# *Chemistry of Pongamol. Part II.**

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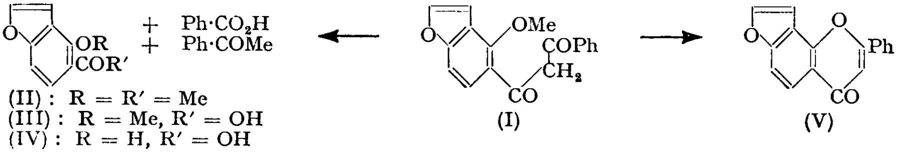
Pongamol, the second crystalline component of the seed oil of *Pongamia glabra*, is shown to be benzoyl-*O*-methylkaranjoylmethane (5-benzoylacetyl-4-methoxybenzofuran) (I) by a study of its fission with alkali and demethylation with hydriodic acid. It is the first example of a naturally occurring diketone related to flavones.

In Part I * pongamol was shown to have the molecular formula $C_{18}H_{14}O_4$ and to contain one methoxyl group. Though it gave a ferric chloride colour indicative of a phenolic or enolic hydroxyl group, it did not undergo methylation or benzoylation under ordinary conditions. Oxidation of pongamol with permanganate gave benzoic acid. Further, its colour reactions with concentrated sulphuric acid and with magnesium and hydrochloric acid were somewhat similar to those of karanjin, 3-methoxyfurano(2′ : 3′-7 : 8)flavone. It was believed therefore, that pongamol had a closely related structure.

Subsequently, fission of pongamol was carried out with aqueous-alcoholic potassium hydroxide. This gave a mixture which has now been analysed by paper-chromatography. The products were first separated into neutral and acid fractions. In the latter, benzoic acid was readily characterised, because of its higher solubility in water. The remaining portion consisted of a mixture of karanjic (IV) and *O*-methylkaranjic acid (III), which were largely separated by using the solubility difference in water but not fully purified. However, methylation afforded pure *O*-methylkaranjic acid. Obviously, the primary product of fission was this *O*-methylkaranjic acid and some of it suffered demethylation in alkali. The neutral fraction was also a mixture, consisting of acetophenone and a solid ketone, $C_{11}H_{10}O_3$, having one methoxyl group and giving no ferric reaction. That it was 5-acetyl-4-methoxybenzofuran (II) was confirmed by its conversion into *O*-methylkaranjic acid and its synthesis from *O*-methylkaranjoyl chloride and ethyl acetoacetate. This ketone, karanjic acid, and its methyl ether all give pronounced colours in concentrated sulphuric acid.

The fission is simpler with absolute methyl-alcoholic potassium hydroxide, yielding almost entirely benzoic acid and the ketone (II).

The results given above lead to the conclusion that pongamol is benzoyl-*O*-methylkaranjoylmethane (5-benzoylacetyl-4-methoxybenzofuran) (I), its degradations being represented as in the following scheme. In accordance with this structure, it gives a copper complex and a pronounced ferric chloride reaction and when demethylated undergoes ring-closure as discussed below.



(II) : R = R′ = Me
(III) : R = Me, R′ = OH
(IV) : R = H, R′ = OH

(I)

(V)

In Part I, demethylation of pongamol by hydriodic acid and by aluminium chloride in benzene was reported. The former yielded a neutral product $C_{17}H_{12}O_4$. This demethylation with hydriodic acid has now been found to proceed best under milder conditions; the product which is nonphenolic and does not undergo acetylation or methylation is a monohydrate and the anhydrous substance agrees with the requirements for furano-(2′ : 3′-7 : 8)flavone (V), the simplest member of this group of furanoflavones and hitherto unknown. Demethylation by aluminium chloride in benzene cannot be simple because of the ability of benzene to add to the furan ring (Krishnaswami and Seshadri, *Proc. Indian Acad. Sci.*, 1942, **15**, *A*, 437).

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* Part I, *Proc. Indian Acad. Sci.*, 1942, **15**, *A*, 419.

The elucidation of the constitution of pongamol is of importance in connection with the biogenesis of sap-soluble pigments. This structure, which is closely related to flavones, has not been found to occur in Nature before. Robinson's theory (*Nature*, 1936, **137**, 172; *Phil. Trans.*, 1939, **230**, *B*, 149) of the evolution of the $C_{15}$ skeleton suggests a stage of this type. But normally when a free hydroxyl group is present in the *o*-position, the compound would undergo ring-closure. In pongamol, an earlier stage of methylation has rendered this diketone stable.

