

# NUCLEAR OXIDATION IN FLAVONES AND RELATED COMPOUNDS

## Part XXII. A Synthesis of Pectolarigenin

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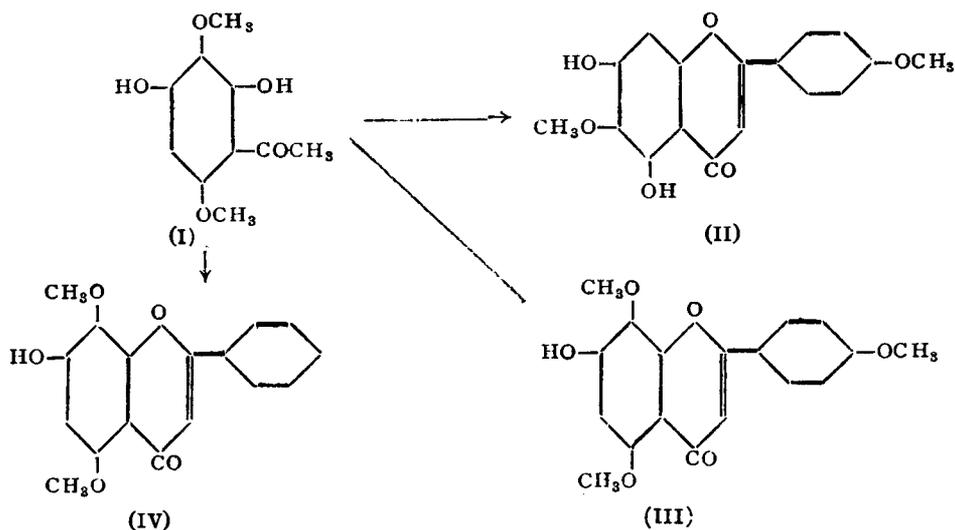
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Received May 30, 1949

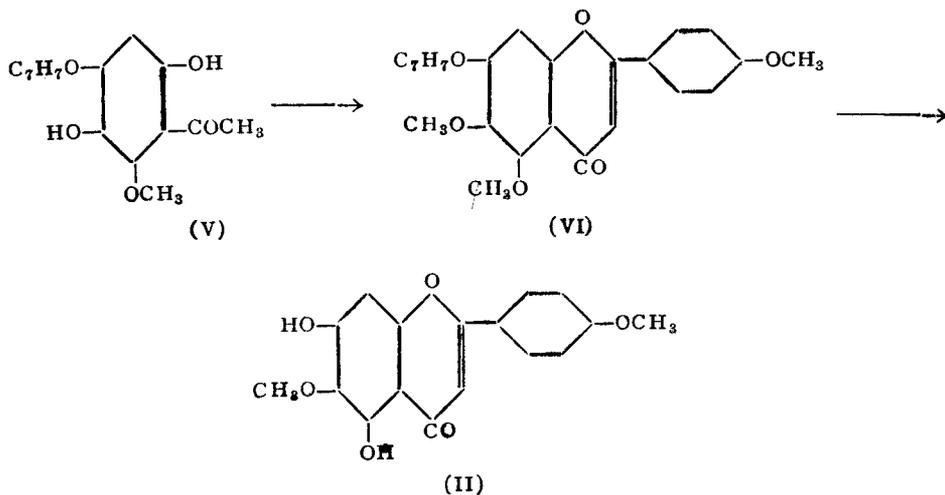
THE glycoside pectolarin which was isolated from the flowers of *Linaria vulgaris*<sup>1</sup> yielded on hydrolysis an aglycone, pectolarigenin, having the molecular formula  $C_{17}H_{14}O_6$ . It was a dimethyl ether of scutellarein. The position of one of the methoxyl groups could be easily located since it yielded anisic acid by alkali fission. The other methoxyl was considered to be in the 6-position since the compound was found to be identical with the 6:4'-dimethyl ether of scutellarein (II) obtained synthetically by Wessely and Moser.<sup>2</sup> The sugar residue could be allotted the position 7 because the glycoside was unchanged when treated with diazomethane and hence had the free hydroxyl group in the resistant 5-position. Subsequently the synthesis of the glycoside itself has been effected using the aglycone and hexa-acetyl- $\beta$ -rutosidyl bromide.<sup>3</sup>

The synthesis of pectolarigenin by Wessely and Moser<sup>2</sup> was not a direct one and was due to the Allan-Robinson condensation taking an unexpected course. They fused 2:4-dihydroxy-3:6-dimethoxy acetophenone (I) with anisic anhydride and sodium anisate and instead of the expected 7-hydroxy-5:8:4'-trimethoxy flavone (III), obtained a dimethyl ether of scutellarein (II). This was explained as due to partial demethylation during the condensation and favoured ring closure to yield the 5:6:7-arrangement instead of the 5:7:8-arrangement of groups.

