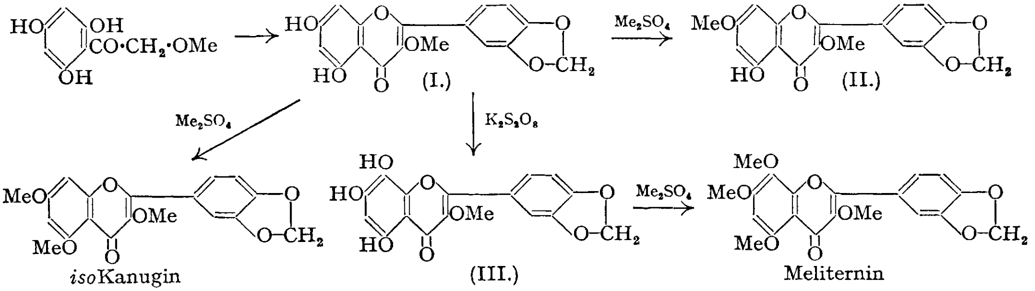
460. *Flavonols from the Bark of* Melicope ternata. *Part II. A Synthesis of Meliternin,* iso*Kanugin, and Allied Flavonols.*

By Lindsay H. Briggs and R. H. Locker.

Meliternin, *iso*kanugin, 5 : 8-*dihydroxy*-3-*methoxy*-3′ : 4′-*methylenedioxyflavone*, 5-*hydroxy*-3 : 8-*dimethoxy*-3′ : 4′-*methylenedioxyflavone*, and 5 : 7 : 8-*trihydroxy*-3-*methoxy*-3′ : 4′-*methylenedioxyflavone* have been synthesised by standard methods.

Using Allan and Robinson's flavonol synthesis (*J.*, 1924, 2192) and Rao and Seshadri's method of nuclear oxidation (*Proc. Indian Acad. Sci.*, 1947, **26**, 182 and earlier papers), meliternin (3 : 5 : 7 : 8-tetramethoxy-3′ : 4′-methylenedioxyflavone), *iso*kanugin (3 : 5 : 7-trimethoxy-3′ : 4′-methylenedioxyflavone), 5 : 7-*dihydroxy*-3-*methoxy*-3′ : 4′-*methylenedioxyflavone*, 5-*hydroxy*-3 : 7-

dimethoxy-3′ : 4′-*methylenedioxyflavone* and 5 : 7 : 8-*trihydroxy*-3-*methoxy*-3′ : 4′-*methylenedioxyflavone* have been synthesised according to the annexed scheme.



Condensation of 2 : 4 : 6-trihydroxy-ω-methoxyacetophenone with piperonylic anhydride in the presence of potassium piperonylate at 170—180° in a vacuum afforded 5 : 8-dihydroxy-3-methoxy-3′ : 4′-methylenedioxyflavone (I), converted by partial methylation into 5-hydroxy-3 : 8-dimethoxy-3′ : 4′-methylenedioxyflavone (II) and by complete methylation into *iso*kanugin (3 : 5 : 8-trimethoxy-3′ : 4′-methylenedioxyflavone) whose identity with the natural product was confirmed by mixed melting point.

Nuclear oxidation of (I) with potassium persulphate introduced a phenolic group at $C_{(8)}$ forming 5 : 7 : 8-trihydroxy-3-methoxy-3′ : 4′-methylenedioxyflavone (III) which, on complete methylation, produced 3 : 5 : 7 : 8-tetramethoxy-3′ : 4′-methylenedioxyflavone, identical in all respects with meliternin, the structure of which, suggested in Part I (preceding paper), is thus confirmed.

EXPERIMENTAL.

(M. p.s are corrected.)