A matter of further significance is the occurrence of pongamol and karanjin together, both being methylation products, but belonging to different types. Clearly, when the methylation mechanism of the plant functions, the nuclear hydroxyl group in pro-pongamol (pyrone ring open) is methylated whereas in pro-karanjin it is protected by chelation so that the second hydroxyl group is methylated instead, flavone ring-closure being the final stage.

As a structure analogous to pongamol should be mentioned eugenone (Meijer and Schmid, *Helv. Chim. Acta*, 1948, **31**, 1603), which is 2 : 4 : 6-trimethoxybenzoylacetone, a diketone related to the chromones and present in *Eugenia caryophyllata*. Here too stability has been conferred on it by the methylation of the *o*-hydroxyl groups.

## EXPERIMENTAL

Pongamol was extracted directly from the seeds of *Pongamia glabra*. A modified purification will be described elsewhere. When an ethereal solution of pongamol was shaken with saturated aqueous copper acetate the ethereal layer became green and a yellowish-green precipitate was formed at the interface. When crystallised from chloroform–ether, this copper complex melted at 226—227°.

*Fission with Aqueous-alcoholic Potassium Hydroxide.*—Pongamol (0·75 g.), dissolved in alcohol (38 c.c.), was treated with aqueous potassium hydroxide (2·8 g. in 56 c.c.). The clear yellow solution was refluxed on a water-bath for 3 hr., the solution becoming turbid. Alcohol was distilled off as completely as possible. The distillate gave a copious precipitate with 2 : 4-dinitrophenylhydrazine; the product crystallised from alcohol as fine needles, m. p. 239° alone or mixed with acetophenone 2 : 4-dinitrophenylhydrazone. The aqueous alkaline solution was acidified with sulphuric acid and extracted with ether and the ethereal solution extracted successively with aqueous sodium hydrogen carbonate and aqueous sodium hydroxide, the latter removing very little. Examination of the ethereal residue (C) is reported below.

A portion of the carbonate extract (A) was acidified and extracted with ether. Circular paper-chromatography of the whole of the extracted acid showed the presence of three components ($R_F$, at 23°, 0·61, 0·56, and 0·51; solvent, *n*-butanol saturated with ammonia) when bromophenol-blue (0·04% in alcohol) was used as the indicator, and of one component giving a blue ring ($R_F$ 0·61) with ferric chloride (1% solution in alcohol). The $R_F$ values of karanjic, *O*-methylkaranjic, and benzoic acid were found to be 0·61, 0·56, and 0·51 respectively.

The bulk of the carbonate extract (A) was acidified and the solid (B) (0·25 g.) was filtered off. This gave a blue colour with alcoholic ferric chloride, a colourless solution with concentrated sulphuric acid becoming blue when warmed (pure karanjic and *O*-methylkaranjic acids gave a similar colour reaction with sulphuric acid), m. p. 126° with sintering at 96°. It was boiled with water, most of it dissolving. The insoluble part was filtered off and washed with hot water to remove the more soluble partion completely; it then crystallised from dilute alcohol as colourless needles which sintered at 196° and melted at 206° (decomp.); the m. p. of karanjic acid is 218° (decomp.). It gave a blue colour with alcoholic ferric chloride and a negative test for methoxyl. The hot aqueous filtrate, when kept in the refrigerator, gave a crystalline solid which after another crystallisation from hot water formed rectangular tablets, m. p. 142—144°; the m. p. of *O*-methylkaranjic acid is 148°. It still gave a blue ferric reaction and contained 13% of methoxyl (*O*-methylkaranjic acid requires OMe, 16·1%). The filtrate from (A) was extracted with ether; the colourless residue obtained on removal of the ether was crystallised twice from water, forming colourless plates, m. p. 120°, identical with benzoic acid.

From the remaining ethereal solution (C) the solvent was distilled off. The oily residue of 5-*acetyl*-4-*methoxybenzofuran* solidified and crystallised from light petroleum as rectangular tablets, m. p. 59° (0·19 g.). These gave no colour with alcoholic ferric chloride and dissolved in concentrated sulphuric acid to a yellow solution becoming green when warmed (Found : C, 69·2; H, 5·5; OMe, 15·6. $C_{11}H_{10}O_3$ requires C, 69·5; H, 5·3; OMe, 16·3%). It gave a 2 : 4-dinitrophenylhydrazone crystallising from alcohol as stout needles and rectangular rods, m. p. 221°.