However, attempts to synthesise oroxylin-A by employing the same ketone and benzoic anhydride and sodium benzoate were unsuccessful.<sup>4</sup> Only wogonin methyl ether (IV) was obtained. Even in anisoylation Wessely and Moser got the normal product (III) in one of a large number of experiments and Furukawa and Tamaki<sup>5</sup> reported that the condensation proceeded normally in their experiments to yield 5:8:4'-trimethoxy-7-hydroxy flavone (III). Hence a more definite synthetic route for scutellarein-6:4'-dimethyl-ether was needed and this has now been provided by the synthesis of the



compound on the same lines as oroxylin-A.<sup>6</sup> By fusing 2:5-dihydroxy-4-benzyloxy-6-methoxy acetophenone (V) with sodium anisate and anisic anhydride and methylating the product, is obtained 5:6:4'-trimethoxy-7-benzyloxy flavone (VI). It undergoes debenylation and partial demethylation in the 5-position with hydrobromic acid and the product is a dimethyl ether having all the properties of pectolarigenin (II). Its diacetate also agrees with the description of pectolarigenin diacetate. We have also repeated the synthesis by the method of Wessely and Moser<sup>2</sup> and find that the product is identical with the one obtained by the new method, the same being the case with the diacetate obtained from it.



## EXPERIMENTAL

*Allan-Robinson condensation*

An intimate mixture of 2:5-dihydroxy-4-benzyloxy-6-methoxy-acetophenone (V) (2.5 g.), anisic anhydride (16 g.) and sodium anisate (6.0 g.) was heated under reduced pressure for 4 hours. The product was suspended in alcohol, aqueous potassium hydroxide (8 g. in 10 c.c. of water) added and the mixture refluxed for half-an-hour. The alcohol was removed under reduced pressure, the residue dissolved in water, the deep reddish-brown solution filtered and saturated with carbon dioxide. The alkaline solution along with the fluffy solid that had separated out was repeatedly extracted with ether and the solvent distilled off. A bright yellow solid was left behind which was boiled with aqueous alcoholic sodium carbonate (5%, 25 c.c.) for two hours. The yellow solution was filtered and acidified and the product crystallised from alcohol. It melted indefinitely between 210 and 230° and gave a green ferric chloride colour (yield, 0.7 g.). It was, therefore, considered to be a mixture of 5-methoxy and 5-hydroxy compounds and hence was directly subjected to methylation.

*5:6:4'-Trimethoxy-7-benzyloxy-flavone (VI)*

The yellow solid obtained above (0.5 g.) was dissolved in dry acetone (50 c.c.), redistilled dimethyl sulphate (0.8 c.c.) and ignited potassium carbonate (5 g.) were added and the mixture refluxed for 30 hours. The product could be crystallised from acetone-alcohol mixture when it was obtained as colourless rods and prisms melting at 184–5°; yield, 0.4 g. (Found: C, 71.6; H, 5.5;  $C_{25}H_{22}O_6$  requires C, 71.8; H, 5.3%.)

*5:7-Dihydroxy-6:4'-dimethoxy flavone: Pectolinarigenin (II)*

The trimethoxy-benzyloxy flavone (VI) (0.5 g.) was dissolved in glacial acetic acid (15 c.c.), the solution treated with hydrobromic acid in glacial acetic acid solution (40%; 10 c.c.) and the mixture heated on a water-bath at 60° for one hour. It was then cooled, diluted with a large volume of water and extracted with ether. On removing the solvent, a yellow solid was left behind which, on crystallisation from alcohol, was obtained as yellow elongated rectangular plates melting at 216–7°. Yield, 0.1 g. It gave a reddish-brown colour with alcoholic ferric chloride, and dissolved to a yellow solution in aqueous sodium hydroxide. It was identical with the sample obtained by the method of Wessely and Moser and the mixed melting point was undepressed. (Found: C, 64.7; H, 4.7;  $OCH_3$ , 19.9;  $C_{17}H_{14}O_6$  requires C, 65.0; H, 4.5 and  $OCH_3$  19.7%.)

The compound was acetylated with acetic anhydride and sodium acetate. The diacetate crystallised from alcohol as colourless needles melting at 152–3°; the mixture with the acetate of the sample obtained by the method of Wessely and Moser melted at same temperature.

#### SUMMARY

Employing 2:5-dihydroxy-4-benzyloxy-6-methoxy acetophenone and following the procedure very similar to the one adopted for the synthesis of oroxylin-A, the 6:4'-dimethyl ether of scutellarein has now been obtained. Its properties agree closely with those of pectolinarigenin and it is found to be identical with the dimethyl ether prepared by the method of Wessely and Moser.

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