COLOURING MATTER OF TAMBUL SEEDS

Part II. Constitution of Tambuletin: Synthesis of O-Tetraethyl Tambuletin

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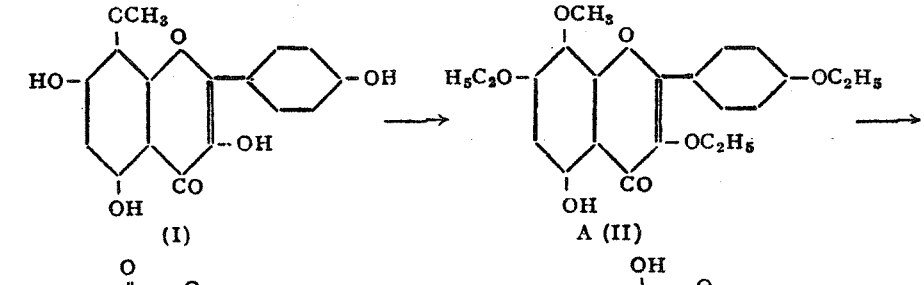
Received May 12, 1947

IN Part I[1] were described the isolation and properties of tambuletin. It was shown to be a monomethyl ether giving herbacetin on demethylation and its pentamethyl ether on methylation. From an examination of its reactions with dilute alkali, ferric chloride and *p*-benzoquinone the methoxyl group was considered to be in the 8-position. This constitution of tambuletin (I) as 8-O-methyl herbacetin has now been confirmed by the experiments described in this paper.

By the use of a restricted quantity of ethyl iodide tambuletin undergoes ethylation to form a triethyl ether (A) which exhibits the reactions for a free hydroxyl in the 5-position. This compound is oxidised readily with nitric acid yielding a quinone,[2] reduction of which yields a quinol which is found to be identical with a synthetic sample of 3:7:4′-triethoxy-5:8-dihydroxy flavone (III). It should therefore be concluded that the oxidation of O-triethyl tambuletin involves demethylation and this could happen only if the methoxyl group in tambuletin were in the 8-position. The transformations involved could be represented as below. The partial ethyl ether

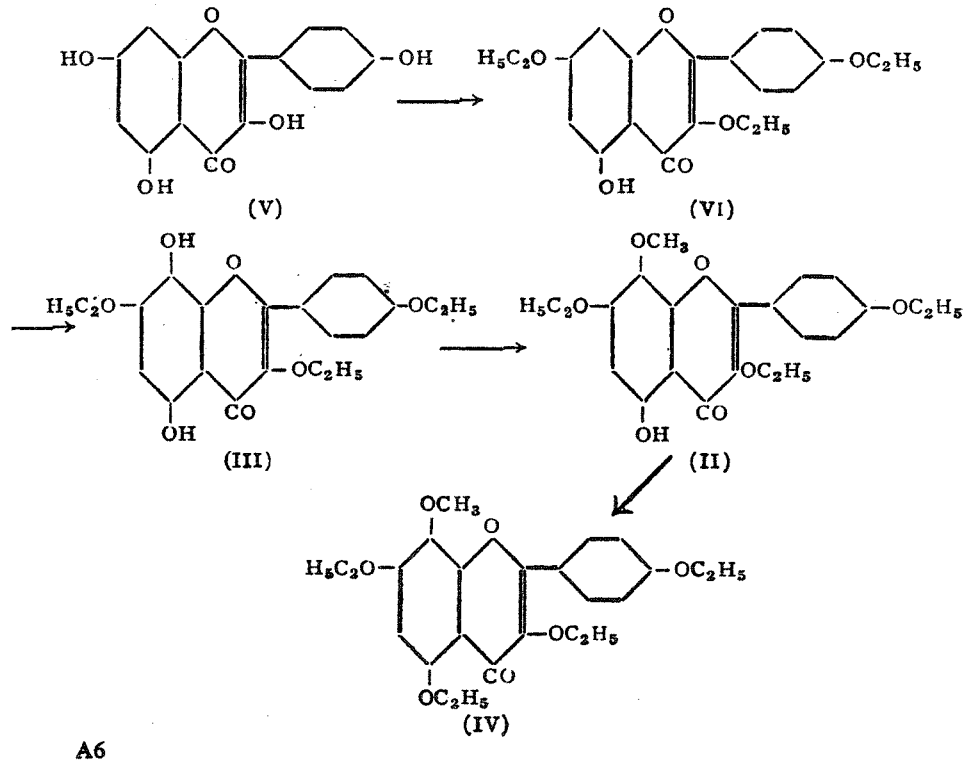


(III)

(A) should have the constitution (II) and this has been established by synthesis mentioned later on.

