

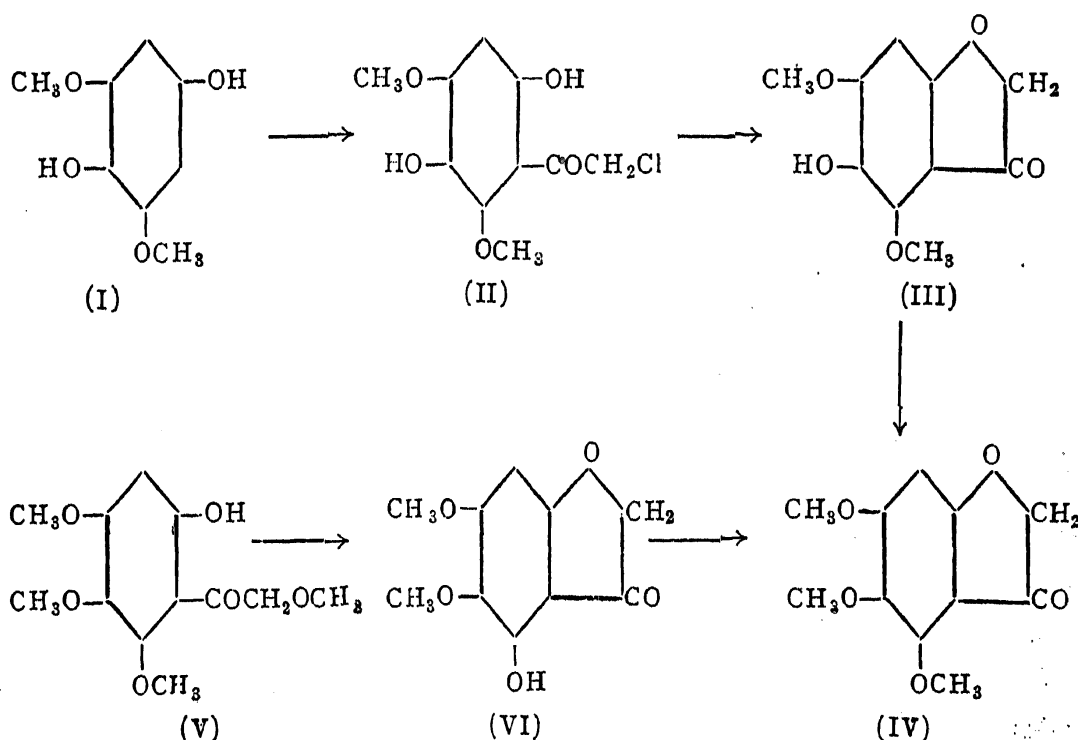
A NOTE ON 4:5:6-TRIMETHOXY-COUMARAN-3-ONE

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IN connection with a method for distinguishing between flavones and flavonols, the preparation of a number of coumaranones and their derivatives was earlier investigated.¹ As a continuation, the preparation and properties of 4:5:6-trimethoxy-coumaranone (IV) is here described. The starting material is 2:6-dimethoxy quinol (I) which is unreactive in the Hoesch condensation for the preparation of ketones. But it reacts smoothly with chloracetyl chloride in the presence of anhydrous aluminium chloride in the cold and the product is found to be 2:5-dihydroxy-4:6-dimethoxy- ω -chloroacetophenone (II); no demethylation occurs during this condensation. Under the same conditions the quinol does not enter into reaction with acetyl chloride. Treatment with sodium acetate in hot alcoholic solution converts (II) into 4:6-dimethoxy-5-hydroxy-coumaranone (III) which yields 4:5:6-trimethoxy-coumaranone (IV) by methylation. This sample is found to be identical with the product obtained by the degradation of quercetagetol-tetramethyl ether (V)² in the following manner. When this ω -methoxy ketone is heated with 40% aqueous hydrogen bromide,



it yields a coumaranone giving ferric chloride reaction. Obviously partial demethylation takes place in the course of this reaction in the 4-position (VI). It is therefore directly methylated whereby the trimethoxy compound (IV) is obtained.

