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THE ALKALOIDS OF *PLATYDESMA CAMPA NULATA* 
MANN

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DOCTOR OF PHILOSOPHY 
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by Frank Werny
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Inez and Mark
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A. Botanical

*Platydesma campanulata* Mann is a member of the plant family Rutaceae, which is a prominent contributor to the flora of the warmer regions of the earth. Three endemic genera of this family are found in the Hawaiian Islands. They are *Platydesma*, *Pelea*, and *Fagara*, all of which are classified by Engler and Prantl in the Xanthoxylae group of the subfamily Rutoideae. In this group *Platydesma* is placed between the Mexican genus *Choisya* and the New-Caledonia genus *Dutaillyea*. Stone, however, considers *Platydesma* most closely related to *Medicosma*, which is an Australian genus. If Stone is correct, the origin of *Platydesma* is in the Old World. A study of the alkaloids occurring in *Platydesma* may shed some light on this point since the alkaloids of *Medicosma* and *Choisya* have been investigated. A comparison of the alkaloids found in these two genera with those to be isolated from *Platydesma* may point to a relationship of *Platydesma* with *Medicosma* or *Choisya*.

*Platydesma campanulata* is usually found as a small tree in the rain forests of the Hawaiian Islands. It occurs most commonly at an elevation of 2000-5000 feet but is never a frequent member of the vegetation. Its most outstanding visible feature are the large lush leaves which may be as wide as twenty centimeters and as long as fifty centimeters.
When crushed, these leaves emit an odor of essential oils and the bark emits a semeniferous odor. Cuttings of the plant when left to dry in the laboratory were found to be strong attractants for the male Oriental fruitfly, Dacus dorsalis Hendel.

The Hawaiian name of Platycladus campanulata is Pilo kea, but the plant is apparently not mentioned in the sparse literature on medicinal uses of Hawaiian plants.

B. Chemical

Of the approximately 1300 species of the Rutaceae fewer than twenty percent have been investigated for the presence or absence of alkaloids. According to a survey published in 1955, one hundred and seventy-three species had been examined; of these, seventy-four gave a positive test for alkaloids while ninety-nine gave a negative test. By 1959 the number of rutaceous species in which alkaloids had been detected had risen to one hundred and eighty-one. On the basis of these surveys it would seem that the family Rutaceae is a moderately promising source of alkaloids.

Normally, a given plant family will produce alkaloids of a certain structural type. For example, alkaloids which have been isolated from Apocynaceae are structurally related to indole (I) while those from Papaveraceae are related to isoquinoline (II).
The behavior of the Rutaceae is in sharp contrast to this norm. Among the molecular species which have been isolated are evodiamine (indole type, I), berberine (isoquinoline type, II), melicopine (acridone type, III), dictamnine (furoquinoline type, IV), and arborine (quinazolone type, V). It therefore was of interest to investigate an Hawaiian representative of the family.

In a preliminary survey the presence of alkaloids was detected in all three Hawaiian genera. One species of the widely distributed genus *Fagara* has been investigated more closely. The genus *Platydesma* was chosen for closer scrutiny because it is wholly endemic to the Hawaiian Islands.
and the species *campanulata* was selected since it promised a reasonable supply of raw material.

Some genera which are closely related to *Platydesma* have been found to contain alkaloids. A species of *Medicosma* yielded medicosmine (VI), and a species of *Choisyia* yielded skimmianine (VII), evoxine (VIII), and an alkaloid (C₁₉H₂₁O₅N) of undetermined structure.

![Chemical structures](attachment:alkaloid_structures.png)

All three alkaloids are elaborations of the dictamine skeleton (IX) and *Platydesma* might possibly yield alkaloids which are related to dictamine. About a dozen other substituted dictamnines have been isolated from Rutaceous plants.
Furoquinolines constitute perhaps the most characteristic group of alkaloids isolated from Rutaceae.

\[
\begin{array}{c}
\text{O} \\
\text{O} \\
\text{CH}_3 \\
\end{array}
\]

IX

Dictamnine itself is physiologically active against urogenital diseases\(^{12}\) and has pharmacological properties.\(^{13}\) Derivatives of this base may therefore be reasonably expected to exhibit physiological activity.

An investigation of the alkaloids of *Platydesma campanulata* is therefore of interest to the chemist because of the variety of alkaloid types which occur in Rutaceae; to the botanist because chemical knowledge may assist him in attempts to correlate chemical structure of plant constituents with plant morphology\(^{14}\) and taxonomy;\(^{15}\) and to the pharmacologist because *Platydesma campanulata* may produce physiologically active alkaloids.\(^{16}\)

The object of this research was to isolate pure alkaloids from *Platydesma campanulata* and to determine molecular structures of the principal constituents.
CHAPTER II
EXPERIMENTAL

All melting points were determined on a Fisher-Johns melting point apparatus and are uncorrected.

Elemental and functional group analyses were performed by Dr. A. Bernhardt, Mulheim, Germany.

Infrared absorption spectra were obtained with a Beckmann IR-5 double beam instrument either in chloroform solution or as potassium bromide pellets. Ultraviolet absorption spectra were obtained on a Beckmann DK 2 spectrophotometer.

The N.M.R. Spectra were measured by Dr. Leon Mandell, Emory University, Atlanta, Georgia and a mass spectrum was determined by Dr. Klaus Biemann, Massachusetts Institute of Technology, Cambridge, Massachusetts.

Alumina Woelm of activity grade I was used and all other adsorbents were used as supplied by the manufacturers.

Alkaloid tests were considered positive, if Mayer's and Dragendorff's reagents gave a precipitate.19

A. Procurement and Preparation of Plant Material

Plant material for a preliminary investigation was collected in the Koolau Range on Oahu, mostly along the Ridge Trail in the Pupukea area. Material for the major work-up was collected on Kauai and on Hawaii.

On Kauai a sufficient supply of P. campanulata
was found in the Kokee area south of the Ranger Station. Taxonomic identification was made by Dr. B. C. Stone. On Hawaii *P. campanulata* was collected in the Kohala mountains south of Hawi and taxonomic identity was confirmed by Mr. I. E. Lane.

All plant material was prepared for extraction by drying in a forced draft oven for 48 hr. at 60°C, followed by grinding in a Wiley mill to pass 16 mesh.

B. Isolation of Alkaloids

The alkaloids were isolated by conventional methods. 17, 18, 19

The bark and whole root from Kauai, that from Hawaii and the combined leaves, were worked up separately. For each of the three work-ups a different scheme was used (Figs. 1, 2, 3,). An attempt was made to correct shortcomings of a scheme during a subsequent work-up.

1. Root and Bark (Kauai)

The entire extraction scheme is summarized in a flowsheet (Fig. 1).

Dried and ground stem bark (6.4 kg.) and whole root (4.5 kg.) was extracted with hexane under reflux for 36 hr. The hexane extract gave a positive alkaloid test, but attempts to isolate alkaloids failed.

The plant material was next extracted with reflux-
Bark and Root Wood
   \[\text{Hexane}\]
   \[\text{Hexane Extract} \quad \text{Bark and Root Wood} \quad \text{(discarded)}\]
   \[\text{Methanol}\]
   \[\text{Methanol Extract} \quad \text{Bark and Root Wood} \quad \text{(discarded)}\]
   \[\text{Aqueous Tartaric Acid}\]
   \[\text{Solid} \quad \text{Aqueous Solution} \quad \text{(discarded)}\]
   \[\text{Chloroform}\]
   \[\text{Chloroform Extract} \quad \text{Aqueous Solution} \quad \text{(discarded)}\]
   \[\text{Butanol}\]
   \[\text{5% Hydrochloric Acid}\]
   \[\text{Acidic Extract} \quad \text{Butanol Solution} \quad \text{(discarded)}\]
   \[\text{Chloroform}\]
   \[\text{Aqueous Solution} \quad \text{(discarded)}\]
   \[\text{Chloroform Extract}\]
   \[\text{Florisil Chromatography}\]
   \[\text{Bases A, B, and C}\]

Fig. 1. Scheme for extraction of bark and root wood (Kauai).
ing methanol for 48 hr. The methanolic extract was concentrated to 4 l. in a steam-jacketed vacuum evaporator. To the concentrated methanolic extract 4 l. of 5% aqueous tartaric acid was added and the mixture was filtered using Kenite filter aid and sand. The resulting solid was washed with 5% tartaric acid, followed by 5% HCl. The washings were combined with the original filtrate. This combined aqueous acidic solution was then extracted with chloroform in a continuous liquid-liquid extractor for 24 hr. Removal of the chloroform in a rotary evaporator under water pump vacuum yielded 119 g. of brown oil. Further extractions of the aqueous fraction at pH 7 and pH 10 yielded solutions giving positive alkaloid tests, but subsequent chromatography did not yield crystalline alkaloids. The brown oil was now taken up in 1 l. of butanol and extracted with 20 X 100 ml. portions of 5% HCl. The acidic extract was again extracted continuously with chloroform for 48 hr. Upon concentration of the chloroform extract a brown oil, ca. 12 g., was obtained.

This oil was dissolved in benzene and chromatographed in a column containing 500 g. of Florisil. Thirty fractions were collected upon successive elution with the following solvents: 2 l. of benzene, 1 l. of 1:1 chloroform-benzene, 1 l. of chloroform, 1 l. of 1:1 chloroform-acetone, 1 l. of acetone, 2.5 l. of methanol. Only fractions 1-14 showed promising spots on ascending paper chromatograms using
ethyl acetate, pyridine, and water in the ratio 7.5 : 2.3 : 1.65 as developing solution. These 14 fractions were therefore combined and rechromatographed in a column containing 100 g. of Florisil. Elution was started with 300 ml. of benzene and continued as follows: 200 ml. of 3:1 benzene-chloroform, 100 ml. of 1:1 benzene-chloroform, 300 ml. of chloroform, 200 ml. of 1:1 chloroform-acetone, 200 ml. of acetone, and 500 ml. of methanol. Twenty-two fractions were collected. The first 6 fractions gave a positive alkaloid test, and fractions 4, 5, and 6 crystallized.

