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PONGAGLABRONE, A NEW COMPONENT OF THE SEEDS OF *PONGAMIA GLABRA*: ITS CONSTITUTION AND SYNTHESIS

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Abstract—From the seeds of *Pongamia glabra*, pongaglabrone, a new furano-flavone has been isolated and its structure established as 3′,4′-methylenedioxy-furano-(2″:3″-7:8)-flavone. It has been confirmed by synthesis in two ways.

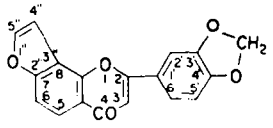
IN A recent publication the isolation of kanjone [6-methoxy-furano-(2″:3″-7:8)-flavone] from the light petroleum extract of the seeds of *P. glabra*, collected in 1959, was reported.[1] In another extraction using the seeds collected in 1961 and adopting a more efficient method of fractionation, besides kanjone a new compound was isolated in small yield from a light petroleum extract. This was found to be a simple member of the furano-flavone series unsubstituted in the condensed benzene ring and has been named pongaglabrone. It is a colourless and fat soluble compound melting at 233°, with the molecular formula $C_{18}H_{10}O_5$ and no methoxyl group. Its insolubility in aqueous sodium hydroxide and lack of ferric reaction indicates that there are no enolic or phenolic hydroxyl groups. But it gives a violet colour on warming with concentrated sulphuric acid; it may be mentioned that other components of the seeds, karanjin, pongamol and pongapin also give definite colours with this acid. The formation of a bright green colour with gallic and sulphuric acids indicates the presence of a methylenedioxy group. The relatively high melting point and low solubility of the compound may also be attributed to the presence of this group. Its IR spectrum includes the following characteristic bands. A strong absorption at 1640 cm^{-1} is characteristic of a flavone carbonyl. A strong band at 1035 cm^{-1} and a weak band at 935 cm^{-1} are the most characteristic for the methylenedioxy group.[2] The UV absorption spectrum shows two bands at 249 and 331 mμ which are similar to those of pongapin[3] and gamatin[4] in wave-length and intensitites (see Table 1), and indicate a furano-flavone skeleton for pongaglabrone. The furano-flavone structure with a methylenedioxy group accounts for all the requirements of the molecular formula.

TABLE 1. UV SPECTRA

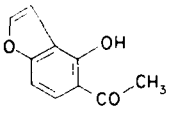
Compound	λ_{max} (mμ)	log ε max	λ_{max} (mμ)	log ε max
Pongapin	251·5	4·34	332·5	4·34
Gamatin	251·5	4·52	334	4·39
Pongaglabrone	249	4·44	331	4·32

[1] R. Aneja, R. N. Khanna and T. R. Seshadri, *J. Chem. Soc.* In press.
[2] L. H. Briggs, L. D. Colebrook, H. M. Fales and W. C. Wildman, *Analyt. Chem.* **29**, 904 (1957).
[3] L. R. Row, *Aust. J. Sci. Res.* **A5**, 754 (1952).
[4] S. K. Pavanaram and L. R. Row, *Aust. J. Chem.* **9**, 132 (1956).

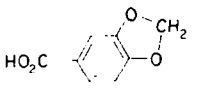
The position of the methylenedioxy group and that of the furan ring had to be determined. Fission of pongaglabrone with absolute alcoholic potash yields an acid, m.p. 220°, giving a positive test for the methylenedioxy group and identified as piperonylic acid (III) and a hydroxy ketone m.p. 95° giving a prominent ferric reaction. Piperonylic acid was accompanied by a small amount of karanjic acid. So the ketone should be 4-hydroxy-5-acetyl coumarone (II), which was obtained earlier[5] by direct alkali fission of pongamol and m.p. recorded as 86°. For comparison it has now been perpared by a modified method using two stages. Demethylation of pongamol gives the furano-(2″:3″-7:8)-flavone (VI)—first made by Rangaswami and Seshadri[6] and later found to occur free in *Tephrosia lanceolata* and called lanceolatin B[7]. Fission of VI affords 4-hydroxy-5-acetyl coumarone (II) m.p. 95°, and not 86° as reported earlier. The mixed m.p. with the fission ketone of pongaglabrone was undepressed and consequently pongaglabrone may be represented as 3′,4′-methylenedioxy-furano-(2″:3″-7:8)-flavone (I). It is unsubstituted in the condensed benzene ring just like lanceolatin B, but the side phenyl has a condensed methylenedioxy group.



