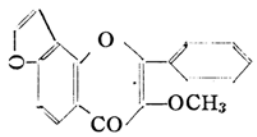
Synthetic Studies on the Benzofuran Derivatives. Part I. A New Synthesis of Karanjin

By Yoshiyuki KAWASE, Takashi MATSUMOTO and Kenji FUKUI

(Received February 4, 1955)

Karanjin, a kind of flavonol, was isolated in colorless needle crystals, $C_{18}H_{12}O_4$, m.p. 158.5°C as an unsaponifiable matter from the seed oil of a leguminous plant *Pongamia glabra Vent.* karanjia by Limaye[1] and by Beal and Katti[2].

The chemical structure of this substance was studied by Limaye[3] and Manjunath, Seetharamiah and Siddappa[4], and was proved to have a constitutional formula (I). The



(I)

total synthesis of this karanjin (I) was reported by Seshadri and Venkateswarlu[5] and Row and Seshadri[6], but the yields were not so good. We also have been studying the synthesis of this substance independently and have obtained karanjin more easily and in higher yield.

Starting from 7-hydroxy-3-methoxyflavone-

1) D.B. Limaye, *Proc. Indian Sci. Congr.*, **1925**, 118; **1926**, 151.
2) Beal and Katti, *J. Am. Pharm. Assoc.*, **14**, 1086 (1926).
3) D.B. Limaye, *Rasayanam*, I, 1 (1936); I, 119 (1937).
4) B.L. Manjunath, A. Seetharamiah and S. Siddappa, *Ber.*, **72B**, 93 (1939).
5) T.R. Seshadri and V. Venkateswarlu, *Proc. Indian Acad. Sci.*, **13A**, 404 (1941).
6) L.R. Row and T.R. Seshadri, ibid, **33**, 168 (1951).

8-aldehyde (II) as Seshadri[7] and Limaye[8] did, 3-methoxyflavone-7,8-furan-α-carboxylic acid (IV) was synthesised in a good yield by the method of Tanaka[9] for benzofuran synthesis;—that is, the aldehyde (II) and ethyl bromomalonate were made to react in acetone in the presence of potassium carbonate, and the condensation product was hydrolysed to the acid (IV), m.p. 283°C (decomp.), yield 88.2%. As the intermediate product of this reaction, the colorless needle crystals, m.p. 183°C, were obtained and were found to be identical with the ethyl ester (IIIa) of the above mentioned acid (IV); therefore, it is clear that the ethyl ester of furan-α-carboxylic acid was produced in this reaction as the intermediate product.

Then, this acid (IV) was decarboxylated in quinoline in a stream of nitrogen gas with copper powder into colorless needle crystals, m.p. 159°C, yield 26.5%, the melting point of which was not depressed by admixture with natural karanjin (I). Further, this synthetic karanjin was derived to 3-hydroxy and 3-acetoxy derivatives and was decomposed into benzoic acid, methoxymethylkaranjketone (VI) and karanjic acid (VII) by alkaline hydrolysis. The melting points of these substances (I, Va, Vb, VI and VII) coincided well with those of the natural products, as shown in the following Table.

We are grateful to the Institute of Organic Chemistry, Osaka City University for carrying out microanalyses and to Prof. T. R. Seshadri for giving us the sample of natural Karanjin.

Experimental[10]

7-Hydroxy-3-methoxyflavone-8-aldehyde (II).—This aldehyde (II) was prepared from 7-hydroxy-3-methoxyflavone by the methods of Seshadri[7] and Limaye[8].

3-Methoxyflavone-7,8-furan-α-carboxylic acid (IV).—A Mixture of 7.5 g. of 7-hydroxy-3-methoxyflavone-8-aldehyde (II), 8 g. of ethyl bromomalonate, 30 g. of anhydrous potassium carbonate in 620 cc. of absolute acetone was refluxed under stirring for 10.5 hours on a steambath. After distilling off the acetone, the residue was mixed with a solution of 5 g. of potassium hydroxide in 50 cc. of water and heated on a steambath for one hour, then diluted with water, decolorised, filtered and acidified with dilute sulfuric acid. The precipitate was collected and dissolved in sodium bicarbonate solution, followed by filtering and acidifying with dilute sulfuric acid. The precipitates were collected, washed with water and recrystallised from alcohol in colorless plates of

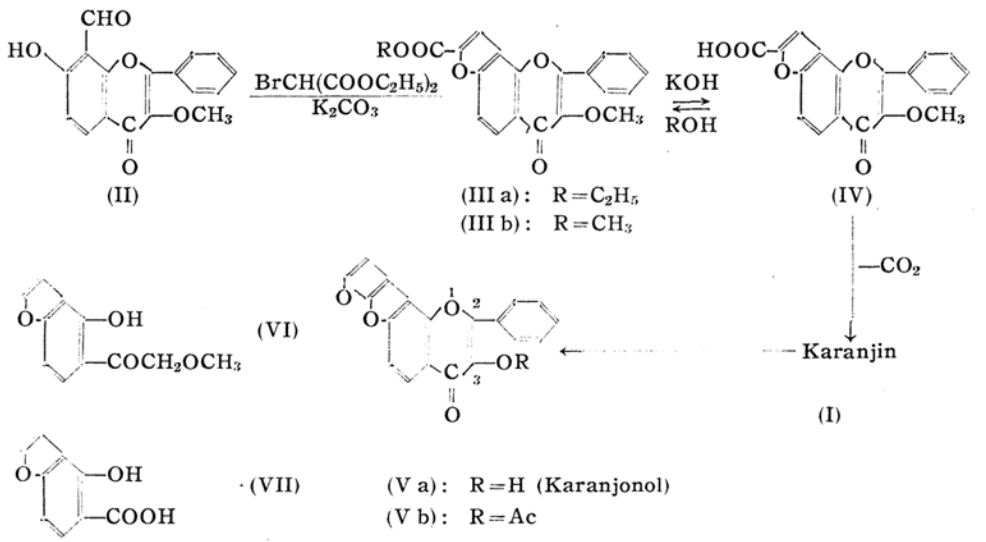


TABLE
THE MELTING POINTS OF KARANJIN AND ITS DERIVATIVES (°C)

