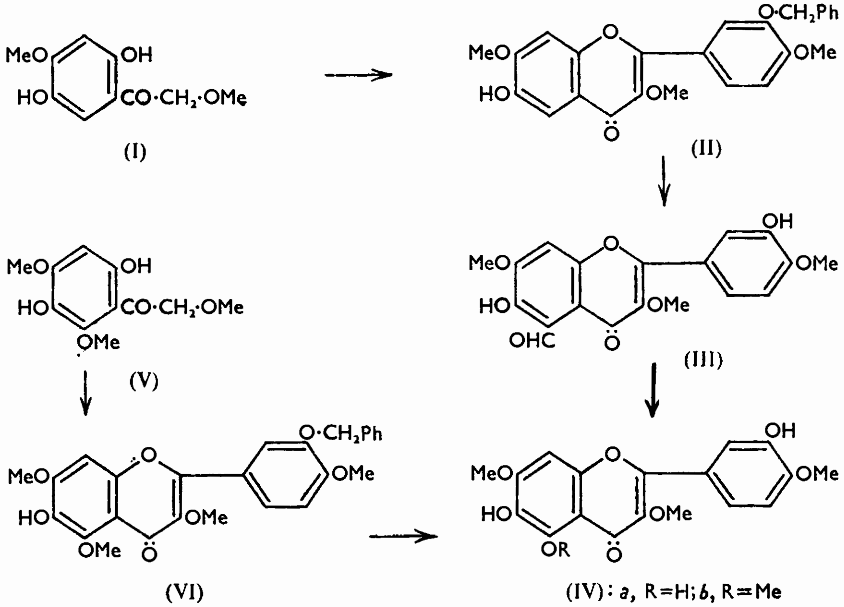
277. *Synthesis of Oxyayanin-B.*

By R. N. Goel, A. C. Jain, and T. R. Seshadri.

The partial methyl ether, oxyayanin-B (IV*a*), has been synthesised by two methods.

A general method for the synthesis of flavonols of the quercetagetin series was recently described [1] which is particularly suitable for the preparation of partial methyl ethers having 5- and 6-hydroxyl groups. Oxyayanin-B [2] has now been synthesised; 3′-benzyloxy-6-hydroxy-3 : 7 : 4′-trimethoxyflavone (II), prepared by the Allan–Robinson reaction from 2 : 5-dihydroxy-ω : 4-dimethoxyacetophenone (I) and the anhydride and sodium salt of *O*-benzyl*iso*vanillic acid, was condensed with hexamine. During hydrolysis of the product with hydrochloric acid, debenzylation also occurred, yielding 5-formyl-6 : 3′-dihydroxy-3 : 7 : 4′-trimethoxyflavone (III). Subsequent Dakin oxidation yielded oxyayanin-B (IV*a*) having all the properties of the natural sample.



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[1] Jain, Seshadri, and Sreenivasan, *J.*, 1955, 3908.
[2] King, King, and Stokes, *J.*, 1954, 4587.

The older method of Row and Seshadri[3] can also be used. Allan–Robinson condensation of 2 : 5-dihydroxy-ω : 4 : 6-trimethoxyacetophenone (V) with the anhydride and sodium salt of *O*-benzyl*iso*vanillic acid yielded 3′-benzyloxy-6-hydroxy-3 : 5 : 7 : 4′-tetramethoxyflavone (VI) which underwent smooth debenzylation (to IV*b*) and partial demethylation in the 5-position, to form oxyayanin-B (IV*a*).

EXPERIMENTAL

3′-*Benzyloxy*-6-*hydroxy*-3 : 7 : 4′-*trimethoxyflavone* (II).—2 : 5-Dihydroxy-ω : 4-dimethoxyacetophenone (4 g.), *O*-benzyl*iso*vanillic anhydride (32 g.), and sodium *O*-benzyl*iso*vanillate (8 g.) were heated under reduced pressure at 180—184° for 4 hr. and the cooled product refluxed with 8% alcoholic potassium hydroxide (80 c.c.) for 30 min. After removal of alcohol in a vacuum and dissolution of the residue in water (200 c.c.), carbon dioxide was passed through the solution. The yellow precipitate (3·5 g.) crystallised from alcohol as deep yellow rectangular prisms, m. p. 190—191° (Found : C, 69·3; H, 5·2. $C_{25}H_{22}O_7$ requires C, 69·1; H, 5·1%). This *flavone* gave no colour with ferric chloride and was sparingly soluble in aqueous sodium hydroxide.