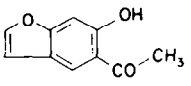
I



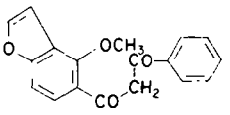
II



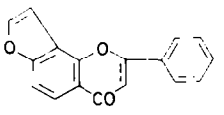
III



IV

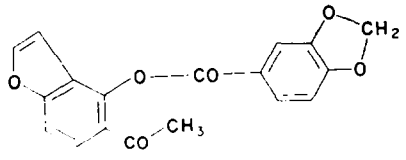


V

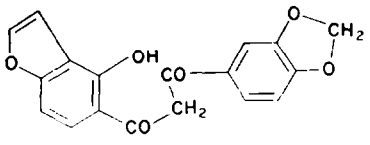


VI

The structure of pongaglabrone has been confirmed by synthesis using the hydroxy-acetyl coumarone (II). The piperonyl ester (VII), prepared by the use of piperonyl chloride in the presence of acetone and potassium carbonate[8] or in the presence of dry pyridine, does not undergo the Baker-Venkataraman rearrangement when refluxed with acetone and potassium carbonate but it proceeds smoothly when skaken with solid potassium hydroxide in pyridine solution. The resulting diketone (VIII) may be converted into flavone (I) by heating with glacial acetic acid and hydrochloric acid.



VII



VIII

[5] B. Rao and V. Venkateswarlu, *Curr Sci, India* 357 (1956).

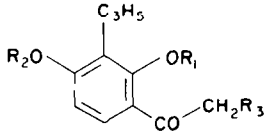
[6] S. Rangaswami and T. R. Seshadri, *Proc. Indian Acad. Sci.* **15A,** 421 (1942); S. Narayanaswami, S. Rangaswami and T. R. Seshadri, *J. Chem. Soc.* 1871 (1954).

[7] S. Rangaswami and B. V. Sastry, *Curr Sci., India,* **24,** 12 (1955).

[8] V. N. Gupta and T. R. Seshadri, *J. Sci. Ind. Res. India* **16B,** 116 (1957).

The synthetic product was identical with the natural pongaglabrone in melting point, colour reactions, solubility and spectral characteristics.

A total synthesis involves 7-hydroxy-8-allyl-3′,4′-methylenedioxy-flavone (XIV) which may be prepared from 3-allyl-resacetophenone (IX). Treatment of ketone IX with potassium carbonate, acetone and piperonyl chloride gives only a poor yield of the diketone XII which could not be purified. The pyridine and acid chloride method gives mainly 4-O-piperonyl-3-allyl-resacetophenone (X), and no di-O-piperonyl derivative (XI) was isolated. This resistance of IX to give the diester may be attributed to the following factors: (1) The activity of the chelated hydroxyl group at position 2 is further reduced due to the steric hindrance caused by the allyl group at the adjacent carbon atom. Similar cases may be mentioned in the flavone series; 6-alkyl-5-hydroxy flavones[9] are very resistant to methylation but the present case seems to be the first where complete esterification could not be achieved due to the steric factors. (2) The piperonyl chloride is probably less reactive than benzoyl chloride, because a similar related system, 2,4-dihydroxy-3-allyl-5-methoxy acetophenone undergoes dibenzoylation.[1] Though the diketone obtained by the acetone-carbonate method could be cyclized to the hydroxy flavone ester (XIII) and hydrolysed to XIV, the over all yields were poor.

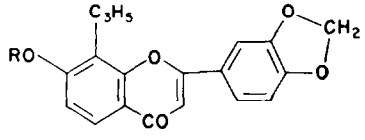


IX $R_1 = R_2 = R_3 = H$

X $R_1 = R_3 = H, R_2 = Pip.$

XI $R_1 = R_2 = Pip., R_3 = H$

XII $R_1 = H, R_2 = R_3 = Pip.$

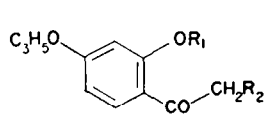


XIII R = Pip.