With excess of ethyl iodide tambuletin gives rise to a tetraethyl ether. This tetraethyl tambuletin is found to be identical with a sample of 8-methoxy-3:5:7:4'tetramethoxy flavone (IV) obtained by unambiguous synthesis.

The synthesis of the compounds (II), (III) and (IV) has been accomplished in an easy manner by the application of the new discovery of facile nuclear oxidation in the flavone series.[3] Kaempferol (V) is the starting point for this synthesis. It is subjected to partial ethylation with the requisite quantity of ethyl iodide in order to form O-triethyl kaempferol (VI). This has a free hydroxyl in the 5-position and has all the characteristic properties. Oxidation with alkaline persulphate yields the quinol (III). That the oxidation takes this course has been proved in the analogous case of trimethyl-kaepmferol.[4] Partial methylation with dimethyl sulphate and potassium carbonate converts it into the 8-methyl ether (II), the more resistant 5-hydroxyl being left out. Subsequent ethylation yields the 8-monomethyl-3:5:7:4'-tetraethyl-ether of herbacetin (IV). This synthesis of O-tetraethyl-tambuletin finally confirms the constitution of tambuletin as already proposed (I).



In tambuletin and wogonin[5] the selective partial methylation taking place in the 8-position is rather remarkable. Equally interesting are the analogous cases of oroxylin-A[6] and patuletin[7] in which the 6-position is involved whereas in the mono-methyl ethers of the more common flavones and flavonols the position affected is either 7, 3, 3′ or 4′.

Experimental

O-Triethyl-tambuletin (A)

Tambuletin (1 g.) was dissolved in dry acetone (100 c.c.) and potassium carbonate (15 g.) and ethyl iodide (1·2 c.c.) were added. The contents were refluxed for 6 hours and the potassium salts were filtered off and washed with acetone. When the filtrate was concentrated, cooled and diluted with water, the partially ethylated compound separated out. It was crystallised from alcohol when it was obtained as pale yellow needles melting at 119–20°. (Found: C, 65·9; H, 6·3; $C_{22}H_{24}O_7$ requires C, 66·0; H, 6·0%.)

The compound was sparingly soluble in aqueous alkali and with alcoholic ferric chloride gave an olive green colour.

Oxidative Demethylation

The above compound (0·5 g.) was treated with nitric acid (2 c.c., d. 1·25) at 15–20° and the mixture stirred well for 15 minutes. A clear red solution was first produced and soon a brown-red solid separated. The mixture was then diluted with water and the solid filtered and washed free of nitric acid. The flavoquinone was crystallised from dilute acetic acid when it came out as reddish-brown needles melting at 140–42°.

Reduction to quinol (III)

The above quinone (0·2 g.) was suspended in rectified spirit and a current of sulphur dioxide passed. After the reduction was complete, the clear bright yellow solution was concentrated. The crystalline substance that separated out was filtered and recrystallised from absolute alcohol when it was obtained as bright yellow needles melting at 194–96°. (Found: C, 64·9; H, 5·9; $C_{21}H_{22}O_7$ requires C, 65·3; H, 5·6%.)

The compound was soluble in aqueous sodium hydroxide to give a reddish-brown solution. With alcoholic ferric chloride it gave a transient green colour which changed to reddish-brown. It produced a reddish brown colour with *p*-benzoquinone in absolute alcoholic solution.

O-Tetra-ethyl-tambuletin (IV)

Tambuletin (0·2 g.) was dissolved in dry acetone (50 c.c.) and anhydrous potassium carbonate (6 g.) and ethyl iodide (1 c.c.) were added. The contents were boiled for 30 hours. The potassium salts were filtered off

and washed with hot acetone. The filtrate was concentrated on a water-bath until all the acetone was removed. The solid that remained behind was stirred up with water and filtered. The tetra-ethyl ether was crystallised from alcohol when it was obtained as colourless hexagonal prisms melting at 109–110°. (Found: C, 66·8; H, 6·2; $C_{24}H_{28}O_7$ requires C, 67·3; H, 6·5%). It was insoluble in sodium hydroxide and did not give any colour with ferric chloride in alcoholic solution. It gave a bright red colour with concentrated nitric acid.