Fractions 1-3 were extracted with hot petroleum ether (b.p. 30-60°). Upon cooling the combined extracts 30 mg. of a crystalline substance, m.p. 115-116°, was isolated.

After extraction with hot petroleum ether the fractions 1-3 were taken up in hot benzene. Upon addition of petroleum ether (b.p. 30-60°) to cloudiness and subsequent cooling slightly yellow rosettes crystallized. Those from fractions 1 and 2 melted at 124-128° and those from fraction 3 melted at 134-135°.

Thin-layer chromatography on aluminum oxide G in 1:1 benzene-chloroform of the 3 crystalline fractions thus obtained showed that the crystals melting at 134-135° were a pure base, labelled B. Those melting at 115-116° and those melting at 124-128° appeared to be mixtures of two alkaloid base B and a base, labelled A.

Altogether 252 mg. of chromatographically pure
base B was obtained from fraction 3 and by recrystallization of the mixed crystals from benzene-petroleum ether (b.p. 30-60°). Attempts to obtain pure base A from the mixture of the two bases failed.

Trituration of fractions 4-6 with absolute ethanol yielded 18 mg. of a white crystalline solid, m.p. 164-167°, which was labelled base C.

2. Root and Bark (Hawaii)

The entire extraction scheme is summarized in a flowsheet (Fig. 2).

A total of 12 kg. of stem bark and whole root was extracted with refluxing methanol for 48 hr. The extract was concentrated to 4 l., to which 7.6 l. of 5% HCl was added. A solid precipitated which was filtered off and repeatedly extracted with 5%, 10%, and 20% HCl in succession. The acidic extracts were combined with the acidic filtrate and the solid was discarded.

The aqueous acidic solution was neutralized with cooling using concentrated ammonium hydroxide and then extracted with chloroform for 24 hr. in a liquid-liquid extractor. The chloroform solution was evaporated to near-dryness in a rotary evaporator under water pump vacuum and then triturated with ether. The original chloroform extract was thus separated into an ether-soluble fraction, weighing 190 g., and an ether-insoluble fraction, weighing 158 g.
Fig. 2. Scheme for extraction of bark and root wood (Hawaii).
a. The Ether-Soluble Fraction

The ether was removed on a rotary evaporator under water pump vacuum and the residual oil was taken up in 1 l. of benzene and subsequently extracted, first with 1 l. of 5% HCl and then with 1 l. of 10% HCl. The acidic extracts were brought to pH 6 with solid sodium bicarbonate and extracted with chloroform for 24 hr. About 30 g. of a viscous oil remained after distillation of the chloroform on a rotary evaporator under water pump vacuum. The viscous oil was dissolved in 50 ml. of benzene and chromatographed in a column containing 500 g. of Florisil. Elution was started with benzene, gradually changed to chloroform, then to ethanol and finally to methanol. Fractions of 25 ml. each were collected with an automatic fraction collector. The first 50 fractions gave positive alkaloid tests. Thin-layer chromatography on aluminum oxide G showed that the 50 fractions were resolved poorly. The fractions were therefore combined, dissolved in 2:1 benzene-carbon tetrachloride and rechromatographed on basic alumina (Woelm). The column was eluted with the following solvents: 1 l. of 2:1 benzene-carbon tetrachloride, 1 l. of benzene, 1 l. of 9:1 benzene-chloroform, 2 l. of 4:1 benzene-chloroform, 2.5 l. of 1:1 benzene-chloroform, 1 l. of chloroform, 1 l. of ethyl acetate, and 1 l. of acetone. In this manner 425 fractions of 25 ml. each were collected. Only fractions 150-299 gave a positive alkaloid test. These were combined in benzene and
chromatographed on 100 g. of silica gel G. Elution with chloroform-benzene mixtures (1:9, 1:4, 2:3, 1:1, 3:1) brought down several crystalline fractions. Fractions 109-124 of the silica gel G column could be shown by thin-layer chromatography (1:1 benzene-chloroform on aluminum oxide G) to contain alkaloids with $R_f$ values of bases A, B, and C. They were again combined and chromatographed in a column containing 50 g. of silica gel G. The alkaloids were eluted with 1:9 chloroform-benzene followed by 1:6 chloroform-benzene. Fractions 31-62 and 87-110 contained the alkaloids. Fractions 87-110 were combined and recrystallized from ethanol to yield 67 mg. of base C, m.p. 169-169.5°.

Hot petroleum ether extracted 27.7 mg. of base B from fractions 31-62. Upon recrystallization from hot petroleum ether, it melted at 134-135°. An examination of the mother liquors by thin-layer chromatography showed the presence of bases A and B. Attempts to separate the two were unsuccessful.

b. The Ether-Insoluble Fraction

The ether-insoluble oil was mixed with 4 lbs. of sand, filled into a column and extracted in succession with 3 l. of 5% HCl, 2 l. of 10% HCl, and 4 l. of 20% HCl. The extracts were neutralized with solid sodium bicarbonate, combined, and extracted with chloroform for 2d hr. The chloroform was distilled off and the residual oil was taken
up in 80% methanol which was extracted with carbon tetrachloride for 3 days. The methanol solution was evaporated to near-dryness and triturated with benzene. Upon evaporation of the solvent the combined carbon tetrachloride and benzene fractions gave 12 g. of a viscous brown oil. The oil was separated into two fractions, one which was eluted from 500 g. aluminum oxide G with chloroform, and one which was eluted with ethanol. The ethanol eluate yielded no alkaloids. The chloroform eluate was dissolved in benzene and applied to a column containing 150 g. of silica gel G. The alkaloids were eluted with 500 ml. of 3:1 benzene-chloroform, 1 l. of 7:3 benzene-chloroform, 500 ml. of 3:2 benzene-chloroform, 500 ml. of 1:1 benzene-chloroform, 500 ml. of 1:3 benzene-chloroform, 1 l. of chloroform, and 1 l. of 5% methanol in chloroform. Three hundred and twenty-five fractions were collected. Fractions 1-38 and 274-325 contained no alkaloids. It could be shown by thin-layer chromatography (aluminum oxide G in chloroform) that fractions 39-130 contained non-alkaloidal substances and an alkaloid of $R_f 0.6-0.7$. Similarly, fractions 269-273 could be shown to contain an alkaloid with $R_f 0.2$. In order to purify the fractions picrates of the alkaloidal components were prepared by dissolving the fractions in a minimum amount of hot ethanol and then adding 1-2 ml. of concentrated picric acid solution in methanol. The results of this work-up are summarized in table I.
Table I. Results of Work-up

<table>
<thead>
<tr>
<th>Fraction</th>
<th>Melting Point</th>
<th>Weight of Picrate</th>
<th>M.P. after 1st recryst. from EtOH</th>
<th>After 2nd recryst.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-38</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>39-65</td>
<td>160-170°</td>
<td>48 mg.</td>
<td>not cryst.</td>
<td>-</td>
</tr>
<tr>
<td>66-69</td>
<td>172-178°</td>
<td>39 mg.</td>
<td>177-180°</td>
<td>193-195°</td>
</tr>
<tr>
<td>(dec.)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>70-89</td>
<td>171-172°</td>
<td>91 mg.</td>
<td>185-185,5°</td>
<td>-</td>
</tr>
<tr>
<td>90-130</td>
<td>205-207°</td>
<td>54 mg.</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>131-210</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>211-216</td>
<td>92-96°</td>
<td>168 mg.</td>
<td>98-99°</td>
<td>107-109°</td>
</tr>
<tr>
<td>217-268</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>269-273</td>
<td>234-245°</td>
<td>105 mg.</td>
<td>234-235°</td>
<td>(dec.)</td>
</tr>
<tr>
<td>(dec.)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>274-325</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

By thin-layer chromatography, comparison of ultraviolet and infrared absorption spectra, and melting points it was established that 1) the picrates from fractions 39-65 and 66-69 were mixtures of the picrates of the bases A and B isolated previously; 2) the picrate from fractions 70-89 was a mixture of picrates of previously found bases A, B, and C; 3) the picrate from fractions 90-130 was identical with the picrate of base C; 4) the picrate from fractions 211-216 was the picrate of a new base, labelled D; and 5) the picrate from fractions 269-273 was the picrate of another new base, labelled E.
3. The Leaves

The entire extraction scheme is summarized in a flowsheet (Fig. 3).