XIV R = H

Pip.= Piperonyl

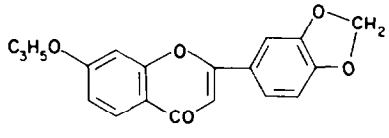
A more feasible synthesis of the hydroxy-allyl-flavone (XIV) was achieved from 4-O-allyl-resacetophenone (XV). The pyridine-acid chloride method or acetone, potassium carbonate and acid chloride method converted XV into its O-piperonyl



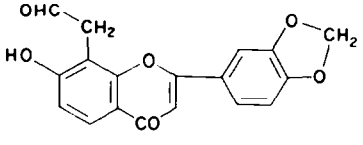
XV $R_1 = R_2 = H$

XVI $R_1 = Pip., R_2 = H$

XVII $R_1 = H, R_2 = Pip.$



XVIII



XIX

[9] S. K. Mukerjee and T. R. Seshadri, *Proc. Indian Acad. Sci.* **38A**, 211 (1953).

derivative (XVI), which was smoothly rearranged to the diketone (XVII). Subsequent cyclization proceeds easily to the flavone (XVIII).

Application of the Claisen migration to XVIII yields 7-hydroxy-8-allyl-3',4'-methylene-dioxy-flavone (XIV). The constitution of this product is based on analogy with the related flavone derivatives studied by Chibber *et al.*[10] where the migration takes place to the 8-position. Closing the furan ring was effected by following the

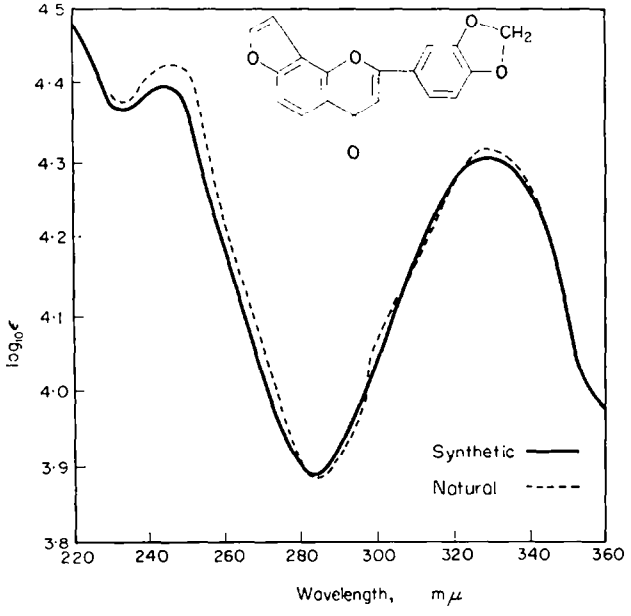


FIG. 1.

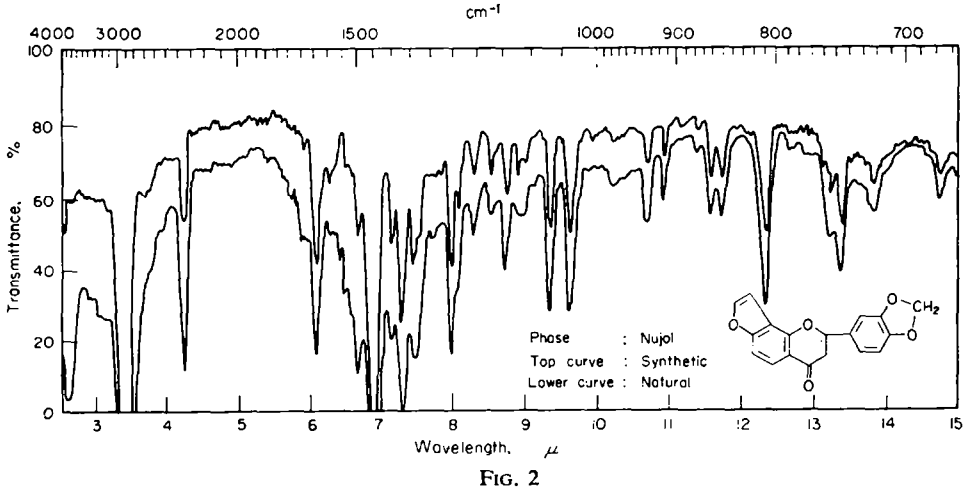


FIG. 2

[10] S. S. Chibber, A. K. Ganguly, S. K. Mukerjee and T. R. Seshadri, *Proc. Indian Acad. Sci.* **46A**, 19 (1957).

method of Aneja *et al.*[11] using ozone to form the corresponding acetaldehyde (XIX) and then closing the ring with polyphosphoric acid. The synthetic product agreed with the natural pongaglabrone in all respects.

