# A SYNTHESIS OF MELIBENTIN

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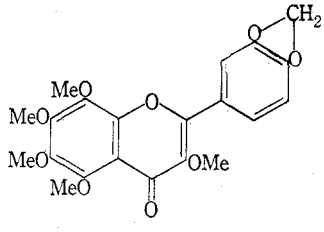
*Summary*

Melibentin (I), a new, fully alkylated flavone from *Melicope broadbentiana* Bail., has been synthesized from meliternatin (II).

## Introduction

In a forthcoming communication to this Journal the isolation of a new, fully alkylated flavone, melibentin, from *Melicope broadbentiana* Bail. and evidence leading to its structure (I) will be described by Stephanie T. K. Vautin, E. Ritchie, and W. C. Taylor. We are indebted to Dr. Ritchie for this information prior to publication and the opportunity of attempting its synthesis with our other work in this field.




(I)

## Synthesis of Melibentin

Meliternatin, a fully alkylated flavone from *M. ternata* J. R. & G. Forst., which has been shown to have the structure (II) by degradation[1,2] and synthesis,[3] has been used as the starting material for the synthesis of melibentin (I).

It has already been reported[2] that meliternatin reacts with sodium methoxide to give 6-hydroxy-3,5,7-trimethoxy-3′,4′-methylenedioxyflavone (III). Methylation of (III) with dimethyl sulphate and potassium carbonate afforded melisimplexin (IV)[4] which has already been synthesized[5] and converted by selective demethylation to

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[1] Briggs, L. H., and Locker, R. H., *J. Chem. Soc.*, 1949, 2157.

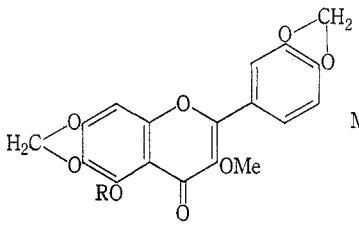
[2] Briggs, L. H., and Locker, R. H., *J. Chem. Soc.*, 1951, 3131.

[3] Anderson, B. F., Briggs, L. H., Cebalo, T., and Trotman, Margaret A., *J. Chem. Soc.* (in press).

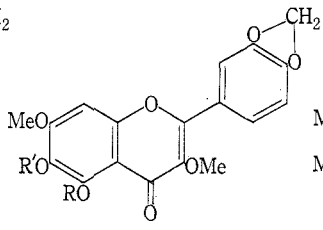
[4] Briggs, L. H., and Locker, R. H., *J. Chem. Soc.*, 1950, 2376.

[5] Briggs, L. H., and Locker, R. H., *J. Chem. Soc.*, 1950, 2379.

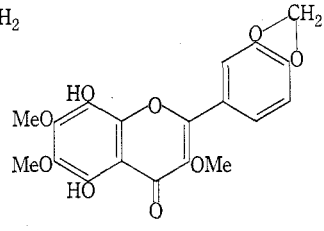
melisimplin (V).[5] Persulphate oxidation of melisimplin gave 5,8-dihydroxy-3,6,7-trimethoxy-3′,4′-methylenedioxyflavone (VI), converted by complete methylation into 3,5,6,7,8-pentamethoxy-3′,4′-methylenedioxyflavone (I), identical with melibentin.



(II) R = Me
(VIII) R = H



(III) R = Me; R′ = H
(IV) R = R′ = Me
(V) R = H; R′ = Me
(VII) R = R′ = H



(VI)

Rao and Seshadri have reported[6] that the reaction of aluminium chloride on 3,5-dimethoxyflavones in nitrobenzene leads to dealkylation in both positions. By the use of one mole of aluminium chloride, however, dealkylation occurs in the 5 position. By this method flavone (III) was converted into 5,6-dihydroxy-3,7-dimethoxy-3′,4′-methylenedioxyflavone (VII) which underwent partial methylation to give melisimplin (V). Similar dealkylation of meliternatin led to 5-hydroxy-3-methoxy-6,7 : 3′,4′-dimethylenedioxyflavone (VIII), previously obtained from meliternatin by the action of aluminium chloride in ethereal solution.[2] Unlike meliternatin, flavone (VIII) was unreactive towards sodium methoxide.

## Experimental

Analyses were by Dr. A. D. Campbell and associates, University of Otago, New Zealand. Infrared spectra were measured in KBr disks with an Infracord instrument.

(*a*) *6-Hydroxy-3,5,7-trimethoxy-3′,4′-methylenedioxyflavone* (*III*).—The following procedure gives an improved yield over that previously reported.[2] Meliternatin* (1·6 g) was refluxed with sodium methoxide (24 g sodium in 560 ml absolute methanol) for 9 hr, and the mixture acidified after standing overnight. After concentration almost to dryness it was extracted with boiling dilute alkali. The solid obtained on bubbling $CO_2$ through the combined basic extracts crystallized from ethanol in hexagonal plates (1·33 g), m.p. and mixed m.p. with 6-hydroxy-3,5,7-trimethoxy-3′,4′-methylenedioxyflavone,[2] 241–243°. The infrared spectra were also identical: $\nu_{max.}$ 3175 (OH), 1634 $cm^{-1}$ (CO).