A total of 4.8 kg. of dried and milled leaves was extracted with refluxing methanol for 48 hr. The methanolic extract was concentrated to a volume of 4 l. on a steam-jacketed vacuum evaporator. Four liters of 5% HCl was added to the concentrate. The resulting oily precipitate was filtered and washed with 2 l. of 5% HCl. The combined acidic extracts had a pH of 2 and were extracted with chloroform for 48 hr. to yield 175 g. of a viscous brown oil upon evaporation of the chloroform. The aqueous solution was now adjusted to pH 8 with concentrated ammonium hydroxide and again extracted with chloroform for 48 hr. to yield 20 g. of a brown oil upon evaporation of the chloroform. The pH of the aqueous solution was now raised to 13-14 with solid sodium hydroxide and once more extracted with chloroform for 48 hr. Upon evaporation of the solvent 30 g. of dark brown oil was obtained.

a. The pH 2 Extract

The oil (175 g.) was taken up in 300 ml. of methanol and 1200 ml. of 5% HCl was added. An oily precipitate formed which was filtered off on a Buchner funnel. The acidic filtrate was extracted with chloroform for 48 hr. Evaporation of the chloroform gave 35 g. of a brown oil. This
Fig. 3. Scheme for extraction of leaves.
oil was now dissolved in a minimum amount of chloroform and chromatographed in a column containing 500 g. of basic alumina (Woelm). Elution was started with chloroform and gradually changed to ethanol. Only early fractions which were eluted with pure chloroform gave positive alkaloid test. Upon thin-layer chromatography of these fractions on aluminum oxide G in 1:1 benzene-chloroform only one alkaloidal spot was noticed. The alkaloidal fractions were therefore combined, dissolved in 100 ml. of ethanol, and 1 g. of picric acid was added. The mixture was heated to boiling. Upon cooling, a non-crystalline yellow picrate was collected. Crystallization from ethanol yielded 71 mg. of fine yellow needles, melting 205-207.5°. Its infrared absorption spectrum and a melting point showed this picrate to be identical with the picrate of base C isolated from the root and bark.

b. The pH 8 Extract

The oil (20 g.) was dissolved in 50 ml. of chloroform and chromatographed on 600 g. of basic alumina (Woelm). Fractions 1-58 resulted from elution with pure chloroform. Fractions 59-160 were eluted with 20% ethanol in chloroform, and the remainder with ethanol. Only fractions 14-74 gave alkaloidal spots on a thin-layer chromatogram. These fractions were therefore combined and dissolved in 50 ml. of 95% ethanol and 5 ml. of concentrated methanolic picric acid was added. The solution was brought to the boiling point and
then slowly evaporated to dryness. Upon trituration with acetone, a yellow picrate remained. Recrystallization from ethanol yielded 145.5 mg. of yellow needles. The infrared absorption spectrum and a mixture melting point showed this base to be identical with base E, which had been isolated from the root and bark.

c. The pH 14 Extract

The oil (30 g.) was dissolved in 50 ml. of chloroform and chromatographed in a column containing 500 g. of basic alumina (Woelm). Chloroform eluted two bands. More polar solvents eluted no further alkaloids. The fractions eluted with chloroform were combined and dissolved in benzene. The benzene solution was chromatographed in a column containing 250 g. of aluminum oxide G. Elution was started with benzene, continued with 1:1 benzene-chloroform, and then with chloroform. The fractions eluted with the 1:1 benzene-chloroform showed one alkaloidal spot on a thin-layer chromatogram. They were combined in chloroform and about 4 ml. of concentrated methanolic picric acid was added. The solution was brought to the boiling point and then cooled resulting in precipitation of a yellow picrate. By fractional crystallization from ethanol the picrate could be separated into the picrates of the previously found base E and a new base F. Base F picrate began to soften at 195° and decomposed from 203-216°. There was 71 mg. of this picrate.
C. Characterization of the alkaloids

1. The Mixture of the Bases A and B

The mixture of the bases A and B which was obtained from both extractions of root and bark was chromatographed on a thin layer of aluminum oxide G in 1:1 benzene-chloroform concurrently with pure base B and an authentic sample of evolitrine. Development with modified Dragsendorff's reagent yielded results which are summarized in Table II.

Table II. Chromatography of the Mixture of The Bases A and B

<table>
<thead>
<tr>
<th>Pure Base B</th>
<th>Authentic Evolitrine</th>
<th>Mixture Spot 1</th>
<th>Mixture Spot 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rf Value</td>
<td>0.58</td>
<td>0.61</td>
<td>0.58</td>
</tr>
<tr>
<td>Color</td>
<td>Dark Purple</td>
<td>Tan</td>
<td>Dark Purple</td>
</tr>
</tbody>
</table>

Since attempts to separate bases A and B failed, base A could not be further characterized.

2. Base B

Base B could be recrystallized by dissolving it in a minimum amount of benzene, adding petroleum ether to appearance of cloudiness, and subsequent cooling. It sublimed readily at 107⁰/3 X 10⁻² mm. The analytically pure base melted 134-135⁰. It was very soluble in chloroform, alcohol, benzene and carbon tetrachloride; sparingly soluble
in acetone and petroleum ether (b.p. 30-60°); and insoluble in water, and aqueous base, but it did dissolve slowly in 5% HCl. The base was chromatographically pure. The Rf values on aluminum oxide G were 0.58 in 1:1 benzene-chloroform and 0.44 in 3:1 benzene-chloroform.

Anal. Calcd. for C_{13}H_{11}O_3N: C, 68.11; H, 4.84; 2 OCH_3, 27.08. Found: C, 68.37, 68.24; H, 5.06, 4.86; OCH_3, 25.77.

The ultraviolet absorption spectrum (Fig. 4) in 4.4 X 10^{-5} M 95% ethanol solution showed the following maxima and minima: \( \lambda_{\text{max}} \) 350 m\( \mu \) (log \( \varepsilon \) 4.68), 333 (4.75), 307.3 (5.04), 295.5 (4.99) 284 sh (4.81), 260.7 (4.91), 248.8 (6.01), 238 (6.10); \( \lambda_{\text{min}} \) 342 (4.63), 324.2 (4.68), 267 (4.62), 220 (5.85).

The major peaks in the infrared absorption spectrum (Fig. 5) occurred at the following wavelengths:

\( \lambda_{\text{max}} \) chloroform 3.40\( \mu \) (m), 6.18 (s), 6.33 (s), 6.49 (m), 6.64 (s), 6.83 (s), 7.07 (m), 7.33 (s), 7.67 (s), 7.92 (m), 8.11 (s), 8.23 (s), 8.67 (s), 9.01 (s), 9.15 (s), 9.68 (m), 10.10 (m), 10.20 (m), 11.78 (w), 12.06 (m), 14.30 (w).

A picrate of base B was prepared by dissolving 4.5 mg. of the base in 1 ml. of absolute ethanol. Upon addition of 2 drops of concentrated methanolic picric acid, the picrate precipitated immediately as fine yellow needles. Recrystallization from ethanol gave fine needles melting with decomposition at 195-196°.
Fig. 4.—Ultraviolet spectrum of base B in 95% ethanol.
Fig. 5. Infrared spectra of base B (upper) and base C (lower) (Chloroform).
The Iso Compound. - Base B (112 mg.) was sealed in a Pyrex tube with 2 ml. of methyl iodide and left overnight at 100°. After opening of the tube the solvent was evaporated and the residue extracted with three 5 ml. portions of chloroform. The extract was concentrated to 5 ml. in a stream of nitrogen and applied to a column containing 10 g. of basic Alumina (Woelm). Three successive colored fractions could be eluted with chloroform gave a crystalline residue, m.p. 206-209°. The residue was recrystallized by dissolving it in a minimum amount of cold absolute ethanol, warming the solution, and then adding water until the solution appeared cloudy. Colorless crystals separated overnight in the refrigerator. This compound melted from 214-216°. The crystals slowly turned pink on standing.

Anal. Caled. for C_{13}H_{11}O_{3}N: C, 68.11; H, 4.84. Found: C, 67.82; H, 4.82.

Upon melting, cooling, and remelting the iso-compound melted from 208-210°. An authentic sample of 6-methoxyisodictamine^{23} melted at 211.5-212.5°. Upon cooling and remelting it melted from 208-210°. Two samples when mixed by fusion followed by cooling, had on remelting, a melting point of 208-210.5°.

The ultraviolet absorption spectrum (Fig. 6) in 4.39 \times 10^{-5} M 95% ethanol solution showed the following maxima and minima: \( \lambda_{\text{max}} \) 361 m\( \mu \) (log 3.66), 344 (3.64), 329 (3.38), 302 (3.07), 290 (3.19), 264.5 (4.15), 255 (4.03).
Fig. 6.—Ultraviolet spectrum of 6-methoxyisodictamine in 95% ethanol.
243 (4.11), 216.5 (3.91); \( \lambda_{\text{min.}} \) 350 (3.53), 310 (2.88), 260 (3.99), 250 (3.94), 225 (3.86).

The infrared absorption spectrum (Fig. 7) gave the following peaks:

\[ \lambda_{\text{max.}} \text{chloroform} 3.39 \mu \text{m}, 6.17 (s), 6.28 (s), 6.49 (s), 6.63 (s), 6.80 (m), 6.98 (m), 7.42 (w), 7.65 (s), 8.08 (s), 8.37 (m), 8.44 (m), 8.60 (m), 8.84 (w), 9.02 (m), 9.63 (w), 9.88 (w), 11.12 (w), 11.34 (w), 12.32 (w).

3. Base C

Recrystallization of base C from absolute ethanol gave needles melting 169-169.5\(^\circ\). The base was found to be soluble in chloroform, ethanol, and methanol. It was slightly soluble in benzene, ether, and 5% HCl. It was insoluble in water, aqueous base, and petroleum ether.

Anal. Calcd. for \( \text{C}_{12}\text{H}_{13}\text{O}_4\text{N} \): C, 64.86; H, 5.05.

Found: C, 65.12, 64.08; H, 5.39, 5.20.