EXPERIMENTAL

The ripe seeds were collected from the President's Estate, New Delhi in March 1961 and the general extraction carried out as in earlier work.[1] However oil A and oil B have been examined by a more efficient method.

Oil A: karanjin, pongamol and pongaglabrone

Oil A was continuously extracted in a liquid–liquid extractor with alcohol (1 l.) for 40 hr and the extract concentrated under red. press. to a dark brown oil (175 cc), which on standing in a refrigerator for 10 days, deposited karanjin (4 g). The oil was decanted off, the crystals washed with light petroleum and the washings evaporated and the residue mixed with the decanted oil. The oil in benzene solution was passed over a column of alumina (5·6 × 35 cm.). Light petroleum (4 l.) eluted a mixture of fatty oil and pongamol and separation was effected by counter current distribution between aqueous acetic acid and light petroleum which gave pongamol (8 g). Further washings with light petroleum (4 l.) and light petroleum–benzene (1:1, 1·5 l.) eluted karanjin (1 g). Benzene (4·4 l.) eluted a new product (pongaglabrone) which crystallized from alcohol as silky needles, m.p. 233° (50 mg). Alcohol (2·5 l.) eluted a brownish-yellow oil (10 cc). Further work on this fraction is in progress.

Oil B: karanjin, pongapin, kanjone and pongaglabrone

Oil B when left in a refrigerator for 10 days deposited karanjin (1 g). The decanted oil and that obtained from washing the crystals with light petroleum were dissolved in benzene and passed over a column of alumina (3 × 44 cm.). Light petroleum (1·2 l.) eluted karanjin (1 g). Light petroleum-benzene mixture (1:1, 2 l.) eluted pongapin (10 mg), and benzene (2·5 l.) eluted kanjone (100 mg). Further elution with benzene (1·5 l.) yielded a colourless compound (10 mg), m.p. 233°, alone or mixed with pongaglabrone obtained from oil A. Alcohol (4 l.) eluted a brownish yellow oil (2 cc). Further work on this fraction is in progress.

Pongaglabrone is a colourless fat soluble compound. With warm conc sulphuric acid it gives a violet colour and with gallic and sulphuric acids a bright green colour (Found: C, 68·5; H, 4·0; $C_{18}H_{10}O_5,\frac{1}{2}H_2O$ requires: C, 68·6; H, 3·5%). The sample dried *in vacuo* at 110° exhibited a marked tendency to absorb moisture.

Alkaline hydrolysis of pongaglabrone. Pongaglabrone (30 mg) was refluxed with absolute alcoholic potash (2 cc; 8%) for 8 hr. The solvent was completely removed under red. press. water (15 cc) added and the reddish brown solution acidified with hydrochloric acid yielding a pale yellow crystalline solid. The mixture was taken up in ether, extracted successively with aqueous sodium hydrogen carbonate (5%; 3 × 8 cc) and with aqueous sodium hydroxide (5%; 3 × 5 cc). The hydrogen carbonate extract was acidified and the mixture centrifuged. The mother liquor was decanted off and the residue crystallized from methanol, yielding a crystalline solid, m.p. 180–190°. This was subjected to vacuum sublimation at 130°. The residue (1 mg), m.p. 220°d; gives a blue ferric reaction and agrees with karanjic acid. The colourless sublimate (7 mg) has a m.p. 219–220° alone or mixed with an authentic sample of piperonylic acid. The aqueous sodium hydroxide extract was acidified and the precipitated product centrifuged and the mother liquor decanted off. The residue crystallized from aqueous methanol as pale yellow needles (3 mg), m.p. 95° alone or mixed with an authentic sample of 4-hydroxy-5-acetyl coumarone (II) prepared by the alkaline hydrolysis of furano-(2″:3″-7:8)-flavone (VI) (see below). Evaporation of the residual ether solution, gave a small amount of oil which could not be purified.

