COLOURING MATTER OF TAMBUL SEEDS

Part IV. Synthesis of Tambuletin

By K. J. Balakrishna and T. R. Seshadri, F.A.Sc.

(From the Department of Chemistry, Andhra University, Waltair)

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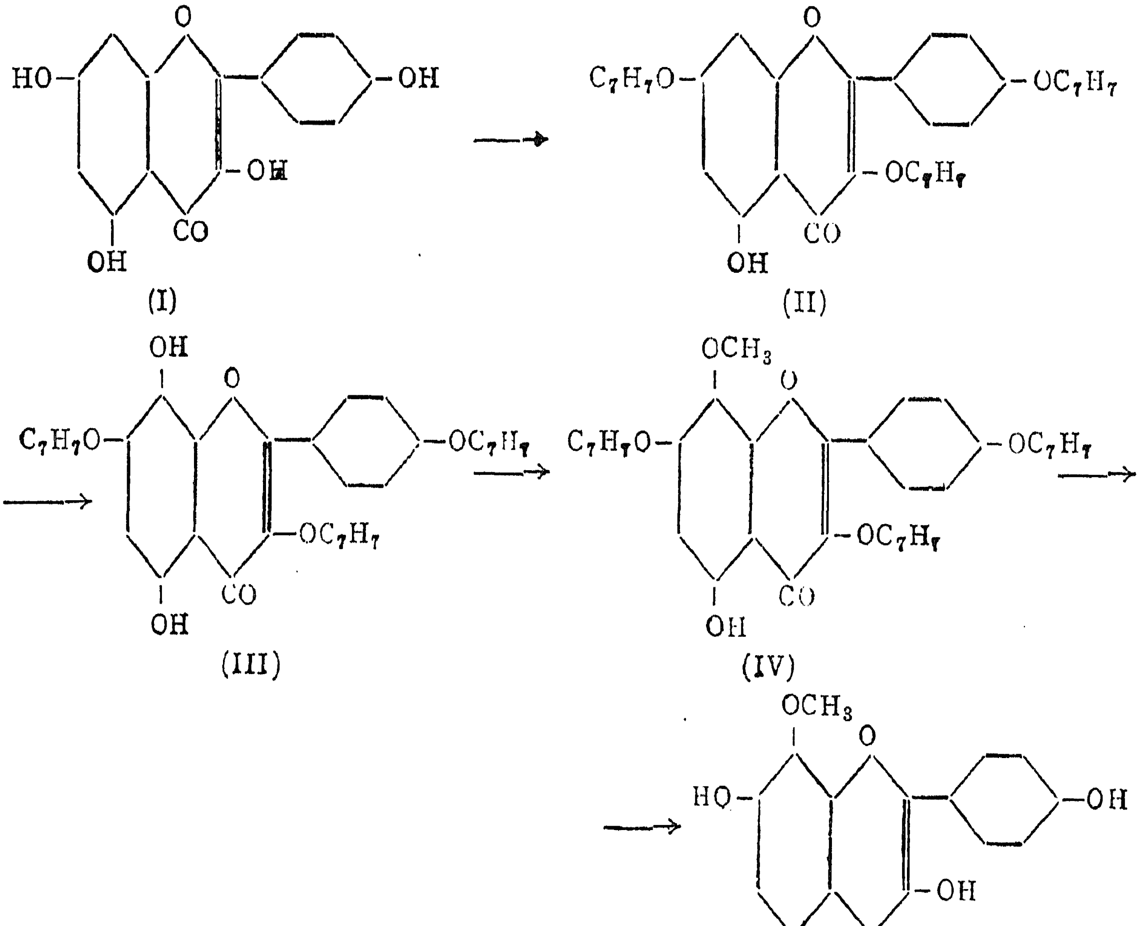
From a consideration of the properties and reactions of tambuletin, it was given the constitution of the 8-methyl-ether of herbacetin.[1] This constitution was subsequently confirmed[2] by the preparation of its tri- and tetraethyl ethers and by their identity with 3:7:4′-triethoxy-8-methoxy-5-hydroxy flavone and 3:5:7:4′-tetraethoxy-8-methoxy flavone respectively. The synthesis of tambuletin itself has now been achieved and is reported in this paper.