The ultraviolet absorption spectrum (Fig. 8) in 3.86 \( \times \) 10\(^{-5}\) M 95% ethanol showed the following maxima and minima:

\[ \lambda_{\text{max.}} \text{334 m} \mu \text{m (log} \epsilon \text{3.53), 323 (3.64), 352 (4.23), 246 (4.17); } \lambda_{\text{min.}} \text{315 (3.60), 263 (2.71).}

The infrared absorption spectrum (Fig. 5) in 0.13 M chloroform showed the following peaks:

\[ \lambda_{\text{max.}} \text{3.36 } \mu \text{m}, 3.52 (w), 6.13 (m), 6.43 (w), 6.62 (s), 6.71 (s), 6.81 (m), 6.90 (m), 7.53 (s), 7.91 (s), 8.38 (w), 8.50 (s), 8.60 (s), 8.72 (m), 9.09 (s), 9.46 (m), 9.60 (w), 9.82 (s), 10.04 (m), 10.52 (m), 11.63 (m), 14.22 (w), 15.13 (w).}
Fig. 7. Infrared spectra of the iso-compound of base B (upper) and 6-methoxyisodictamnine (lower) (Chloroform).
Fig. 8.—Ultraviolet spectrum of kokusaginine in 95% ethanol.
The base (5 mg.) was dissolved in 10 drops of methanol and 3 drops of concentrated methanolic picric acid were added. A precipitate formed immediately. After recrystallization from ethanol it melted 205-207° (dec.). An authentic sample of kokusaginine picrate had m.p. 204-206° (dec.) and the melting point of the mixed compounds was 205-208° (dec.). The infrared absorption spectrum of base C picrate and that of kokusaginine picrate were identical.

4. Base D

Base D Picrate. - The base was isolated as the picrate. The picrate after recrystallization from methanol softened around 93° and melted 107-109°.

Anal. Calcd. for C_{15}H_{17}O_{3}N_{4}C_{6}H_{3}O_{7}N_{3}: C, 51.64; H, 4.13. Found: C, 51.55, 51.75; H, 4.24, 4.11.

Base D. - The free base was obtained from the picrate by absorbing 50 mg. on 2 g. of aluminum oxide G and placing this mixture on 20 g. of 10 g. aluminum oxide G in a column. Elution with chloroform and evaporation of the solvent gave 21.3 mg. of crystalline base.

Base D dissolved readily in benzene, chloroform, and ethanol; it was slightly soluble in 5% HCl; and insoluble in petroleum ether. It was recrystallized from benzene-petroleum ether, yielding white rosettes of needles, m.p. 137-139°.

Its ultraviolet absorption spectrum (Fig. 9) show-
Fig. 9.—Ultraviolet spectra of base D: —; in 95% ethanol; ---, in 0.01 N hydrochloric acid in 95% ethanol.
ed the following maxima and minima. In $3.86 \times 10^{-5} \text{ M}$ 95% ethanol: $\lambda_{\text{max}}$ 320.5 μ (log ε 3.55), 307.2 (3.49), 294.5 sh (3.24), 283 (3.65), 272 (3.73), 262.3 (3.65), 253.5 (3.50), 238.1 (4.43), 229.3 (4.57); $\lambda_{\text{min}}$ 314 (3.38, 292 (3.23), 278.3 (3.59), 266.5 (3.64), 248.5 (3.43), 236.5 (4.42). $3.86 \times 10^{-5} \text{ M in 0.01 N HCl in 95% ethanol: } \lambda_{\text{max}}$ 315 (3.69), 302.5 (3.87), 291.5 (3.89), 240.2 (4.33), 236 (4.40), 215.8 (4.39); $\lambda_{\text{min}}$ 312 (3.68), 253 (3.24), 226 (4.23).

The mass spectrum of the base showed two principal peaks at 259 and 200 m/e. The infrared absorption spectrum (Fig. 10) of the base gave the following peaks: $\lambda_{\text{max}}$ chloroform 2.79 μ (w), 3.36 (s), 6.11 (s), 6.29 (s), 6.59 (s), 6.91 (m), 7.90 (s), 7.16 (s), 7.31 (s), 7.49 (m), 7.64 (m), 7.72 (m), 8.08-8.31 (m), 8.47 (m), 8.58 (m), 8.72 (w), 8.91 (s), 9.08 (s), 9.82 (s), 10.04 (m), 10.50 (m).

5. Base E

Base E Picrate. - The picrate of base E was soluble in acetone and 95% ethanol. Recrystallization from 95% ethanol yielded yellow needles m.p. 234-236°, dec. 237°.

Anal. Calcd. for $C_{11}H_{11}O_3N\cdot C_6H_3O_7$: C, 50.75; H, 3.51; N, 13.93; OCH$_3$, 0. Found: C, 51.19, 51.39; H, 3.79, 3.73; N, 13.78; OCH$_3$, 0.

The picrate of base E (60 mg.) was absorbed on 2 g.
Fig. 10. - Infrared spectra of base D (upper) and base F (lower) (Chloroform).
of aluminum oxide G by dissolving the picrate in acetone, adding the adsorbent and subsequently evaporating the solvent on a rotary evaporator under water pump vacuum. The resultant mixture was placed on top of a column containing 10 g. of aluminum oxide G. The base was eluted with 10% methanol in chloroform. Evaporation of the solvent gave 23 mg. of slightly yellow needles of base E.

Base E. - The free base was soluble in chloroform, hot benzene, ethanol, methanol, and 5% HCl. It was recrystallized from chloroform-petroleum ether or from benzene. It crystallized as fine needles which turned to prisms at 174° and melted sharply at 178-179°.

Anal. Calcd. for C_{11}H_{11}ON: C, 76.27; H, 6.40.

Found: C, 75.96, 76.10; H, 6.51, 6.46.

The ultraviolet absorption spectrum (Fig. 11) showed the following maxima and minima. In 5.78 X 10^{-5} M 95% ethanol: \(\lambda_{\text{max.}} = 335.5 \text{ m}\mu (\log E = 3.994), 321.5 \text{ (3.96), 310 (3.72), 290 (3.29), 279 (3.17), 266 (2.97), 239.5 (4.20), 206.7 (4.44); } \lambda_{\text{min.}} = 327.5 \text{ (3.89), 261 (2.92), 222.5 (3.97); 5.78 X 10^{-5} M in 0.01 N HCl in 95% ethanol: } \lambda_{\text{max.}} = 302.8 \text{ (3.95), 247.1 (2.95), 233.1 (4.70); } \lambda_{\text{min.}} = 257.5 \text{ (2.84, 219 (4.27).}

The infrared absorption spectrum (Fig. 12) in 0.21 M chloroform showed the following peaks: \(\lambda_{\text{max.}} = 3.25 \mu (w), 3.34 (s), 6.23 (s), 6.32 (m), 6.65 (s), 6.78 (m), 6.42 (m), 6.97 (w), 7.05 (m), 7.22 (w), 7.41 (w), 7.56 (m), 7.86 (m),
Fig. 11. Ultraviolet spectra of base E: --, in 95% ethanol; ---, in 0.01 N hydrochloric acid in 95% ethanol.
Fig. 12. - Infrared spectra of base E (upper) and 1,2,3-trimethyl-4-quinolone (lower) (Chloroform).
8.45 (m), 8.61 (w), 8.92 (w), 9.24 (m), 9.61 (m), 9.73 (w),
11.08 (m), 11.86 (m).

The N.M.R. spectrum of base E (Fig. 13) showed a
3-proton peak at 140 c.p.s., a 3-proton peak at 215 c.p.s.,
a 1-proton peak at 363 c.p.s., a split 3-proton peak at 443
c.p.s., and a split 1-proton peak at 499 c.p.s. Tetramethyl-
silane was the standard and deuteriochloroform the solvent.

6. Base F

Base F Picrate. - Base F was isolated as the pic­
rate. It could be recrystallized from absolute ethanol.
The picrate softened at 194°, began to turn brown at 203°,
and was decomposed by 216°.

Anal. Calcd. for C_{16}H_{21}O_{3}N•C_{6}H_{5}O_{7}N_{3}: C, 52.38;
H, 4.80; 1 OCH_{3}, 6.16; 1 NCH_{3}, 5.75. Found: C, 52.51, 52.56;
H, 4.35, 4.39; OCH_{3}, 5.69; NCH_{3}, 9.48.

The infrared absorption spectrum is shown in
Fig. 14.

The picrate (0.11 g.) was adsorbed on 2 g. of alu-
minum oxide G and added to the top of a column containing
10 g. aluminum oxide G. Elution with chloroform brought
down the free base. Fifty milligrams of the free base was
collected.

Base F. - Base F could not be obtained crystalline.
Attempts were made to crystallize base F from benzene, 95%
ethanol acetate, ether, benzene-petroleum ether,
Fig. 13.—Nuclear magnetic resonance spectra of base E (upper) and 1,2,3-trimethyl-4-quinolone (lower) in deuteriochloroform at 60 mc. The frequency is relative to tetramethylsilane.
Fig. 14. - Infrared spectra of base F picrate (upper) and the picrate of the oxidation product of base F (lower) (KBr).
chloroform-petroleum ether, ethanol-water, and ethyl acetate-petroleum ether. The base always appeared as a whitish opaque oil.

Thin-layer chromatography of the base on aluminum oxide G with chloroform as the developer gave a single spot of $R_f$ 0.35.

The ultraviolet absorption spectra (Fig. 15) of this oil had the following maxima and minima. In $4.76 \times 10^{-5} \text{ M}$ 95% ethanol: $\lambda_{\text{max}}$ 336.5 m$\mu$ ($\log \varepsilon$ 4.39), 324.8 (4.34), 291.6 sh (3.75), 281 sh (3.66), 248 (4.72), 242 (4.74), 230.8 sh (4.63), 215 (4.68); $\lambda_{\text{min}}$ 276 (3.64), 223.4 (4.61), 205 (4.62); $4.76 \times 10^{-5} \text{ M}$ in 0.01 N HCl in 95% ethanol: $\lambda_{\text{max}}$ 336 (3.94), 322 (4.01), 308.7 (3.96), 248 sh (5.34), 234 (5.51), 215 (4.30); $\lambda_{\text{min}}$ 275.4 (3.47), 220.5 (4.28), 210 (4.27).