5-*Formyl*-6 : 3′-*dihydroxy*-3 : 7 : 4′-*trimethoxyflavone* (III).—The preceding flavone (3·0 g.) was heated with acetic acid (150 c.c.) and hexamine (12 g.) on a boiling-water bath for 7 hr. Boiling dilute hydrochloric acid (1 : 1; 70 c.c.) was then added and heating continued for 30 min. more. The resulting mixture was cooled, diluted with water, and extracted exhaustively with chloroform. The chloroform layer was washed with sodium hydrogen carbonate solution followed by water, dried, and treated with ether. The insoluble impurities were filtered off and the clear orange solution was concentrated. The residual *aldehyde* crystallised from benzene as very pale yellow prisms, m. p. 209—211° (0·8 g.). It gave a reddish-brown colour with alcoholic ferric chloride and was soluble in 5% aqueous sodium carbonate (Found : C, 61·2; H, 4·8. $C_{19}H_{16}O_8$ requires C, 61·3; H, 4·3%). The 2 : 4-dinitrophenylhydrazone crystallised from acetic acid as orange-yellow needles, m. p. 286° (decomp.).

Oxyayanin-B (IV*a*).—The aldehyde (0·5 g.) was dissolved in 6% aqueous sodium hydroxide (3·5 c.c.) and pyridine (5 c.c.), cooled in ice, and treated during 15 min. with 5% hydrogen peroxide solution (1·5 c.c.) with shaking. The mixture was allowed slowly to reach room temperature, vigorously shaken for 2 hr., then neutralised to Congo-red, and extracted with ether, and the extract washed with water, dried and concentrated. The residue crystallised from ethyl acetate–light petroleum as pale yellow needles, m. p. 207—208° (Found : C, 60·1; H, 4·5. Calc. for $C_{18}H_{16}O_8$: C, 60·0; H, 4·4%). The mixed m. p. with the natural sample was undepressed. It gave an olive-green colour with alcoholic ferric chloride, a crimson colour with magnesium and hydrochloric acid, and a green solution becoming orange in hot 5% aqueous sodium carbonate. The triacetate crystallised from ethyl acetate as colourless needles, m. p. 214—216° (Found : C, 59·2; H, 4·8. Calc. for $C_{24}H_{22}O_{11}$: C, 59·2; H, 4·5%), in agreement with the natural sample.[2]

3′-*Benzyloxy*-6-*hydroxy*-3 : 5 : 7 : 4′-*tetramethoxyflavone* (VI).—2 : 5-Dihydroxy-ω : 4 : 6-trimethoxyacetophenone (3 g.), *O*-benzyl*iso*vanillic anhydride (25 g.), and sodium *O*-benzyl*iso*vanillate (6 g.) were heated at 175—180° under diminished pressure for 4 hr. and worked up as mentioned earlier. The *flavone* (VI) crystallised from alcohol as yellow needles and rectangular rods, m. p. 168—169° (3·5 g.) (Found : C, 66·7; H, 5·2. $C_{26}H_{24}O_8$ requires C, 67·2; H, 5·2%). It gave no ferric reaction.

6 : 3′-*Dihydroxy*-3 : 5 : 7 : 4′-*tetramethoxyflavone* (IV*b*).—The preceding flavone (1 g.) was heated with acetic acid (30 c.c.) and concentrated hydrochloric acid (15 c.c.) on a steam-bath for 1 hr. The product was diluted with water and extracted with chloroform; the chloroform layer was washed with sodium hydrogen carbonate solution followed by water, dried, and concentrated. The residual *flavone* crystallised from ethyl acetate as very pale yellow rectangular plates and prisms, m. p. 236—238° (0·4 g.) (Found : C, 60·6; H, 4·7. $C_{19}H_{18}O_8$ requires C, 61·0; H, 4·8%). It gives no ferric reaction and dissolves easily in aqueous sodium hydroxide to a yellow solution.

Oxyayanin-B (IV*a*).—(*a*) The above 6 : 3′-dihydroxyflavone (0·25 g.) was refluxed with anhydrous aluminium chloride (1 g.) in dry ether (20 c.c.) for 6 hr., ether was distilled off, and the complex decomposed with dilute hydrochloric acid. The pale yellow precipitate (0·15 g.) was collected, dried, and acetylated by acetic anhydride–pyridine. The acetate crystallised

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[3] Row and Seshadri, *Proc. Indian Acad. Sci.*, **1946**, **23***A*, 24.

from ethyl acetate as colourless needles, m. p. 214—216°. It was deacetylated by refluxing alcoholic hydrochloric acid (1 : 1; 15 c.c.) for 1 hr. Alcohol was distilled off and water added to the remaining mixture; oxyayanin-B, which separated, crystallised from ethyl acetate as pale yellow needles, m. p. and mixed m. p. 207—208°.

(*b*) 3′-Benzyloxy-6-hydroxy-3 : 5 : 7 : 4′-tetramethoxyflavone (VI) (0·5 g.) was refluxed with concentrated hydrochloric acid (30 c.c.) and acetic acid (20 c.c.) for 6 hr. The product was treated with crushed ice and extracted with chloroform. The extract, treated as above, yielded oxyayanin-B triacetate, m. p. 214—216°, and thence oxyayanin-B (0·2 g.).

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UNIVERSITY OF DELHI, DELHI-8. INDIA. [*Received, October 27th*, 1955.]