When the fission was carried out by boiling for 8 hr., the yield of the component (karanjic acid) insoluble in hot water was greater.

*Methylation of the Acid Fraction* (*B*).—The acid fraction (B) (0·1 g.) was heated in a small volume of dry acetone with excess of methyl iodide (0·2 c.c.) and anhydrous potassium carbonate (0·2 g.) under reflux for 45 hr. The solution was filtered and, after removal of the acetone, water was added and the mixture extracted with ether. The extract was evaporated and the residue boiled with 25% aqueous sodium hydroxide (2 c.c.) until clear. After acidification with hydrochloric acid, the precipitate was crystallised from hot water, giving *O*-methylkaranjic acid as colourless rectangular plates, m. p. 148° (no colour with alcoholic ferric chloride; $R_F$ 0·56).

*Fission with Absolute Methanolic Potassium Hydroxide.*—Pongamol (0·2 g.) was heated with methyl-alcoholic potassium hydroxide (0·4 g. in 6 c.c.) under reflux for about 8 hr. As much of the alcohol as possible was then distilled off and the residue treated with water. After cooling in ice, the solid product (II) was filtered off. On crystallisation from light petroleum it had m. p. and mixed m. p. 59° (yield 85 mg.). When the aqueous alkaline solution was acidified with hydrochloric acid only a small precipitate was obtained, giving a positive ferric reaction. It was filtered off and the solution extracted with ether, which yielded benzoic acid.

*Oxidation of the Ketone* (II) *to* O-*Methylkaranjic Acid.*—A solution of the ketone (0·15 g.) and iodine (0·2 g.) in pyridine (1 c.c.) was heated on a water-bath for 1 hr.; a crystalline product separated. The mixture was kept in the refrigerator before the solid was filtered off. The solid was heated on a water-bath with 2% aqueous potassium hydroxide (8 c.c.) for 45 min., then the whole was cooled and acidified with hydrochloric acid. The precipitate was dissolved in aqueous sodium hydrogen carbonate and reprecipitated with acid; it then crystallised from hot water as rectangular plates, m. p. 148° alone or mixed with *O*-methylkaranjic acid, m. p. 148°; it gave no ferric reaction.

*Synthesis of* 5-*Acetyl*-4-*methoxycoumarone* (II).—*O*-Methylkaranjic acid (Seshadri and Venkateswarlu, *Proc. Indian Acad. Sci.*, 1941, **13**, *A*, 407) (1 g., 1 mol.) and thionyl chloride (5 c.c.) were refluxed on a water-bath for 1 hr. Excess of chloride was removed under reduced pressure. The residue was treated with dry carbon tetrachloride and again distilled to remove the last traces of thionyl chloride. A viscid mass remained. Ethyl acetoacetate (0·8 g., 1·2 mols.) was added to finely granulated sodium (0·25 g., 2·2 mols.) in anhydrous ether (10 c.c.) and shaken. After about 1 hr. the acid chloride was added in dry ether (15 c.c.). The mixture was kept overnight, then boiled for 4 hr. It was treated first with ether and then with water. The ethereal layer, on evaporation, gave a liquid product which was mixed with water (8 c.c.); 10% aqueous potassium hydroxide (9 c.c.) was then added gradually during 2 hr. The clear mixture was gently boiled for 2 hr., cooled, and extracted with ether; the ethereal extract yielded the benzofuran as rectangular plates and tablets (from light petroleum), m. p. and mixed m. p. 60° (Found: C, 69·1; H, 5·3%) giving a 2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 221°.

*Demethylation of Pongamol* [*Furano*(2′ : 3′-7 : 8)*flavone* (V)].—Pongamol (0·5 g.) was dissolved in acetic anhydride (8 c.c.) and cooled in ice, and hydriodic acid (*d* 1·7; 8 c.c.) was added carefully. The mixture was heated for 40 min. at 115° and poured into aqueous sodium hydrogen sulphite. The brown solid product was crystallised twice from aqueous alcohol, forming woolly needles (0·31 g.), m. p. 146° (sinters at 115°; dehydration). *Furano*(2′ : 3′-7 : 8)*flavone* gave no colour with ferric chloride and did not dissolve in aqueous sodium hydroxide. It dissolved in concentrated sulphuric acid giving a yellow solution which became deep blue when warmed (Found, in a sample dried at 110° for 4 hr. : C, 77·5; H, 3·9. $C_{17}H_{10}O_3$ requires C, 77·8; H, 3·8%). An alcoholic solution gave an orange colour with magnesium and hydrochloric acid.

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