The infrared absorption spectrum (Fig. 10) showed the following peaks: $\lambda_{\text{max}}$ chloroform 2.73 $\mu$ (w), 3.34 (s), 3.48 (sh), 3.53 (sh), 6.14 (s), 6.22 (s), 6.37 (m), 6.79 (m), 6.90 (w), 7.06 (w), 7.41 (w), 7.53 (w), 7.60 (w), 7.85 (w), 8.46 (w), 8.61 (w), 9.23 (w), 9.68 (w), 10.29 (w), 11.56 (w), 11.71 (w).

Oxidation of Base F.25 - The base (50 mg.) was dissolved in 6 ml. of glacial acetic acid and a solution of 100 mg. of chromic anhydride in 10 ml. of 90% acetic acid was added dropwise. No immediate change in color was noted. Upon standing, the solution turned dark. After one hour at
Fig. 15.—Ultraviolet spectra of base F: --, in 95% ethanol; ---, in 0.01 N hydrochloric acid in 95% ethanol.
room temperature the solution was slowly poured into 30 ml. of concentrated ammonium hydroxide with cooling. The basic solution was extracted with 25 ml. portions of chloroform. The chloroform solution was washed with 100 ml. of water and dried by pouring it through a bed of sodium sulfate on a funnel. The solution was evaporated to dryness on a rotary evaporator under water pump vacuum. The resulting brown oil was dissolved in 10 ml. of 95% ethanol and treated with 15 ml. of 2,4-dinitrophenylhydrazine reagent. After refrigeration overnight the solution became cloudy but no crystals could be detected. The cloudy solution was slowly neutralized with 5% sodium bicarbonate solution. At pH 1.5 the salt of unreacted 2,4-dinitrophenylhydrazine precipitated. Neutralization was continued with potassium hydroxide pellets and the solution was thus brought to pH 10 and extracted with three 50 ml. portions of chloroform. Upon evaporation of the chloroform the residual solid was taken up in 10 ml. of absolute ethanol, and 2 ml. of concentrated methanolic picric acid was added. No picrate precipitated. Addition of 5 ml. of 10% acetic acid and cooling overnight yielded a crystalline picrate. Recrystallization from absolute ethanol gave fine yellow needles, melting without decomposition from 187-190°. The ultraviolet absorption spectrum of this picrate was identical with that of base F picrate, but their infrared spectra (Fig. 14) differed.
Anal. Calcd. for $C_{16}H_{19}O_3N^+C_6H_3O_7N_3$: C, 52.58; H, 4.42. Found: C, 52.57, 52.66; H 4.32, 4.31.

D. Syntheses

1. Synthesis of 2,3-Dimethyl-4-quinolone

a. By the Niemontowski Reaction

Butanone-2 (1.35 moles) and anthranilic acid (0.73 mole), 100 g. of each, were heated in a 500 ml. 3-neck flask equipped with a thermometer and a downward condenser above an air cooled reflux condenser. The mixture was first heated to 90° and held there 0.5 hr. and then to 190-200° for 1.5 hr. On cooling a white precipitate appeared which was washed with boiling benzene. Recrystallization from 95% ethanol yielded fine colorless needles (7 g., 5.5%), m.p. ca. 295°. After two additional recrystallizations from 95% ethanol, the melting point was 305-307° (dec.).

Anal. Calcd. for $C_{11}H_{11}ON$: C, 76.28; H, 6.40; N, 8.09; act. H, 0.58. Found: C, 76.45, 76.52; H, 6.31, 6.53; N, 8.23; act. H, 0.58.

The ultraviolet absorption spectrum showed the following maxima and minima. In $2.89 \times 10^{-5}$M 95% ethanol: $\lambda_{\text{max}}$ 335.4 $\mu$m ($\log \varepsilon$ 4.09), 327.4 (4.08), 292.4 sh (3.44), 279 sh (3.27), 245.8 (4.46), 238.2 (4.49); $\lambda_{\text{min}}$ 328.7 (4.03), 256.8 (3.14), 221 (4.17); $2.89 \times 10^{-5}$M in 0.01 N HCl in 95% ethanol: $\lambda_{\text{max}}$ 335.6 sh (3.50), 321 (3.81), 309.7 (3.33), 281.7 sh (3.97), 267.2 sh (3.40), 246 sh (4.19), 232 (4.62),
b. From o-Acetamidopropiophenone

o-Nitropropiophenone. To 425 ml. of fuming nitric acid (d. 1.5 g./ml.) in a 3-neck round bottom flask equipped with a stirrer, thermometer and dropping funnel was added 67 g. of freshly distilled propiophenone (0.5 mole). The ketone was added so as to keep the temperature of the ice-cooled mixture around 10°. After addition of the ketone the mixture was stirred for 10 min. and then poured into 2 l. of water. After cooling to room temperature, the mixture was filtered. The filtrate was extracted with three 200 ml. portions of benzene and the benzene extract was warmed and used to dissolve the product on the filter. The resulting benzene solution was then concentrated on a rotary evaporator under water pump vacuum. When no more benzene distilled, the remaining oil was taken up in 500 ml. of 95% ethanol and cooled overnight. The white crystalline precipitate (m-nitropropiophenone) was filtered and washed with 95% ethanol. The filtrate as well as the washings were evaporated to dryness. A yellow oil remained. It was distilled at 180°/20 mm. About 15 ml. was collected at this temperature and pressure. Upon addition to the distillate of a small amount of benzene crystals appeared.

o-Acetamidopropiophenone.- The benzene solution of o-nitropropiophenone was diluted to 100 ml. with benzene.
To this solution, 4 g. of palladium-charcoal (10%) was added and the mixture was placed under 42 lbs. of hydrogen pressure for 5 hr. with shaking. After separation of the catalyst by filtration the benzene solution was combined with 60 ml. of acetic anhydride and 60 ml. of glacial acetic acid and heated for 2 hr. on a steam bath, which removed the benzene. The reaction mixture was poured into 900 ml. of water. The green oil which separated crystallized overnight in the refrigerator. It was recrystallized from aqueous ethanol to yield 7.4 g. of crystals, m.p. 70.5-71.5°. (Literature m.p. 71.0°.)

Anal. Calcd. for C_{11}H_{13}O_{2}N: C, 69.11; H, 6.85.
Found: C, 69.00, 69.06; H, 6.75, 6.69.

2,3-Dimethyl-4-quinolone.- A solution of 7 g. (0.037 mole) of o-acetamidopropiophenone, 450 ml. of water, 150 ml. of ethanol, and 4.5 ml. of 40% aqueous sodium hydroxide was refluxed for 3 hr. on a steam bath. The ethanol was then distilled and the solution cooled. On cooling crystals (3.7 g., 58%) separated which had a melting point and infrared absorption spectrum identical with the compound which was synthesized by the Niementowski reaction (See part a.).

2. Synthesis of 1,2,3-Trimethyl-4-quinolone
a. Using Methyl Iodide
2,3-Dimethyl-4-quinolone (2 g., 0.012 mole) was
mixed with 0.3 g. (0.013 mole) of sodium and 6 ml. of methanol and warmed slightly until solution was complete. The solution was then sealed in a pyrex tube with 7 ml. of methyl iodide. After 20 hr. at 100° the solvent was evaporated and the residue chromatographed on 50 g. of basic alumina (Woelm). Upon evaporation of the solvent fraction 1 gave a white crystalline residue m.p. 187-189°. Only 5 mg. (0.2%) of this substance was obtained in addition to the unchanged starting material.

b. Using Dimethyl Sulfate

To a solution of 0.5 g. (0.009 mole) of potassium hydroxide in 30 ml. of methanol 1 g. (0.006 mole) of 2,3-dimethyl-4-quinolone was added. The solvent was evaporated and an excess of dimethyl sulfate (about 10 ml.) was added slowly. The solution was then heated for 0.5 hr. on a steam bath. Excess dimethyl sulfate was destroyed by slowly adding 40% potassium hydroxide to a pH of 10. The aqueous solution was then extracted with chloroform. The chloroform solution was dried over sodium sulfate and evaporated to dryness. The residue was recrystallized twice from benzene to yield 59 mg. (53%) of colorless prisms m.p. 188-189°.

Anal. Calcd. for C_{12}H_{13}ON: C, 76.99; H, 7.00.
Found: C, 76.51, 76.64; H, 7.61, 6.96.

