

NUCLEAR OXIDATION IN FLAVONES AND RELATED COMPOUNDS

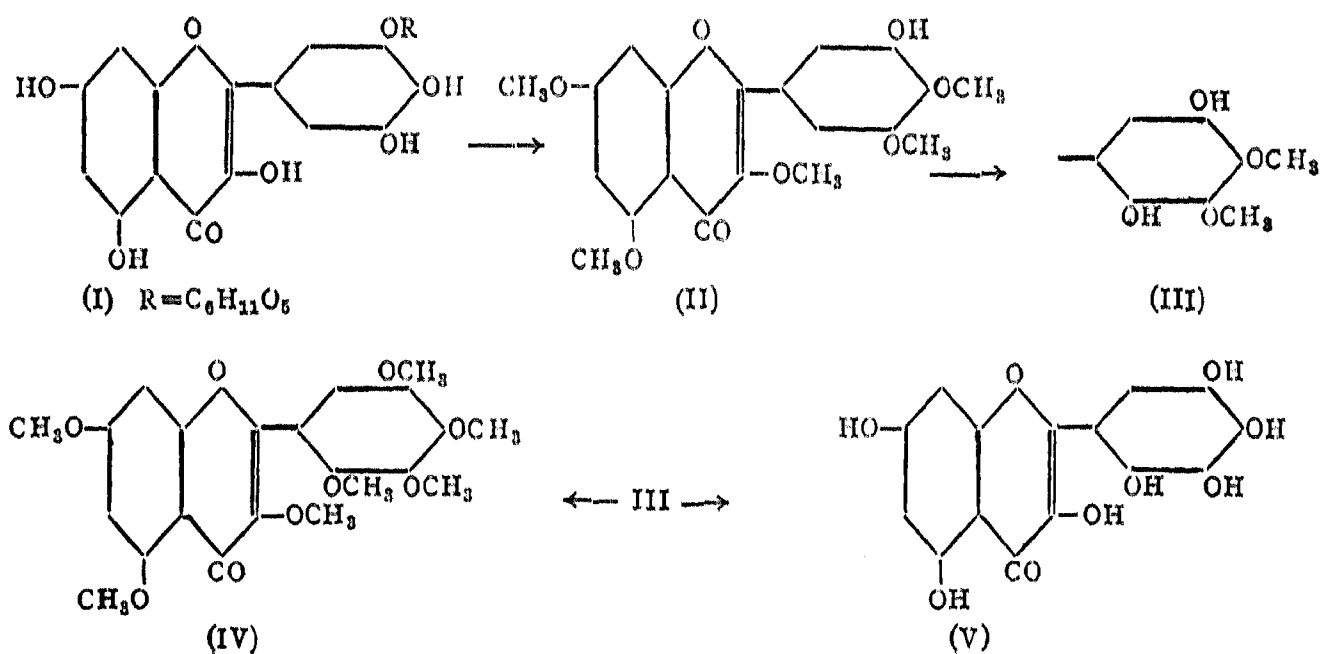
Part XXXIV. Para-oxidation in the Side-Phenyl Nucleus : Preparation of 6'-Hydroxy-myricetin

BY K. J. BALAKRISHNA, N. PRABHAKARA RAO AND T. R. SESHADRI, F.A.SC.

(From the Departments of Chemistry, Andhra and Delhi Universities)

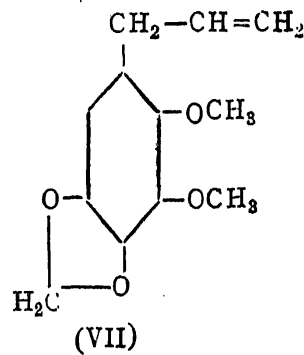
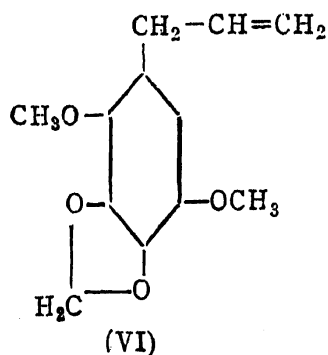
Received December 11, 1950

IN previous parts was described para-oxidation in the condensed benzene ring of flavones and flavonols using alkaline persulphate. As far as the side-phenyl nucleus was concerned the two-stage ortho-oxidation was applied for the conversion of a quercetin derivative into myricetin¹ and of a fisetin derivative into robinetin.² The feasibility of para-oxidation in this part of the molecule has not so far been tested. This has now been done using as a convenient material the pentamethyl ether of myricetin (II) which is easily made from the glucoside cannabiscitrin (I) by methylation and hydrolysis.³ It is soluble in aqueous alkali and smoothly undergoes oxidation with persulphate to yield the quinol (III). On methylation it yields 3:5:7:3':4':5':6'-heptamethoxy flavone (IV) and on demethylation 6'-hydroxy-myricetin (V). Though it is a more highly hydroxylated compound, its alkali colour reactions are not more prominent than those of myricetin. With a view to make sure that hydriodic acid has not brought about any other changes besides demethylation the product is remethylated. The



resulting methyl ether is found to be identical with the original heptamethoxy flavone obtained from (III) and the mixed melting point is undepressed.