5 : 7-*Dihydroxy*-3-*methoxy*-3′ : 4′-*methylenedioxyflavone*.—2 : 4 : 6-Trihydroxy-ω-methoxyacetophenone (5 g.; Slater and Stephen, *J.*, 1920, 312), piperonylic anhydride (20 g.; Rao and Seshadri, *Proc. Ind. Acad. Sci.*, 1946, **23**, 148), and potassium piperonylate (8·5 g.) were ground together and heated at 170—180°/25 mm. for 2 hours. The purple reaction mass was ground and boiled with 10% aqueous alcoholic (1 : 10) potassium hydroxide (300 c.c.) for 15 minutes. The pasty mass of yellow crystals, formed after removal of the solvent in a vacuum, was dissolved in water (500 c.c.), and carbon dioxide bubbled into the solution until it was acid to phenolphthalein. The precipitated solid (4·9 g.), after repeated crystallisation from acetone, formed yellow needles, m. p. 273·5—274·5°, of 5 : 7-*dihydroxy*-3-*methoxy*-3′ : 4′-*methylenedioxyflavone* (Found : C, 61·8; H, 4·0; OMe, 8·6. $C_{17}H_{12}O_7$ requires C, 62·2; H, 3·6; 1OMe, 9·45%). It dissolves in sodium hydroxide, but not in carbonate, solution with a yellow colour. Reduction with magnesium and hydrochloric acid as well as with sodium amalgam followed by acidification gave a strong scarlet colour. Its bright-yellow solution in concentrated sulphuric acid rapidly became green on addition of gallic acid. It gave a stable pale yellow colour in a buffer at pH 9·8, and a brown colour with ferric chloride solution.

The *diacetate*, formed by acetylating the flavone (20 mg.) with excess of acetic anhydride and 60% perchloric acid (1 drop) for ½ hour and pouring the mixture into water, crystallised from methyl alcohol in slender, colourless needles, m. p. 188·5° (14 mg.) (Found : C, 61·4; H, 3·9. $C_{21}H_{16}O_9$ requires C, 61·2; H, 3·9%).

5-*Hydroxy*-3 : 7-*dimethoxy*-3′ : 4′-*methylenedioxyflavone*.—5 : 7-Dihydroxy-3-methoxy-3′ : 4′-methylenedioxyflavone (800 mg.), dissolved in acetone (50 c.c.), was heated under reflux with methyl sulphate (0·27 c.c.) and anhydrous potassium carbonate (3·0 g.) for 6 hours. The solution was filtered, concentrated until crystallisation set in, and allowed to cool. The yellow needles produced (610 mg.), after repeated crystallisation from alcohol, had m. p. 183·5° (Found : C, 63·5; H, 4·55. $C_{18}H_{14}O_7$ requires C, 63·2; H, 4·1%). The partly methylated flavone is insoluble in concentrated hydrochloric acid and in both sodium carbonate and hydroxide (10%) solutions. It gives a brown colour with ferric chloride solution and a scarlet colour on acid and alkaline reduction.

One drop of perchloric acid (60%) was added to a mixture of the flavone (26 mg.) in acetic anhydride (0·5 c.c.). A red colour was produced but complete dissolution did not occur even on the addition of a further c.c. of acetic anhydride. The yellow insoluble plates formed after ½ hour were probably the perchlorate of the acetylated flavone. After the mixture had been poured into water to decompose the perchlorate, the *acetate*, repeatedly crystallised from alcohol, formed slender, colourless needles, m. p. 192—193° (Found : C, 62·7; H, 4·5. $C_{20}H_{16}O_8$ requires C, 62·5; H, 4·2%).

iso*Kanugin*.—5 : 7-Dihydroxy-3-methoxy-3′ : 4′-methylenedioxyflavone (100 mg.), dissolved in acetone (15 c.c.), was heated under reflux with methyl sulphate (0·4 c.c.) and anhydrous potassium carbonate (1 g.) for 6 hours. The solution was filtered, concentrated until crystallisation set in, and cooled. The product, *iso*kanugin (70 mg.), crystallised from alcohol in long, colourless, rectangular plates, m. p. 198—199°, undepressed by an authentic specimen kindly provided by Professor T. R. Seshadri. *iso*Kanugin is soluble in concentrated hydrochloric acid with an intense yellow colour.