EXPERIMENTAL

2:5-Dihydroxy-4:6-dimethoxy- ω -chloroacetophenone (II):

Anhydrous aluminium chloride (16 g.) was added in small quantities at a time to dry ether (50 c.c.), cooled in ice, followed by 2:6-dimethoxy-1:4-dihydroxy benzene (I) (7 g.). Chloracetyl chloride (4 g.) was then added gradually in drops and the mixture allowed to stand overnight. Ice-cold water (50 c.c.) and concentrated hydrochloric acid (50 c.c.) were added in small quantities alternately, all the while allowing the ether to evaporate. The reaction mixture was then heated on a boiling water-bath for one hour, cooled and the separated solid filtered off. It crystallised from alcohol as light yellow elongated rectangular rods melting at 154°. Yield 4 g. (Found: C, 48.4; H, 4.8; OCH₃, 25.5; Cl, 14.0; C₁₀H₁₁O₅Cl requires C, 48.7; H, 4.5; OCH₃, 25.2; Cl, 14.4%). With alcoholic ferric chloride it gave a brown colour and was soluble in aqueous alkali. It produced an irritating sensation when it came in contact with the skin.

4:6-Dimethoxy-5-hydroxy-coumaran-3-one (III)

The above compound (II) (4 g.) was dissolved in a small quantity of alcohol and an aqueous solution of sodium acetate (10 g. in 100 c.c.) was added to it. The mixture was boiled for 15 minutes when a grey solid separated out. It was cooled and filtered. It crystallised from methyl alcohol as light grey hexagonal prisms melting at 88–89°. Yield 2 g. (Found: C, 57.2; H, 5.0; OCH₃, 29.1; C₁₀H₁₀O₅ requires C, 57.2; H, 4.8; OCH₃, 29.5%). With alcoholic ferric chloride it did not give any colour but it was soluble in aqueous alkali.

4:5:6-Trimethoxy-coumaran-3-one (IV):

(i) The above hydroxy compound (III) (1 g.) was dissolved in dry acetone (25 c.c.) and treated with anhydrous potassium carbonate (5 g.) and dimethyl sulphate (3.0 c.c.). The mixture was refluxed for three hours and the potassium salts were filtered off. On concentrating the filtrate, the trimethyl ether separated out. It crystallised from alcohol as pale yellow prisms melting at 108–09°. Yield 0.4 g. (Found: C, 58.7; H, 5.6; C₁₁H₁₂O₅ requires C, 58.9; H, 5.4%). With alcoholic ferric chloride it did not give any colour and was insoluble in aqueous alkali.

(ii) Quercetagetol-tetramethyl ether (V) (2.0 g.) was treated with aqueous hydrobromic acid (40%, 10 c.c.) and the mixture heated on a boiling water-bath for three hours. Water was added and the solid that separated out was extracted with ether. Removal of ether gave a solid which even after a crystallisation from methyl alcohol did not have a sharp melting point, gave colour with alcoholic ferric chloride and was almost completely soluble in aqueous alkali. It therefore seemed to consist largely of 4-hydroxy-5:6-dimethoxy-coumaranone arising out of partial demethylation in the course of the reaction. It was methylated completely using excess of dimethyl sulphate and anhydrous potassium carbonate in dry acetone medium according to the procedure described above. The trimethoxy-coumaranone (IV) thus obtained crystallised from alcohol as pale yellow prisms melting at 108–09°. The mixed melting point with the sample obtained in (i) was not depressed. Yield 0.1 g.

SUMMARY

4:5:6-Trimethoxy-coumaranone is obtained from quercetagetol-tetramethyl ether by treatment with hydrobromic acid and methylation of the product. It is conveniently synthesised from 2:6-dimethoxy-quinol which undergoes Friedel and Craft's reaction with chloracetyl chloride satisfactorily.

REFERENCES

1. Balakrishna, Rao and Seshadri .. *Proc. Ind. Acad. Sci.*, 1949, **29A**, 394.
2. Row and Seshadri .. *Ibid.*, 1945, **22A**, 215 ; 1946, **23A**, 23.