The ultraviolet absorption spectra (Fig. 16) gave the following maxima and minima. In 5.4 X 10^{-5} M 95% etha-
Fig. 16.—Ultraviolet spectra of 1,2,3-trimethyl-4-quinolone:
—, in 95% ethanol; ---, in 0.01 N hydrochloric acid in 95% ethanol.
The infrared absorption spectrum (Fig. 12) had the following peaks: \[ \lambda \text{max. chloroform } 3.36 \mu \text{ (s), } 6.18 \text{ (s), } 6.25 \text{ (s), } 6.36 \text{ (s), } 6.46 \text{ (s), } 6.79 \text{ (s), } 6.87 \text{ (m), } 6.97 \text{ (m), } 7.04 \text{ (m), } 7.29 \text{ (m), } 7.40 \text{ (m), } 7.64 \text{ (s), } 7.72 \text{ (s), } 8.34 \text{ (m), } 8.89 \text{ (m), } 9.88 \text{ (m), } 10.31 \text{ (m), } 14.38 \text{ (m), } 15.12 \text{ (m).} \]

3. Synthesis of 1,2-Dimethyl-4-quinolone by the Conrad-Limpach Method

a. 2-Methyl-4-quinolone

To a mixture of 51.5 g. (0.55 mole) of aniline and 66 g. (0.51 mole) of ethyl acetoacetate methylene chloride was added to a volume of 250 ml. After 4 d. at room temperature the solution was washed successively with 100 ml. of 2% HCl, 100 ml. of water, 100 ml. of 0.5 N sodium hydroxide and again with 100 ml. of water. Subsequently, the solution was dried over magnesium sulfate and the solvent evaporated. The residual light brown oil was added to 500 ml. of paraffin oil at 205\(^\circ\) while stirring and distilling off the alcohol as it was formed. After the addition the temperature was raised to 240\(^\circ\) and kept there for 10 min. The mixture was
then cooled with stirring. A solid separated on cooling. It was filtered and washed with benzene. Washing with boiling chloroform removed the final traces of color and left 6.29 g. (7.8%) of a white solid m.p. 234-235.5°. The ultraviolet absorption spectrum was identical with that published by Ewing and Steck for 2-methyl-4-quinolone.

b. 1,2-Dimethyl-4-quinolone

To a solution of 0.71 g. (0.013 mole) of potassium hydroxide in 50 ml. of hot methanol 2 g. (0.013 mole) of 2-methyl-4-quinolone was added. The methanol was then distilled off on a rotary evaporator under water pump vacuum and 5 ml. of dimethyl sulfate was added to the residue. The reaction mixture was refluxed for 0.5 hr. and then taken up in an excess of aqueous potassium hydroxide. The resulting purple solution was extracted with chloroform and the extract was passed through a column containing 50 g. of alumnum oxide. The eluant was evaporated to dryness and then taken up in a minimum of chloroform. Upon addition of 3-4 times as much petroleum ether as there was chloroform purple crystals appeared. These were sublimed at 120°/0.3 mm. A total of 0.3 g. (13%) of white crystals, m.p. 179° (Lit. 174-175°), was collected. Two recrystallizations from benzene raised the m.p. to 179.5-180.5°.

Anal. Calcd. for C_11H_11ON: C, 76.27; H, 6.40; O, 9.24; N, 8.09; NCH_3, 8.66; OCH_3, 0.
Found: C, 76.22, 75.99; H, 6.42, 6.44; O, 9.78; N, 8.15; NCH₃, 7.94; OCH₃, 0.

The ultraviolet and infrared absorption spectra were identical with those of base E shown in Figs. 11 and 12.

4. Results of Other Syntheses

a. The Reaction of Anthranilic Acid and Propanal

A mixture of 100 g. (1.7 mole) of propanal and 100 g. (0.73 mole) of anthranilic acid was heated for 0.5 hr. at about 100°. The temperature was then slowly raised to 210°. The heating was discontinued when no more water was distilled. The solution was left to cool to about 150° and then poured into 200 ml. of benzene. About 35 g. of light yellow precipitate was collected. It could be crystallized from benzene, chloroform, methanol, or ethanol. Recrystallization from ethanol resulted in colorless needles m.p. 225-226°.

Found: C, 73.04, 73.22; H, 6.24, 6.36; N, 6.49.

The ultraviolet absorption spectra showed the following maxima and minima. In 6.34 X 10⁻⁵ M 95% ethanol:

\[ \lambda_{\text{max}} \approx 326.2 \text{ m} \mu \text{c} (\log 3.84), 312.1 (3.77), 298.1 (3.72), 287.2 (3.64), 222 (3.94); \lambda_{\text{min}} \approx 312.4 (3.63), 307.3 (3.68), 252.8 (3.04); 6.34 X 10⁻⁵ M in 0.01 N HCl in 95% ethanol:

\[ \lambda_{\text{max}} \approx 325.6 (3.94), 321.5 (3.84), 299.4 (3.73), 220.6 (3.93); \lambda_{\text{min}} \approx 321.2 (3.79), 255.6 (3.04).

The infrared absorption spectrum showed the
following peaks: $\lambda_{\text{max}}^{\text{KBr}} \approx 3.26 \mu (w), 3.36 (s), 3.42 (m), 3.46 (w), 4.25 \text{ broad (m)}, 5.27 (m), 5.90 (s), 6.12 (s), 6.31 (s), 6.52 (s), 6.71 (m), 6.88 (s), 6.96 (m), 7.08 (s), 7.23 (s), 7.38 (m), 7.48 (m), 7.58 (m), 7.88 (m), 8.19 (s), 8.31 (s), 8.67 (w), 8.89 (w), 9.35 (m), 9.56 (m), 10.01 (s), 10.19 (m), 10.96 (s), 12.46 (m), 12.72 (s), 13.29 (s).

b. Attempted Synthesis of 2-Methyl-4-quinolone Using the Procedure of Stark$^{36}$

A mixture of 51.5 g. (0.55 mole) of freshly distilled aniline and 66 g. (0.51 mole) of ethyl acetoacetate was dissolved in 250 ml. of methylene chloride and warmed on a steam bath to 40$^\circ$ for 48 hr. Four milliliters of water was separated with a separatory funnel. The solution was then dried over magnesium sulfate. Methylene chloride was distilled on a rotary evaporator under water pump vacuum and the resulting light brown oil was heated very rapidly to 240$^\circ$. Heating was stopped to allow the temperature to drop to 235$^\circ$ when it was again raised to 240$^\circ$ and then left to cool. When the temperature had dropped to 100$^\circ$, the red-brown oil was extracted with 300 ml. of boiling water. No crystals appeared on cooling of the aqueous solution. The brown oil was now triturated with two 200 ml. portions of benzene and then two 200 ml. portions of ether. A solid remained. It was filtered and washed again with ether. Upon recrystallization from chloroform, 3.6 g. of white crystalline needles, m.p. 244-245$^\circ$, was isolated. The ultraviolet
absorption spectrum showed a maximum at 256 m\(\mu\).

c. Attempted Synthesis of 1,2-Dimethyl-4-quinolone

\textit{o-Acetamidoacetophenone}. - A mixture of 10 g. (0.074 mole) of \textit{o}-aminoacetophenone, 50 ml. acetic acid and 50 ml. of acetic anhydride was heated for 2 hr. on a steam bath. It was poured into 500 ml. of water, which was then neutralized with sodium bicarbonate. Upon neutralization, the amide precipitated. Recrystallization from ethanol gave 7.9 g. (63\%) of crystals, m.p. 75-76\(^\circ\) (Lit. 76-77\(^\circ\) 37).

\textit{Condensation of the Amide}. - To a solution of 3.5 g. (0.02 mole) of \textit{o-acetamidoacetophenone}, in 325 ml. of water and 110 ml. of ethanol was added 3.25 ml. of 40\% aqueous sodium hydroxide. The solution was refluxed on a steam bath for 3 hr. The ethanol was allowed to distil and the aqueous solution was placed in a refrigerator for cooling. A crystalline white solid precipitated. Filtration and washing with water yielded 1.65 g. (52\%) of crystals, m.p. 223-224\(^\circ\) (4-methylcarbostyril, Lit. m.p. 223\(^\circ\) 38).

The ultraviolet absorption spectrum in 9.5 \texttimes 10^{-5} M 95\% ethanol had the following maxima and minima: \(\lambda_{\text{max}}\), 339.8 m\(\mu\) (log \(\varepsilon\) 3.47), 326.2 (3.62), 314.7 sh (3.53), 276.7 (3.55), 267.6 (3.62), 259.3 sh (3.54), 245 (3.84, 230 (4.34), 224.9 (4.31); \(\lambda_{\text{min}}\), 335.7 (3.47), 288.3 (2.97), 273.3 (3.55), 254.5 (3.50), 242.6 (3.84).
N-Methyl-o-acetamidoacetophenone. - To a solution of 3.54 g. (0.02 mole) of o-acetamidoacetophenone in 50 ml. of benzene was added 0.8 g. (0.035 mole) of sodium ribbon. The mixture was warmed on a water bath till no more sodium was evident. Two milliliters (d. 1.33 g./ml.) of dimethyl sulfate was added slowly and the solution was refluxed for 0.5 hr. on a steam bath. A reddish-purple solution resulted, which was washed by extracted it with three 50 ml. portions of water. The benzene solution was dried over magnesium sulfate and evaporated to dryness. About 2 g. (52%) of crystalline N-methyl-o-acetamidoacetophenone was collected.

1,4-Dimethylcarbostyril. - To a solution of 2 g. (0.01 mole) of N-methyl-o-acetamidoacetophenone in 100 ml. of water and 70 ml. of ethanol was added 2 ml. of 40% aqueous sodium hydroxide. This solution was refluxed on a steam bath for 3 hr. Ethanol was distilled on a rotary evaporator under water pump vacuum. The remaining aqueous solution was extracted with 3 X 50 ml. chloroform. The chloroform extract was dried over magnesium sulfate and evaporated to dryness. The resulting solid was purified by chromatography on aluminum oxide G in chloroform. Recrystallization from benzene gave a crystalline solid, m.p. 130-132°. Thin-layer chromatography gave no indication of the presence of 1,2-dimethyl-4-quinolone.
CHAPTER III
RESULTS AND DISCUSSION

A. Base B

Base B was isolated as a weak base from the root and bark collections on Hawaii and Kauai but not from the leaves. From the plant material collected on Kauai two hundred and fifty-two milligrams (0.0023 percent) of base B was isolated. The yield from the plant material from Hawaii was smaller.