5 : 7 : 8-*Trihydroxy*-3-*methoxy*-3′ : 4′-*methylenedioxyflavone*.—To a solution of 5 : 7-dihydroxy-3-methoxy-3′ : 4′-methylenedioxyflavone (1·5 g.) in sodium hydroxide (1·5 g.) and water (50 c.c.) was

added dropwise during 2 hours and with mechanical stirring a solution of potassium persulphate (2·5 g., 2 mols.) in water (50 c.c.). After the mixture had been kept overnight, the brown gelatinous precipitate was collected, shaken with dilute hydrochloric acid, and heated on the water-bath for ½ hour with a little sodium sulphite solution. On cooling, the chrome-yellow solid (683 mg.) was repeatedly crystallised from alcohol (charcoal), aqueous acetone, and again from alcohol, forming deep-yellow needles, m. p. 259°, of 5 : 7 : 8-*trihydroxy*-3-*methoxy*-3′ : 4′-*methylenedioxyflavone* (Found : C, 59·7; H, 3·8; OMe, 7·1. $C_{17}H_{12}O_8$ requires C, 59·3; H, 3·5; 1OMe, 9·0%). It is slightly soluble in sodium hydrogen carbonate, and readily soluble in sodium carbonate, solution with a bright yellow colour. The solution in 10% sodium hydroxide solution is violet-red in colour. When it was reduced with magnesium and hydrochloric acid in alcohol a wine-red colour was produced. Reduction with sodium amalgam in alcohol caused rapid decolorisation in dilute solution but in more concentrated solution copious green flocks formed, becoming yellow on warming, a colour unchanged on acidification. A solution in a buffer at pH 9·8 passed from yellow through brown to colourless. Ferric chloride gave a brown, whilst the methylenedioxy-test with gallic acid rapidly produced a green, colour.

The *triacetate*, produced as in the first case from 15 mg., crystallised from alcohol in slender, colourless needles, m. p. 213—213·5° (12·5 mg.) (Found : C, 58·8; H, 4·3. $C_{23}H_{18}O_{11}$ requires C, 58·7; H, 3·9%).

Meliternin.—A solution of 5 : 7 : 8-trihydroxy-3-methoxy-3′ : 4′-methylenedioxyflavone (90 mg.) in acetone (5 c.c.) was heated under reflux with methyl sulphate (0·15 c.c.) and anhydrous potassium carbonate (1·5 g.) for 5 hours. The acetone solution was filtered, concentrated to *ca.* 1 c.c., and cooled. Recrystallisation from alcohol of the prisms which formed (34 mg.) afforded almost colourless prisms, m. p. 184·5—185·5°, undepressed by a sample of natural meliternin.

Absorption Spectra.—The absorption spectra of the five synthetic flavonols and 5-hydroxy-3 : 7′ : 3′ : 4′-tetramethoxyflavone for comparison were measured in *ca.* N/20,000 alcoholic solution in a Beckman spectrophotometer, model DU, peaks being obtained as shown in the table. The absorption peaks of synthetic meliternin correspond with those of the natural product (Part I, *loc. cit.*).

Compound.	λ.	log ε.	λ.	log ε.	λ.	log ε.
5 : 7-Dihydroxy-3-methoxy-3′ : 4′-methylenedioxyflavone	250 *	4·23	262 *	4·15	335	4·32
5-Hydroxy-3 : 7-dimethoxy-3′ : 4′-methylenedioxyflavone	254	4·31	269 *	4·21	353	4·28
5 : 7 : 8-Trihydroxy-3-methoxy-3′ : 4′-methylenedioxyflavone	231	4·34	285	4·31	325	4·23
*iso*Kanugin	250	4·35	263 *	4·21	340	4·32
Meliternin (synthetic)	254	—	272	—	353	—
5-Hydroxy-3 : 7 : 3′ : 4′-tetramethoxyflavone	254	4·37	269	4·29	352	4·34

* Points of inflexion.

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AUCKLAND UNIVERSITY COLLEGE, AUCKLAND, NEW ZEALAND. [*Received, April* 13*th*, 1949.]