Preparation of 4-hydroxy-5-acetyl coumarone (II). The furano-(2″:3″-7:8)-flavone (VI) was prepared from pongamol by the method of Narayanaswamy *et al.*[6]. Compound VI (500 mg) was

[11] R. Aneja, S. K. Murkerjee and T. R. Seshadri, *Tetrahedron* **2**, 203 (1958).

boiled with absolute alcoholic potash (40 cc; 8%) for 8 hr and the solution worked up as mentioned in the case of pongaglabrone. The aqueous sodium hydrogen carbonate extract on acidification gave benzoic acid (100 mg), while the aqueous sodium hydroxide extract provided 4-hydroxy-5-acetyl coumarone (125 mg). Crystallization from aqueous methanol gave pale yellow needles, m.p. 95° (Rao and Venkateswarlu[5] recorded m.p. 86°) (Found: C, 67·9; H, 4·5. Calc. for $C_{10}H_8O_3$: C, 68·2; H, 4·5%).

Partial synthesis

3',4'-*Methylenedioxy-furano*-(2'':3''-7:8)-*flavone* (I). (i) A mixture of coumarone (II; 100 mg) and piperonyl chloride (200 mg) and pyridine (1·5 cc) was heated to 50° for 10 min and left overnight and poured into ice-cold hydrochloric acid. The solution was filtered and the residual solid washed with aqueous sodium hydrogen carbonate and finally with water and dried. Crystallization of the residue from aqueous methanol (charcoal) gave colourless silky needles (125 mg) of the piperonyl ester (VII), m.p. 127° (Found: C, 65·9; H, 3·8. $C_{18}H_{12}O_6$ requires: C, 66·6; H, 3·7%).

(ii) The piperonyl derivative (VII; 100 mg) was dissolved in dry pyridine (2 cc) and powdered potassium hydroxide (100 mg) added. The mixture was shaken for 1 hr at 40°, acidified with excess of aqueous acetic acid (20%) and kept overnight. The yellow diketone (VIII) was collected and crystallized from alcohol yielding yellow prisms (60 mg), m.p. 149°, which gave a brown ferric reaction (Found: C, 66·8; H, 4·1. $C_{18}H_{12}O_6$ requires: C, 66·6; H, 3·7%).

(iii) The above diketone (VIII; 30 mg) was refluxed with glacial acetic acid (3 cc) containing a drop of conc hydrochloric acid for 1 hr. On dilution with water, the product precipitated as a colourless solid (20 mg). Crystallization from ethanol yielded colourless silky needles, m.p. 233° alone or mixed with pongaglabrone. It gives all the colour reactions of the natural pongaglabrone (Found: C, 68·2; H, 4·1. $C_{18}H_{10}O_5,\frac{1}{2}H_2O$ requires: C, 68·6; H, 3·5%). The sample dried *in vacuo* at 110° exhibited marked tendency to absorb moisture.

Total synthesis

(*a*) *7-Hydroxy-8-allyl-3',4'-methylenedioxy flavone* (XIV)

Method I

7-Piperonyloxy-8-allyl-3',4'-methylenedioxy flavone (XIII). 3-Allyl-resacetophenone (IX) was prepared from resacetophenone as described by Baker and Lothian.[12] A mixture of 3-allyl resacetophenone (IX; 3·84 g), piperonyl chloride (8·1 g), dry acetone (250 cc) and potassium carbonate (30 g) was refluxed for 40 hr and the mixture filtered. (A) The residue was treated with water, leaving an undissolved colourless solid (4·0 g), giving a brown ferric reaction. Crystallization from ethanol gave pale yellow needles, m.p. 108–110° which could be easily hydrolysed with aqueous alcoholic potash to 3-allyl resacetophenone, indicating that it was 3-allyl-4-O-piperonyl resacetophenone (X) (Found: C, 66·4; H, 4·6. $C_{19}H_{16}O_6$ requires: C, 67·0; H, 4·7%). (B) The acetone filtrate on evaporation yielded a pale yellow residue (500 mg), m.p. 150–160° which could not be purified and was used directly for cyclization by refluxing with glacial acetic acid (30 cc) containing a few drops of conc hydrochloric acid for 1 hr. On addition of water the flavone (XIII) was precipitated as a colourless solid (300 mg). Crystallization from methanol gave thin colourless needles, m.p. 209°. (Found: C, 69·2; H, 4·3. $C_{27}H_{18}O_8$ requires: C, 68·9; H, 3·8%).