The synthetic preparation of tambuletin follows on lines similar to the synthesis of wogonin[3] from chrysin. Starting with kæmpferol (I) it is subjected to partial benzylation using three molecular proportions of benzyl



chloride. The product should be 3 : 7 : 4′-O-tribenzyl-ether (II) having the resistant 5-hydroxyl free. This constitution is supported by its properties since it gives a strong ferric chloride colour and is sparingly soluble in aqueous alkali. Its oxidation to the quinol (III) takes place with some difficulty owing to its sparing solubility in alkali even in the presence of pyridine and only poor yields are obtained. Partial methylation of this quinol yields the 8-methyl ether (IV) which gives the reactions for a free 5-hydroxyl. Final debenzylation takes place smoothly producing 8-methoxy-3 : 5 : 7 : 4′-tetrahydroxy-flavone (V) which is found to be identical in all respects with tambuletin isolated from tambul seeds.[1]

EXPERIMENTAL

5-*Hydroxy*-3 : 7 : 4′-*tribenzyloxy-flavone* (*II*)

Kæmpferol (I) (1·0 g.) was dissolved in dry acetone (50 c.c.) and anhydrous potassium carbonate (8·0 g.) and benzyl chloride (1·13 c.c., 3 mols.) were added. The mixture was refluxed for 20 hours. The potassium salts were filtered off and washed with hot acetone. The filtrate was concentrated on a water-bath as far as possible and the residue stirred up with water. A semi-solid separated out. It crystallised from a mixture of alcohol and acetone as pale yellow small prisms melting at 111–13° (Found: C, 78·0; H, 5·0; $C_{36}H_{28}O_6$ requires C, 77·7; H, 5·0%). It gave a green colour with alcoholic ferric chloride and was sparingly soluble in aqueous alkali.

5 : 8-*Dihydroxy*-3 : 7 : 4′-*tribenzyloxy-flavone* (*III*)

The 5-hydroxy compound (II) (1·7 g.) was dissolved in pyridine (50 c.c.) and an aqueous solution of sodium hydroxide (1·0 g. in 20 c.c. of water) was added. The mixture was stirred for 2 hours while an aqueous solution of potassium persulphate (2·0 g. in 40 c.c. of water) was added gradually drop by drop. The solution was kept aside overnight and acidified to congo red with hydrochloric acid. The unreacted compound was filtered off and the filtrate extracted twice with ether to remove the last traces of it. Sodium sulphite (3·0 g.) and concentrated hydrochloric acid (20 c.c.) were added to the aqueous solution which was then heated over a boiling water-bath for 30 minutes. After cooling the solution, the soild that had separated out was extracted with ether. Removal of ether by distillation left a bright yellow substance. It crystallised from alcohol in the form of bright yellow narrow rectangular plates and flat needles melting at 165–66° (Found: C, 75·3; H, 5·0; $C_{36}H_{28}O_7$ requires C, 75·5; H, 4·9%). It gave a transient green colour changing to brown with alcoholic ferric chloride and was soluble in aqueous alkali producing a reddish-brown solution.

5-*Hydroxy*-8-*methoxy*-3 : 7 : 4′-*tribenzyloxy-flavone* (*IV*)

The 5 : 8-dihydroxy compound (III) (0·8 g.) was dissolved in dry acetone (25 c.c.) and anhydrous potassium carbonate (5·0 g.) and dimethyl sulphate (0·14 c.c., 1 mol.) were added. The mixture was refluxed for 6 hours. The potassium salts were filtered off and washed with hot acetone. The filtrate was concentrated over a water-bath to remove acetone. The solid that remained behind was stirred up with water and filtered. It crystallised from a mixture of alcohol and acetone as pale yellow prismatic needles melting at 113–15° (Found: C, 75·5; H, 5·0; $C_{37}H_{30}O_7$ requires C, 75·8; H, 5·1%). It gave a green colour with alcoholic ferric chloride and was sparingly soluble in aqueous alkali.

8-*Methoxy*-5 : 7 : 3 : 4′-*tetrahydroxy-flavone* (*V*) (*Tambuletin*)

The above 5-hydroxy compound (0·5 g.) was treated with a mixture of glacial acetic acid (5·0 c.c.) and concentrated hydrochloric acid (2·5 c.c.) and the mixture was heated at 100° over a water-bath for one hour. The solution was cooled and diluted with water. A bright yellow solid separated out. It was filtered and crystallised from glacial acetic acid whereby it was obtained as bright yellow short needles melting at 269–70°. It gave a dull green colour with alcoholic ferric chloride and was readily soluble in aqueous alkali to give a bright yellow solution. It gave an orange-red precipitate with neutral lead acetate in alcohol. The mixed melting point with a sample of tambuletin isolated from the seeds of *Zanthoxylum acanthopodium* was not depressed (Found: C, 60·3; H, 4·0; $C_{16}H_{12}O_7$ requires C, 60·7; H, 3·8%).

SUMMARY

The synthesis of tambuletin has been effected. Kæmpferol is first benzylated to the tribenzyl-ether which is subjected to oxidation with alkaline persulphate, partial methylation and debenzylation in succession.

REFERENCES

1. Balakrishna and Seshadri .. *Proc. Ind. Acad. Sci.*, A, 1947, **25**, 449.
2. ———— .. *Ibid.*, 1947, **26**, 72.
3. Rao, Rao and Seshadri .. *Ibid.*, 1947, **26**, 13.

ERRATUM

In Part III, A, 1947, **26**, 216 *read* (VIII), *for* (XIII) at the bottom of the page.