Flavones with four hydroxyl (methoxyl) groups in the side-phenyl nucleus have not been made so far and they have not been isolated from natural products. But in allyl-benzene derivatives which are considered to have a similar phytochemical origin⁴ analogous cases are found in parsley apiole (VI) and dill apiole (VII). Consequently the occurrence in nature of the above highly hydroxylated flavones and their derivatives should be considered a possibility.



EXPERIMENTAL

Following the procedure of Seshadri and Venkateswarlu³ cannabiscitrin was methylated and the methyl ether hydrolysed when 3'-hydroxy-3:5:7:4':5'-pentamethoxy flavone (II) was obtained as clusters of colourless needles melting at 220–21°.

3':6'-Dihydroxy-3:5:7:4':5'-pentamethoxy flavone (III)

The above monohydroxy flavone (II) (1.0 g.) was dissolved in aqueous potassium hydroxide (1.0 g. in 30 c.c.) and the clear yellow solution was stirred and treated with aqueous potassium persulphate (1.2 g. in 25 c.c.) gradually during the course of two hours. The reddish-brown solution was allowed to stand for 24 hours and then rendered slightly acidic to congealed with hydrochloric acid. The substance that separated out was filtered off and washed with water. The filtrate was extracted twice with ether to remove the last traces of the unreacted compound. The clear reddish-brown aqueous layer was treated with sodium sulphite (2.0 g.) and concentrated hydrochloric acid (20 c.c.) and the mixture heated with a boiling water-bath for 30 minutes. After cooling the yellow solid that separated out was repeatedly extracted with ether. Yield, 0.3 g. It crystallised from aqueous alcohol as bright yellow narrow rectangular plates melting at 239–40° (Found: C, 59.6; H, 5.4; $C_{20}H_{20}O_9$ requires C, 59.4 and H, 5.0%). With ferric chloride in alcoholic solution it gave a light brown colour. It was easily

soluble in alcohol and also in aqueous alkali to produce a deep yellow solution.

3:5:7:3':4':5'; :6'-Heptamethoxy flavone (IV)

The above dihydroxy compound (III) (1.0 g.) was dissolved in dry acetone (25 c.c.) and the solution treated with dimethyl sulphate (2.0 c.c.) and anhydrous potassium carbonate (5 g.). The mixture was refluxed for 12 hours and the potassium salts were filtered off. The filtrate was concentrated when the methyl ether separated out. It crystallised from alcohol as colourless rectangular plates melting at 160–61° (Found: C, 60.8; H, 5.8; OCH₃, 49.8; C₂₂H₂₄O₉ requires C, 61.1; H, 5.6 and OCH₃, 50.2%). It did not give any colour with alcoholic ferric chloride and was insoluble in aqueous alkali. The mixed melting point with myricetin pentamethyl ether was depressed to 140–45°.

6'-Hydroxy myricetin (V)

The above dihydroxy compound (III) (1.0 g.) was dissolved in acetic anhydride (5.0 c.c.) and treated with hydriodic acid (2.0 c.c.; d. 1.7). The mixture was heated in an oil-bath at 150° for one hour. After dilution with water the solution was saturated with sulphur dioxide and the solid that separated out was filtered and washed with water. It crystallised from ethyl acetate as bright yellow plates which did not melt below 350° (Found: C, 54.1; H, 3.3; C₁₅H₁₀O₉ requires C, 53.9 and H, 3.0%).

With alcoholic ferric chloride the substance gave an olive-brown colour which later changed to brown. The substance was unstable in alkaline solutions and exhibited colour changes. With sodium carbonate solution (5%) the initial yellow rapidly turned red, green, pink and finally orange-brown. With sodium bicarbonate solution (5%) it turned green, greenish-yellow, greenish-brown, brown reddish-brown, pink and purple in two minutes; stable for one hour and the purple colour then slowly faded. With aqueous sodium hydroxide (5%) an immediate brown-red colour was produced which was stable for one hour and later slowly faded to brown.

6'-Hydroxy myricetin (V) (0.5 g.) was methylated in dry acetone medium using dimethyl sulphate (2.0 c.c.) and anhydrous potassium carbonate according to the procedure already described earlier. The product crystallised from alcohol as colourless rectangular plates melting at 160–61°. Mixed melting point with the sample obtained from (III) was not depressed.

SUMMARY

Para oxidation in the side-phenyl nucleus has now been investigated using potassium persulphate and 3'-hydroxy-3:5:7:4':5'-pentamethoxy

flavone obtained conveniently from cannabiscitrin. The resulting quinol on methylation yields 3:5:7:3':4':5':6'-heptamethoxy flavone and on demethylation 6'-hydroxy myricetin which is the first example of a flavone having four hydroxyl groups in the side-phenyl nucleus.

REFERENCES

1. Rao and Seshadri .. *Proc. Ind. Acad. Sci.*, 1948, 28A, 210.
2. Row, Seshadri and Thiruvengadam .. *Ibid.*, 1949, 29A, 168.
3. Seshadri and Venkateswarlu .. *Ibid.*, 1946, 23A, 302.
4. Robinson .. *Nature*, 1936, 137, 172.
———, *et al.* .. *Phil. Trans. Roy. Soc.*, London, 1939, 230 B, 149.
- Rao, *et al.* .. *Proc. Ind. Acad. Sci.*, 1949, 30A, 114.
- Seshadri and Thiruvengadam .. *Ibid.*, 1950, 32A, 110.