The ultraviolet (Fig. 4) and the infrared absorption spectra (Fig. 5) of base B were typical of furoquino-line alkaloids. Elemental and functional group analyses suggested a composition of $C_{13}H_{11}O_3N$ with two methoxyl groups but without methyl bound to nitrogen. Thus, a methoxydictamnine was indicated. Two such compounds, 7-methoxydictamnine (evolitrine) and 8-methoxydictamnine ($\gamma$-fagarine), had been reported previously. Direct comparison of the base with an authentic sample of $\gamma$-fagarine by infrared absorption and melting point of the mixed compounds showed that base B was not 8-methoxydictamnine. Its physical properties obviously differentiated it from evolitrine. Thus, base B had to be one of the two hitherto unreported monomethoxydictamnines, 5-methoxydictamnine or 6-methoxydictamnine.

A comparison of the ultraviolet absorption spectrum of base B (Fig. 4) with spectra of other known methoxy-substituted dictamnines showed that the spectrum of
base B strongly resembled that of 6,8-dimethoxydictamnine (masculosidine) (Fig. 17); this similarity suggested that base B might be 6-methoxy- rather than 5-methoxydictamnine. If this assumption was correct, then the iso-compound of base B should be identical with 6-methoxyisodictamnine isolated by Lamberton and Price as a degradation product of medicosmine. Isomerisation of base B (X) with methyl iodide at 100° yielded the expected iso-compound (XI). This was shown by comparing the absorption spectra (Fig. 7) with those of an authentic sample and by the melting point of the mixed compounds. This constituted proof that base B was 6-methoxydictamnine, an alkaloid which had not been isolated previously.

This brings to three the number of known mono-methoxydictamnines. 5-Methoxydictamnine remains unknown. It is somewhat surprising that 6-methoxydictamnine has not been isolated from other species of the Rutaceae, since it is so closely related to kokusaginine and may even be a biogenetic precursor of kokusaginine.

Evolitrine has now been isolated from four species
Fig. 17.—Ultraviolet spectrum of maculosidine in 95% ethanol.
and 6-methoxydictamine only from *Platydesma campanulata*, while kokusaginine has been isolated from twelve species in Rutaceae. In three of the cases where kokusaginine was isolated a monomethoxydictamine was also isolated and dictamine was isolated in only five cases. At the present time no taxonomic or biogenetic significance can be attached to this since it is not known whether a monomethoxydictamine or dictamine itself is a necessary biogenetic precursor of the more highly oxygenated compounds.

**B. Base C**

Base C was isolated from all parts of the plant and was found to occur in *P. campanulata* from Kauai and from Hawaii. Only eighteen milligrams was isolated from the Kauai root and bark, but the root and bark from Hawaii yielded ca. one hundred milligrams (0.00083 percent) of base C. Combined with the thirty-eight milligrams which was obtained from the leaves the total yield was 0.0016 percent of base C, which therefore may be considered to be the second major alkaloid of *Platydesma campanulata*.

The melting point of the free base and of its picrate as well as the ultraviolet absorption spectrum clearly suggested that base C was identical with the known alkaloid kokusaginine (6,7-dimethoxydictamine). Direct comparison of the picrate with an authentic sample by infrared spectroscopy and by melting point of the mixed compounds proved
Kokusaginine was first isolated by Terasaka from *Orixia japonica* Thunb. Its structure (XII) was determined by Hughes, Ritchie and coworkers through degradation to 2,4-dihydroxy-6,7-dimethoxyquinoline, which had been synthesized previously.

![Formula XII]

In *Platydesma campanulata* this alkaloid was found to occur together with evolitrine and 6-methoxydictamnine only in the root and bark, while in the leaves it was not accompanied by the two monomethoxy compounds.

**C. Base A**

Base A was isolated from the root and bark but not from the leaves of *P. campanulata*. It was found in the same fractions as were bases B and C. It was possible to isolate the latter two in crystalline form, but attempts to separate the pure base A gave only pure base B and a mixture of bases A and B. Since base B was proven to be 6-methoxydictamnine and base C 6,7-dimethoxydictamnine, base A might well be 7-methoxydictamnine (evolitrine).
Evolitrine had been isolated previously, first by Cooke and Haynes, later by Briggs and Cambie, and by Rapoport and Tian Gwan Hiem. Ohta and Mori proved its structure by synthesis. Interestingly enough kokusaginine (base C) was encountered by both Cooke and Briggs in their work.

Chromatography of an authentic sample of evolitrine parallel with the mixture of bases A and B on a thin layer of aluminum oxide with benzene-chloroform (1:1) as developer showed the following results. The mixture yielded two spots, one with the $R_f$ and the color of evolitrine, and the other with the $R_f$ and color of base B. The origin of the color upon development with Dragendorff's reagent is not known but it does seem to be a criterion for the differentiation of the two alkaloids.

Although this evidence is not conclusive, there is little doubt that evolitrine is a minor alkaloid of *Platydesma campanulata*. It is the fourth recorded occurrence of the alkaloid all of which have been in the same subfamily
of the Rutaceae.

D. Base D

This base occurred in the root and bark of *Platydesma campanulata* which was collected on Hawaii. It was not isolated from the plant material collected on Kauai. A total of one hundred and sixty-eight milligrams of Base D picrate was isolated, which corresponds to a yield of 0.00073 percent.

The elemental and functional group analyses of the picrate best agree with an empirical formula of $C_{15}H_{17}NO_3$. This was further supported by a molecular weight of 259 as determined by mass spectrometry.

The ultraviolet absorption spectra (Fig. 9) in ethanol and in 0.01 N hydrochloric acid were identical with those of dihydrodictamnine (Fig. 18).53

The mass spectrum of the free base24 had only two prominent peaks, the molecular weight peak at 259 m/e units and a peak at 200 m/e units. This latter peak is caused by a fragment after a loss of 59 m/e units. A dihydrodictamnine radical, XIV, has a molecular weight of 200; since the presence of this moiety was also suggested by the ultraviolet absorption spectrum, it may be assumed that the alkaloid is a substituted dihydrodictamnine.

The substitution of the dihydrodictamnine nucleus must be on the non-aromatic part of the molecule, since
Fig. 18.—Ultraviolet spectra of dihydrodictamine: —, in 95% ethanol; ——, in 0.01 N hydrochloric acid in 95% ethanol.
cleavage during electron bombardment occurs most readily at aliphatic or alicyclic bonds. Infrared evidence excluded the possibility that the fragment of weight 59 arose from a \( \text{C}_2\text{H}_3\text{O}_2 \) unit. Furthermore, subtraction of the elements \( \text{C}_{12}\text{H}_{10}\text{O}_2\text{N} \) corresponding to dihydrodictamnine from the molecular formula leaves a \( \text{C}_3\text{H}_7\text{O} \) fragment. A \( \text{C}_3\text{H}_7\text{O} \) radical can only be an ether or an alcohol. A band at 2.79 \( \mu \) in the infrared absorption spectrum (Fig. 10) indicates that an hydroxy group is present in the free base D. There is no evidence for an ether linkage other than the known methoxy group. The 2.79 \( \mu \) band is at a sufficiently long wavelength to have arisen from a tertiary alcohol.

If the alcohol function in the \( \text{C}_3\text{H}_7\text{O} \)-fragment is indeed tertiary, its nature would be as in XV.
A choice of two structures, XVI or XVII, remains for alkaloid D.

Biogenetic reasoning supports structure XVI. Reaction of 4-methoxyquinoline with an isoprene unit as suggested by Ruzicka,\textsuperscript{56} with the aid of an operator as suggested by Robinson\textsuperscript{57} would allow the following biogenetic scheme:
If the 'operator' placed the isoprene unit in a position other than the 3-position of methoxyquinoline, a dihydrodictamine nucleus would not arise. Furthermore, two alkaloids with a skeleton as proposed in XVI have been isolated from *Balfourodendron riedelianum* and from *Lunasia amara* Blanco. Both have structure XVIII and are enantiomeric. Balfourodine is the dextrorotatory and hydroxylunacrine is the levorotatory antipode.

![Structure XVIII]

An oxidation analogous to the one that is proposed in the biogenetic scheme has precedents in the alkaloids maculosine, XIX, and hydroxylunacrine, XX.

![Structure XIX][Structure XX]

Both compounds are oxidized to the glycol stage in the isoprene portion of the molecule.
Thus structure XV for base D appears to be reasonable on biogenetic and chemical grounds.

The alkaloid has been named platydesmine. It is the first dihydrodictamine derivative which has been isolated from natural sources. Its occurrence is therefore, if not surprising, biogenetically interesting, since the loss of an isopropyl alcohol unit would lead to dictamine.

This may well be a clue to the origin of the furan group in furoquinoline alkaloids, which has not been explained to date. 57

E. Base E.

Base E was isolated from the root, bark, and leaves from Hawaii, but not from those from Kauai. The total yield was one hundred and seven milligrams (0.0017 percent).

Elemental analysis of the picrate and of the free base established $C_{11}H_{11}ON$ as the empirical formula of the free base. A methoxyl group was absent.

The ultraviolet absorption spectrum of the base
(Fig. 12) is typical of 4-quinolones.\textsuperscript{34,60} It shows a bifurcated peak between 320 and 340 m\textmu in 95\% ethanol, which is shifted to lower wavelength and appears as a single peak in 0.01 N ethanolic hydrochloric acid. This is typical of 2-methyl substituted 4-quinolones.