3: 7: 4′-*Triethoxy*-5-*hydroxy-flavone* (*VI*)

Kaempferol (V) (1·0 g.) was dissolved in acetone (50 c.c.) and anhydrous potassium carbonate (10 g.) and ethyl iodide (0·88 c.c.) were added. The mixture was refluxed for 5 hours. The potassium salts were filtered off and washed with hot acetone. On concentrating the filtrate and dilution with water the tri-ethyl ether was obtained. It was crystallised from alcohol when it melted at 90–92°. (Found: C, 67·6; H, 6·0; $C_{21}H_{22}O_6$ requires C, 68·0; H, 5·9%.)

It gave a brown colour with ferric chloride in alcoholic solution and was sparingly soluble in aqueous sodium hydroxide and insoluble in sodium carbonate solution.

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

5-Hydroxy-3: 7: 4′-triethoxy-flavone (VI) (1·0 g.) was dissolved in pyridine (20 c.c.) and an aqueous solution of sodium hydroxide (0·54 g. in 20 c.c. of water) was added. The contents were vigorously stirred by means of a mechanical stirrer and a solution of potassium persulphate (1·09 g.) in water (30 c.c.) was added gradually drop by drop in the course of two hours. The reaction mixture was set aside overnight. It was acidified to congo red with dilute hydrochloric acid and the unreacted compound that separated out was filtered off. To remove the last traces of this compound the filtrate was extracted with ether. To the clear aqueous solution sodium sulphite (3 g.) and concentrated hydrochloric acid (20 c.c.) were added. The solution was kept immersed in a boiling water-bath for 30 minutes when the 5: 8-dihydroxy compound separated out. The mixture was cooled and extracted with ether. On distilling off the ether, a bright yellow solid was obtained. It was crystallised from alcohol when it was obtained as needles melting at 194–96°. The mixed melting point with the quinol (III) was not depressed. The compound was soluble in aqueous sodium hydroxide giving a reddish brown solution and gave a green colour which changed to brown with ferric chloride in alcoholic solution. It gave a reddish-brown colour with *p*-benzoquinone in absolute alcoholic solution.

3 : 7 : 4′-*Triethoxy*-8-*methoxy*-5-*hydroxy-flavone* (*II*)

The above compound (III) (0·5 g.) was dissolved in dry acetone (50 c.c.) and anhydrous potassium carbonate (6 g.) and dimethyl sulphate (0.13 c.c.) were added. The contents were refluxed for 5 hours. The potassium salts were filtered off and washed with hot acetone. The filtrate was concentrated until all the acetone was removed. The compound thus obtained was crystallised from alcohol. It came out as pale yellow needles melting at 119–20°. The mixed melting point with triethyl-tambuletin (A) was undepressed. With ferric chloride in alcoholic solution, the compound gave an olive green colour. It was sparingly soluble in aqueous sodium hydroxide.

8-*Methoxy*-3 : 5 : 7 : 4′-*tetraethoxy-flavone* (*IV*)

The above compound (II) (0·2 g.) was dissolved in dry acetone (25 c.c.) and anhydrous potassium carbonate (5 g.) and ethyl iodide (0·2 c.c.) were added. The contents were refluxed for 30 hours. The potassium salts were filtered off and washed with hot acetone. When acetone was removed by distillation from the filtrate, a colourless solid was left behind. It was crystallised from alcohol when it melted at 109–110°. (Found: C, 66·9; H, 6·1; $C_{24}H_{28}O_7$ requires C, 67·3; H, 6·5%.)

It was insoluble in aqueous sodium hydroxide and gave no colour with ferric chloride in alcoholic solution. With concentrated nitric acid it gave a bright red colour. The mixed melting point with tetra-ethyl-tambuletin was not depressed.

Summary

By partial ethylation tambuletin forms a definite triethyl-ether giving reactions for a free hydroxyl group in the 5-position. It undergoes oxidative demethylation thus confirming the location of the methyl-ether group in the 8-position. Complete ethylation yields O-tetraethyl-tambuletin which is found to be identical with 3 : 5 : 7 : 4′-tetraethoxy-8-methoxy-flavone, synthesised from kaempferol using the method of nuclear oxidation.

References

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