(*b*) *3,5,6,7-Tetramethoxy-3′,4′-methylenedioxyflavone* (*Melisimplexin*) (*IV*).—A mixture of flavone (III) (1·36 g), dimethyl sulphate (1·7 ml), and $K_2CO_3$ (5·5 g) in dry acetone (60 ml) was refluxed for 6 hr, the acetone distilled off, and water added to the residue. The insoluble material was filtered off and crystallized from acetone to give 3,5,6,7-tetramethoxy-3′,4′-methylenedioxyflavone (1·25 g) as needles, m.p. and mixed m.p. with melisimplexin[4] 183–185°. The infrared spectra were also identical: $\nu_{max.}$ 1613 $cm^{-1}$ (CO).

(*c*) *5-Hydroxy-3,6,7-trimethoxy-3′,4′-methylenedioxyflavone* (*Melisimplin*) (*V*).— A solution of anhydrous aluminium chloride (495 mg) in nitrobenzene (3 ml) was added to a solution of

* We gratefully acknowledge a generous gift of meliternatin from Dr. E. Ritchie.

[6] Rao, K. V., and Seshadri, T. R., *J. Chem. Soc.*, 1946, 771.

melisimplexin (1·2 g) in nitrobenzene (9·6 ml) and the reaction mixture maintained at 105° for 1 hr. The cooled reaction mixture was poured into dilute HCl and steam-distilled to remove the excess nitrobenzene. Crystallization of the product from acetone gave 5-hydroxy-3,6,7-trimethoxy-3′,4′-methylenedioxyflavone (916 mg) as yellow needles, m.p. and mixed m.p. with melisimplin,[4] 232–234°. The infrared spectra were also identical: $\nu_{max.}$ 1667 $cm^{-1}$ (CO).

(*d*) *5,8-Dihydroxy-3,6,7-trimethoxy-3′,4′-methylenedioxyflavone* (*VI*).—A solution of potassium persulphate (900 mg) in water (20 ml) was added dropwise, with stirring, to a solution of melisimplin (900 mg), dimethylformamide (30 ml), pyridine (30 ml), and tetramethylammonium hydroxide (2·5 g) in water (50 ml) at room temperature over 35 min. The reaction mixture remained a yellow colour. Unchanged melisimplin (600 mg; m.p. 234–235°), which separated overnight, was filtered and the residue extracted with ether, after acidification to Congo red. Concentrated HCl (25 ml) and sodium sulphite (3·6 g) were added to the material insoluble in ether and the mixture heated on a steam-bath for 45 min. The yellow needles (65 mg; m.p. 215–217°), which separated from the cooled reaction mixture, crystallized from ethanol to give *5,8-dihydroxy-3,6,7-trimethoxy-3′,4′-methylenedioxyflavone* as needles, m.p. 218–219·5° (Found: C, 59·5; H, 4·0%. Calc. for $C_{19}H_{16}O_9$: C, 58·8; H, 4·15%). Light absorption: $\lambda_{max.}$ 257, 288, 342 mμ ($\log \epsilon$ 4·07, 4·17, 4·12); $\nu_{max.}$ 3311 (OH), 1664 $cm^{-1}$ (CO).

(*e*) *3,5,6,7,8-Pentamethoxy-3′,4′-methylenedioxyflavone* (*Melibentin*) (*I*).—A mixture of flavone (VI) (28 mg), dimethyl sulphate (30 mg), and anhydrous $K_2CO_3$ (300 mg) was refluxed in anhydrous acetone for 22 hr, the acetone distilled off, and water (25 ml) added to the residue. The insoluble material (17 mg; m.p. 125–127°) crystallized from aqueous ethanol to give 3,5,6,7,8-pentamethoxy-3′,4′-methylenedioxyflavone as rhombs, m.p. and mixed m.p. with melibentin, 127–129·5°. The infrared spectra were also identical: $\nu_{max.}$ 1639 $cm^{-1}$ (CO).

(*f*) *5,6-Dihydroxy-3,7-dimethoxy-3′,4′-methylenedioxyflavone* (*VII*).—A solution of anhydrous aluminium chloride (123 mg) in nitrobenzene (2 ml) was added to a solution of flavone (III) (300 mg) in nitrobenzene (6 ml) and the reaction mixture maintained at 105° for 1 hr. The cooled reaction mixture was poured into dilute HCl (108 ml) and the nitrobenzene removed by steam distillation. The solid product crystallized from aqueous ethanol to give *5,6-dihydroxy-3,7-dimethoxy-3′,4′-methylenedioxyflavone* (232 mg) as yellow needles, m.p. 174–176° (Found: C, 60·35; H, 3·9%. Calc. for $C_{18}H_{14}O_8$: C, 60·3; H, 3·9%).

A mixture of flavone (VII) (36 mg), dimethyl sulphate (13 mg), and $K_2CO_3$ (300 mg) was refluxed in anhydrous acetone for 4 hr, the acetone distilled off, and water (20 ml) added to the residue. The material insoluble in water crystallized from ethyl acetate in needles to give melisimplin,[4] m.p. and mixed m.p. 232–234°.

## Acknowledgments

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