(ii) *7-Hydroxy-8-allyl-3',4'-methylenedioxy flavone* (XIV). The flavone (XIII, 300 mg) was refluxed with alcoholic potash (21 cc; 15%) for 0·5 hr. As much alcohol as possible was distilled off and the solution acidified with hydrochloric acid (10%). The colourless precipitate was filtered, washed with aqueous sodium hydrogen carbonate and then with water and dried. Crystallization from ethanol gave colourless needles (150 mg), m.p. 254° (Found: C, 70·5; H, 4·6. $C_{19}H_{14}O_6$ requires: C, 70·8; H, 4·4%).

Method II

(i) 2-O-*Piperonyl*-4-O-*allyl resacetophenone* (XVI) (a) *Acetone-potassium carbonate method.* A mixture of 4-O-allyl resacetophenone[12] (2 g), piperonyl chloride (4 g), dry acetone (200 cc) and ignited

[12] W. Baker and O. M. Lothian, *J. Chem. Soc.* 628 (1935).

potassium carbonate (30 g) was refluxed for 10 hr. The product crystallized from methanol as colourless silky needles (3 g), m.p. 89° (Found: C, 66·6; H, 5·0. $C_{19}H_{16}O_6$ requires: C, 67·1; H, 4·7%). (b) *Pyridine method.* A solution of 4-O-allyl resacetophenone (2 g) in dry pyridine (15 cc) was treated with excess of piperonyl chloride (4 g) and the mixture heated at 90° for 0·5 hr and left overnight. It was poured into ice-cold hydrochloric acid, the solution filtered, the residual solid washed with aqueous sodium bicarbonate and finally with water and dried. Crystallization from methanol gave colourless silky needles (3 g), m.p. 89° alone or mixed with the compound obtained by method (a).

(ii) 2-*Hydroxy*-4-*allyloxy*-3′,4′-*methylenedioxy dibenzoyl methane* (XVII). The piperonyl derivative (XVI; 2 g) was rearranged using pyridine and potassium hydroxide. The yellow product was collected and crystallized from methanol yielding yellow prisms (1·7 g), m.p. 132–133°. The ferric reaction was brown (Found: C, 67·0; H, 4·7. $C_{19}H_{16}O_6$ requires: C, 67·1; H, 4·7%).

(iii) 7-*Allyloxy*-3′,4′-*methylenedioxy flavone* (XVIII). Cyclization of the diketone (XVII, 1 g) was effected with glacial acetic acid and a drop of hydrochloric acid. Crystallization of the product from ethanol gave pale yellow needles (0·8 g), m.p. 187° (Found: C, 71·0; H, 4·6. $C_{19}H_{14}O_5$ requires: C, 70·8; H, 4·4%).

(iv) 7-*Hydroxy*-8-*allyl*-3′,4′-*methylenedioxy flavone* (XIV). The allyloxy flavone (XVIII; 1 g) was heated for 2 hr under red. press. (20 mm) at 210°. The product was extracted with aqueous potash (5%) and filtered. The alkaline filtrate was acidified and the precipitated product filtered, washed with water and dried. Crystallization from ethanol yielded colourless needles (750 mg), m.p. 254° alone or mixed with the one obtained by method I.

(*b*) 3′,4′-*Methylenedioxy furano*-(2″:3″-7:8)-*flavone* (I)

Ozonized oxygen (3%; 150 cc/min) was passed through a solution of the allyl flavone (XIV; 150 mg) in formic acid (100 cc) at 5° for 7 min. The solution was allowed to warm up to room temp. and then shaken with hydrogen in the presence of palladized charcoal (5%; 100 mg) until the rapid absorption of hydrogen ceased. The filtered solution was evaporated under red. press. on a boiling water bath, leaving a deep yellow solid. It was heated on a boiling water bath with polyphosphoric acid (5 cc) for 20 min, cooled and poured on crushed ice. The solid was filtered, washed with aqueous sodium hydroxide and then with water and dried. It crystallized from ethanol as colourless silky needles (12 mg), m.p. 233° alone or mixed with pongaglabrone; $\lambda_{max}^{C_2H_5OH}$, 249 and 330 mμ.