131. *The Constitution of Oroxylin-A, a Yellow Colouring Matter from the Root-bark of* Oroxylum indicum, *Vent.*

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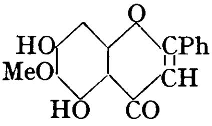
OROXYLIN was isolated by Naylor and Chaplin (" Year Book of Pharmacy," 1890) from the root bark of *Oroxylum indicum*, Vent, an Indian medicinal plant (natural order *Bignoniaceæ*). Naylor and Dyer (J., 1901, **79**, 954) assigned to it the formula $C_{19}H_{14}O_6$ (cf. Warner, *Pharm. J.*, 1898, **7**, 390) and inferred the presence of three hydroxyl groups from the preparation of an acetyl derivative which, from the amount of oroxylin it gave on hydrolysis, was assumed to be a triacetate. Hydrolysis with concentrated alkali yielded phthalic and benzoic acids, and a neutral product which gave the pinewood and hydrochloric acid test for phloroglucinol. Dilute alkali produced benzaldehyde, and potassium permanganate, phthalic acid. Methoxy-, carbonyl, and carboxyl groups appeared to be absent.

The root bark used in the present investigation was purchased from Ahmednagar Ayurvedashram, or collected from the Songadh forests in Gujarat, and was identified by Dr. K. S. Mhaskar of the Haffkine Institute, Bombay, to whom our thanks are due. We isolated oroxylin by a method similar to that of Naylor and Dyer (0·2% yield) and also by a new method (0·86% yield). The properties of our product as regards appearance, m. p., analysis, and production of benzoic acid by alkaline hydrolysis agree with those reported by Naylor and Dyer (*loc. cit.*), but in other respects our results are essentially different. On this account, the name oroxylin-A is suggested for our product, although it is probably identical with that of Naylor and Dyer.

We base our conclusions on the structure of oroxylin-A on the following observations : (a) It gives the magnesium–hydrochloric acid xanthoxine reaction; (b) the formula $C_{16}H_{12}O_5$ satisfies the analytical results as well as the $C_{19}H_{14}O_6$ formula of Naylor and

Dyer; (c) it contains one methoxyl group; (d) it forms a *diacetyl* and a dimethyl derivative and a monomethyl derivative which yields an oxonium platinichloride. These results indicate that it is a dihydroxymethoxyflavone, $C_{15}H_7O_2(OH)_2\cdot OMe$.

(e) It gives benzoic acid on alkaline hydrolysis, indicating that the 2-phenyl group is unsubstituted. (f) It does not contain a 3-hydroxyl group, since it is stable to aerial oxidation in alkaline solution. (g) It gives a reddish-violet coloration with alcoholic ferric chloride, unlike primetin (Nagai and Hattori, *Acta Phytochim.*, 1930, **5**, 1), which gives a green colour. It does not give a brown coloration with ammonium molybdate and acetic acid (cf. Quastel, *Analyst*, 1931, **56**, 311), nor does it reduce ammoniacal silver nitrate. Ortho-related hydroxyl groups are therefore absent. (h) On demethylation it gives demethyloroxylin-A, unchanged in m. p. by admixture with authentic baicalein (5 : 6 : 7-trihydroxyflavone; Shibata, Iwata, and Nakamura, *Acta Phytochim.*, 1923, **1**, 105; Bargellini, *Gazzetta*, 1919, **49**, ii, 47) kindly supplied by Prof. Shibata, to whom we express our best thanks. In all probability, therefore, oroxylin-A is 6-*O*-methyl baicalein (5 : 7-dihydroxy-6-methoxyflavone) (I). This is confirmed by the identity of its mono- and di-methyl derivative with 5-hydroxy-6 : 7-dimethoxyflavone and 5 : 6 : 7-trimethoxyflavone respectively (Bargellini, *loc. cit.*). The synthesis of (I) is in progress.



(I.)

EXPERIMENTAL.