A N.M.R. spectrum (Fig. 13) established the presence of two methyl groups. Since no quinoline alkaloids bearing methyl substituents on the benzene ring had been found previously, it could be assumed that the second methyl group was either in the 1- or 3-position of the molecule. The N.M.R. spectrum of a synthetic sample of 1,2,3-trimethyl-4-quinolone (Fig. 13) showed one additional three-proton peak at lower chemical shift. This indicated that the third methyl group, the one not present in base E, must be in the 3-position, since these hydrogens would show the smallest chemical shift with respect to the internal standard, tetramethylsilane. Base E was therefore proven to be 1,2-dimethyl-4-quinolone.\textsuperscript{61}

2-Methyl-4-quinolone was synthesized by the Conrad-Limpach method.\textsuperscript{32} Methylation with dimethyl sulfate led to the expected 1,2-dimethyl-4-quinolone.\textsuperscript{31} The synthetic base was identical with the natural product in every respect.

The presence of 1,2-dimethyl-4-quinolone in \textit{Platydesma campanulata} came as a surprise, since there has only been one other occurrence of such a simple substituted quinolone in the Rutaceae. Greshoff isolated the alkaloid
echinopsine, XXI, from the seeds of *Echinops ritros*. 62

![Chemical structure of echinopsine, XXI.](image)

Substitution in the two-position, however, is not new. Among the alkaloids of Angostura bark 2-substituted quinolones and quinolines are quite common, but none of them are 2-methylquinolones.

F. Base F.

Base F could not be isolated in crystalline form. It was isolated as the picrate in a yield of 0.00081 percent. It was found only in the leaves.

Its empirical formula rests solely on the analyses of its picrate. \( C_{22}H_{22}O_{10}N_4 \) agrees best, but \( C_{22}H_{24}O_{10}N \) fits well enough to merit consideration. Subtraction of the element of picric acid leaves a free base of formula \( C_{16}H_{19}O_3N \) or \( C_{16}H_{21}O_3N \). Functional group analysis showed the presence of one methoxy group and one methyl group linked to nitrogen.

The ultraviolet absorption spectrum (Fig. 15) of this base was compared with those in the literature. 64 This comparison suggests that base F is a substituted 1-
methyl-8-methoxy-4-quinolone. The shift of its peak to lower wavelength in 0.01 N acid has been suggested to be due to the substituent on the benzene ring. It was noted by Goodwin et al., that an 8-methoxy substituent causes a hypsochromic shift, while a 7,8-methylenedioxy group gives rise to a bathochromic shift of the long wavelength peaks in 0.01 N acid. The infrared absorption spectrum is also consistent with a 4-quinolone structure. A partial structure of 1-methyl-8-methoxy-4-quinolone, XXII, may therefore be proposed.

\[
\begin{array}{c}
\text{CH}_3 \\
\text{CH}_3 \\
\end{array}
\]

XXII

This leaves a \( C_9H_{11}O \) fragment to be placed. The nature of this fragment could not be determined with certainty, but it may be assumed that the five carbons constitute an isoprene unit as has been observed in many other cases. The presence of 'operators' in the plant as suggested by Robinson would make the attachment of such an isoprene unit on the aromatic nucleus possible. A survey of other alkaloids would at first indicate that attachment of such a fragment could be possible almost anywhere on the molecule. However, all 4-quinolones containing an isoprene unit which
have been isolated to date are substituted in the 3-position. Part structure XXII may therefore be expanded to part structure XXIII.

\[
R = C_5H_{9-11}O
\]

XXIII

Presence of a furano group may be excluded since none of the characteristic bands mentioned in the work by Briggs and Colebrook are present in the infrared absorption spectrum. Furthermore, only one oxygen atom remains to be placed. This oxygen atom is clearly part of an alcohol function and gives rise to a peak at 2.72 \( \mu \) in the infrared absorption spectrum (Fig. 10).

An attempt was made to determine the position of the hydroxy group on the side chain. The peak at 2.72 \( \mu \) would indicate that the alcohol is primary or secondary, but this cannot be taken for granted since the accuracy of the spectrometer is \( \pm 0.05 \mu \). Thus, a tertiary alcohol is not excluded.

A small amount of the free base was oxidized with chromic anhydride in acetic acid. A picrate of the product could be isolated. Its ultraviolet absorption spectrum was identical with that of the picrate of the base and exhibited
the three major peaks of base F. The infrared absorption spectrum (Fig. 13) and the melting point of the picrate of the oxidation product were different from those of the picrate of free base F.

The elemental analysis agreed well with a formulation of $C_{16}H_{19}O_3N$. If the empirical formula of base F is $C_{16}H_{21}O_3N$, the formula of the oxidation product would indicate a loss of two hydrogen atoms corresponding to the oxidation of an alcohol to a ketone. Because of the limited accuracy of a hydrogen determination this argument is open to question. No doubt an oxidation took place since the oxidizing agent was reduced. It was an oxidation which was accompanied by a very slight change in percentage composition. This adds some substance to the above argument.

Since the ultraviolet spectrum remained unchanged, the oxidation must have taken place more than one carbon atom away from the aromatic system. This leaves only one likely position for a secondary alcohol. The possibility of a primary alcohol cannot be excluded, but since there are no analogies for it, it must be considered less likely than a secondary alcohol.

The following tentative structure may be proposed for base F, XXIV.
This alkaloid has been named pilokeanine. The name is derived from the Hawaiian name of the plant.

Lunacrine, \( XXV \), and hydroxylunacrine, \( XXVI \), are two alkaloids which have been isolated from \textit{Lunasia amara} \textit{Blanco}.\textsuperscript{59} They differ from each other only by an hydroxyl group in the aliphatic side chain.

If one accepts the tentative structure \( XXIV \) for pilokeanine, analogous though more remote relationship exists in the aliphatic side chains of pilokeanine (\( XXIV \))
and platydesmine (XVI).

Proposed structure XXIV is consistent with all chemical and biogenetic evidence but it cannot be considered definitely established.
CHAPTER IV
CONCLUSION AND SUMMARY

It was shown that at least six bases occur in *Platydesma campanulata*: evolitrine (XIII), 6-methoxydictamnine (X), kokusaginine (XII), platydesmine (XVI), 1,2-dimethyl-4-quinolone (XXVII), and pilokeanine (XXIV).

![Chemical structures](image_url)
The presence of evolitrine was demonstrated by comparison chromatography. The structure of 6-methoxydictamnine was established by isomerization to 6-methoxyisodictamnine, which was a known compound. The presence of kokusaginine was proven by direct comparison of base C picrate with an authentic sample of kokusaginine picrate. The proof of structure of platydesma was based on the use of physical methods and biogenetic principles. Base E was shown to be 1,2-dimethyl-4-quinolone by instrumental methods and by synthesis. A structure has been proposed for pilokeanine. It has not been proven beyond doubt, but it appears to be consistent with all chemical evidence and with currently held biogenetic theories.

6-Methoxydictamnine, platydesmine, 1,2-dimethyl-4-quinolone, and pilokeanine are new natural products. Evolitrine and kokusaginine were isolated previously. The salient data pertaining to these alkaloids are summarized in Table III.

The taxonomic question which was posed in the introduction as to the position of the genus *Platydesma* among the other genera of the subfamily Xanthoxyleae cannot be answered on the basis of the new information. The isolated alkaloids clearly confirm that *Platydesma* is a member of the subfamily Rutoideae. A relationship to the genus *Lunasia* is suggested, but the alkaloids of *Medicago cunninghamii* are not more closely related to those of *Platydesma* than
TABLE III. The Alkaloids of *Platydesma Campanulata* Mann.

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<tbody>
<tr>
<td>Base A evolitrine</td>
<td>114-115°</td>
<td>?</td>
<td>-</td>
<td>-</td>
<td>Root and bark</td>
<td>191-192°</td>
</tr>
<tr>
<td>Base E 6-methoxydictamnine</td>
<td>134-135°</td>
<td>2.3 X 10⁻³%</td>
<td>Fig. 4</td>
<td>Fig. 5</td>
<td>Root and bark</td>
<td>195-196°</td>
</tr>
<tr>
<td>Base C kokusaginine</td>
<td>169-169.5°</td>
<td>1.6 X 10⁻³%</td>
<td>Fig. 8</td>
<td>Fig. 5</td>
<td>Leaves, root and bark</td>
<td>205-208° (dec.)</td>
</tr>
<tr>
<td>Base D platydeshmine</td>
<td>137-138°</td>
<td>7.3 X 10⁻⁴%</td>
<td>Fig. 9</td>
<td>Fig. 10</td>
<td>Leaves, root and bark</td>
<td>107-109°</td>
</tr>
<tr>
<td>Base E 1,2-dimethyl-4-quinolone</td>
<td>178-179°</td>
<td>1.7 X 10⁻³%</td>
<td>Fig. 11</td>
<td>Fig. 12</td>
<td>Leaves, root and bark</td>
<td>234-236° (dec.)</td>
</tr>
<tr>
<td>Base F pilokeanine</td>
<td>oil</td>
<td>7.0 X 10⁻⁴%</td>
<td>Fig. 15</td>
<td>Fig. 10</td>
<td>Leaves</td>
<td>216° (dec.)</td>
</tr>
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are those of *Choisya ternata*.

Pharmacological studies could not be carried out because of the small amount of pure bases which were available. However, the isolation of alkaloids which are related to those isolated from *Lunasia amara* Blanco\(^5^9\) is of potential interest, since the bark of that plant has been used in preparing arrow poisons by the natives of Luzon Island.\(^6^5\)
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