Products	Karanjin (I)	3-OH (Va)	3-OAc (Vb)	Alkaline dec. prod. (VI)	Alkaline dec. prod. (VII)
Natural products[4]	158.5	199–200	177	96	218 (dec.)
Synthetic products	159	200	177	95.5	215–6 (dec.)

7) S. Rangaswami and T.R. Seshadri, *Proc. Indian Acad. Sci.*, 9A, 7, 259 (1939).
8) S.D. Limaye and Limaye, *Rasayanam*, I, 161 (1939).
9) S. Tanaka, *J. Am. Chem. Soc.*, 73, 872 (1951).
10) All melting points were not corrected.

m.p. 283°C (decomp.); yield 7.5 g. (88.2%). Found: C, 67.40; H, 3.83. Calculated for $C_{19}H_{12}O_6$: C, 67.86; H, 3.57%.

Esters (IIIa, IIIb) of the Acid (IV) and the Intermediate Substance of the above Reaction.—This acid (IV) was esterified with methanol or ethanol and sulfuric acid by the usual method. These esters were recrystallised from methanol or ethanol in colorless needles. *Methyl ester*, m.p. 194.5°C (IIIb). Found: C, 68.58; H, 3.96. Calculated for $C_{20}H_{14}O_6$: C, 68.57; H, 4.00%. *Ethyl ester*, m.p. 182°C (IIIa). Found: C, 69.38; H, 4.53. Calculated for $C_{21}H_{16}O_6$: C, 69.23; H, 4.39%.

A part of the residue after distilling off the acetone in the above procedure was recrystallised from alcohol in colorless needles, m.p. 183°C. Found: C, 69.22; H, 4.53. Calculated for $C_{21}H_{16}O_6$: C, 69.23; H, 4.39%. The melting point of this intermediate substance was not depressed by admixture with the ethyl ester (IIIa), m.p. 182°C.

Karanjin (I).—A mixture of 10 g. of 3-methoxyflavone-7,8-furan-α-carboxylic acid (IV), 4 g. of copper powder in 140 cc. of quinoline was heated under stirring in an atomosphere of nitrogen gas for about 40 minutes at 180–190°C until evolution of carbon dioxide ceased. It seems to be important that attention be paid to duration of time and temperature in this decarboxylation. After cooling, a little alcohol was added and the mixture was filtered from copper and was acidified with dilute hydrochloric acid. The brown precipitates thus formed were collected. The mother liquid was made alkaline with sodium hydroxyde and quinoline was distilled off by means of steam distillation. The residue was acidified after cooling and crude precipitates were collected. The crude karanjin thus obtained was recrystallised three times from ethyl acetate with the aid of charcoal in colorless needles, m.p. 159°C; yield 2.3 g. (26.5%). The melting point of this substance was not depressed by admixture with the natural karanjin. Found: C, 74.01; H, 4.04. Calculated for $C_{18}H_{12}O_4$: C, 73.97; H, 4.11%.

3-Hydroxyflavone-7,8-furan (Va) and 3-acetoxyflavone-7,8-furan (Vb).—These compounds (Va and Vb) were prepared according to the directions of Seshadri et al.[11].

A mixture of karanjin and anhydrous aluminium chloride in nitrobenzene was heated for one hour. After the product was worked up in the usual manner, the substance was recrystallised from dilute alcohol in colorless crystals, m.p. 200°C, which gave violet reaction with ferric chloride. This compound (Va) was acetylated to the 3-acetoxy derivate (Vb), m.p. 177°C with acetic anhydride in pyridine.

Alkaline Decomposition of Synthetic Karanjin.—According to the directions of Manjunath et al.,[4] a mixture of 1 g. of synthetic karanjin in alcohol and saturated methanolic potash was refluxed four hours. After distilling off the solvent, the residual solution was acidified and extracted with ether. The ethereal solution was first extracted with aqueous sodium bicarbonate solution and then with aqueous potassium hydroxide solution. Benzoic acid (0.2 g.) m.p. 121°C, and karanjic acid (0.02 g.) (VII), m.p. 215–6°C (decomp.) were obtained from bicarbonate solution; and methoxymethylkaranjketone (0.35 g.) (VI), m.p. 95.5°C, was obtained from potassium hydroxide solution.

Summary

Starting from 7-hydroxy-3-methoxyflavone-8-aldehyde (II), 3-methoxyflavone-7,8-furan-α-carboxylic acid (IV) was synthesised in good yield by the method of Tanaka for benzofuran synthesis and was decarboxylated in quinoline with copper powder into karanjin (I).

Faculty of Liberal Arts and Science, Toyama University, Toyama

11) T. R. Seshadri and V. Venkateswarlu, *Proc. Indian Acad. Sci.*, 17A, 16 (1943).