Improved Method for the Extraction of Oroxylin-A (5 : 7-*Dihydroxy*-6-*methoxyflavone*).—Dried powdered root-bark of *Oroxylin indicum*, Vent, was extracted with acetone and the extract was concentrated and added to an equal volume of 50% alcohol. The precipitate on repeated crystallisation from alcohol gave yellow needles, m. p. 231—232°. Yield, 0·86%. Thus obtained, oroxylin-A dissolves in alkali solution with a red colour which rapidly changes to green. This behaviour is due to the presence of a trace of impurity, for after removal of the green flocculent precipitate and acidification of the filtrate the oroxylin-A obtained has the same m. p. but now dissolves in alkali to a yellow solution which is stable to aerial oxidation. The behaviour of the impurity in alkali corresponds to that of baicalein (5 : 6 : 7-trihydroxyflavone; Bargellini, *loc. cit.*) [Found for oroxylin-A: C, 67·7; H, 4·1; OMe, 10·2. Calc. for $C_{15}H_9O_4(OMe)$: C, 67·6; H, 4·2; OMe, 10·9%]. With magnesium and hydrochloric acid in aqueous-alcoholic solution, it gives an orange-red colour. *Diacetyloroxylin-A* (5 : 7-*diacetoxy*-6-*methoxyflavone*) (acetic anhydride–anhydrous sodium acetate) separated from alcohol in colourless needles, m. p. 131—132° (Found: C, 65·0; H, 4·4. $C_{20}H_{16}O_7$ requires C, 65·2; H, 4·4%), insoluble in alkali and giving no coloration with alcoholic ferric chloride. Naylor and Dyer's supposed triacetyl derivative is stated to melt at 150—152°. *Monobenzoyloroxylin-A* (5-*hydroxy*-7-*benzoyloxy*-6-*methoxyflavone*) (benzoyl chloride–pyridine) separated from alcohol in pale yellow needles, m. p. 210° (Found: C, 71·4; H, 4·3. $C_{23}H_{16}O_6$ requires C, 71·1; H, 4·1%), insoluble in dilute alkali solution and giving a violet coloration with alcoholic ferric chloride indicating a 5-hydroxy-group. Dibenzoylation was attempted without success.

Monomethyloroxylin-A (diazomethane–acetone–ether solution) corresponds in properties and analysis to 5-hydroxy-6 : 7-dimethoxyflavone (Bargellini, *loc. cit.*). This product was also obtained with methyl sulphate and 10% alkali at 40°. The *platinichloride* separated from acetic acid–hydrochloric acid in deep yellow needles, m. p. 185—187° (decomp.). The crystals were dried at 105° [Found: Pt, 20·1. $(C_{17}H_{14}O_5)_2,H_2PtCl_6$ requires Pt, 19·4%]. *Acetylmonomethyloroxylin-A* (5-*acetoxy*-6 : 7-*dimethoxyflavone*) (acetic anhydride–anhydrous sodium acetate) separated from alcohol in colourless needles, m. p. 130—131° (Found: C, 66·8; H, 4·7. $C_{19}H_{16}O_6$ requires C, 67·0; H, 4·7%). *Benzoylmethyloroxylin-A* (5-*benzoyloxy*-6 : 7-*dimethoxyflavone*) (benzoyl chloride–pyridine) separated from acetone in colourless cubes, m. p. 206—207° (Found: C, 71·5; H, 4·7. $C_{24}H_{18}O_6$ requires C, 71·9; H, 4·5%). Both compounds were insoluble in dilute alkali solution and gave no ferric chloride reaction. Dimethyloroxylin-A was obtained from the monomethyl derivative (0·1 g.) by treatment with methyl sulphate (3 c.c.) and 20% potassium hydroxide solution (3 c.c.) in boiling acetone; it corresponds in properties and analysis to 5 : 6 : 7-trimethoxyflavone (Bargellini, *loc. cit.*).

Hydrolysis of Oroxylin-A.—The substance (0·2 g.), dissolved in 10% potassium hydroxide solution (14 c.c.), was heated at 100° in a sealed tube for 8 hours. The resulting alkaline solution was extracted with ether, again after saturation with carbon dioxide, and a third time after acidification with hydrochloric acid. The viscous residue obtained from the first extract smelt strongly of acetophenone and did not give the benzaldehyde test with alkaline silver nitrate. The second extract yielded nothing; the third gave benzoic acid. Hydrolysis of methyloroxylin-A with methyl-alcoholic potash also gave benzoic acid. *Demethylation of Oroxylin-A*.—A mixture of oroxylin-A (0·2 g.), acetic anhydride (5 c.c.), and hydriodic acid (*d* 1·27; 5 c.c.) was refluxed at 145—150° (oil-bath) for 2 hours and poured into saturated sodium hydrogen sulphite solution. The precipitate on successive recrystallisation from alcohol, glacial acetic acid, and xylene had m. p. 265—266°, not depressed by authentic baicalein (5 : 6 : 7-trihydroxyflavone), to which it corresponded also in properties and analysis.

All the analyses except the methoxyl determination of oroxylin-A are micro-determinations by Dr. Schoeller.

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