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Dihydrochalcones from the Fronds of *Pityrogramma chrysophylla* var. *marginata*, Domin

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2′,6′-Dihydroxy-4′-methoxydihydrochalcone (I) and 2′,6′-dihydroxy-4,4′-dimethoxydihydrochalcone (II) were isolated from the fronds of the title fern and were also prepared by hydrogenolysis of the appropriate, known, flavanones.

Recently ceroptene, the yellow pigment of the "goldenbacked fern", *Pityrogramma triangularis*, was re-investigated in this laboratory and was found to be a C-methylated chalcone derivative [1,2]. In the same genus there are also ferns, which are characterised by a white coating on the back of the fronds and in an early investigation of such a "silver fern", *P. calomelanos* (the genus then was given as *Gymnogramme*), Zopf isolated a colourless compound, m.p. 141—142° ($C_{20}H_{22}O_6$?), which he named calomelanene [3].

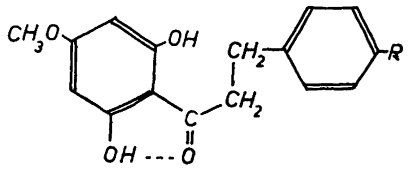
A sample of another silver fern, *P. chrysophylla* var. *marginata* Domin, has now been available for investigation. The white coating was removed by extraction with ether. From the extract a colourless phenol, m.p. 173—175°, was obtained merely by recrystallisation. The mother liquors also contained a small amount of another phenolic component, m.p. 143—145°, which was isolated by partition chromatography.

The compound, m.p. 175°, analysed for $C_{16}H_{16}O_4$ and contained one methoxyl group. It gave rapidly a bright red colour with diazotised benzidine and a strong, brownish red colour with iron(III)chloride. The infrared spectrum indicated the presence of an *o*-hydroxyacylophenone structure, a non-chelated hydroxyl group and a mono-substituted benzene ring.

Among known compounds with these structural features a phenol, m.p. 165°, identified as 2′,6′-dihydroxy-4′-methoxydihydrochalcone (I), has been isolated from the essential oil of *Populus balsamifera* L. by Goris and Canal [4], who also prepared it by mono-methylation of 2′,4′,6′-trihydroxydihydrochalcone [5].

The structure of the present phenol at first was determined indirectly. A Houben-Hoesch condensation of phloroglucinol monomethylether and β-phenylpropionitrile afforded a compound, m.p. 194—197°, which by analogy with acylations with acetonitrile [6] and benzonitrile [7] should be 2′,4′-dihydroxy-

6′-methoxydihydrochalcone. On methylation with diazomethane 2′-hydroxy-4′,6′-dimethoxydihydrochalcone was obtained. The same dimethyl ether was formed on methylation of the natural product also. The position of the methoxyl group was not, however, yet rigidly proved. Hydrogenolysis of flavanones to dihydrochalcones has been successfully applied, *e.g.* for the conversion of naringenin to phloretin [8]. In the present case catalytic hydrogenation of 5-hydroxy-7-methoxyflavanone gave a compound identical with the natural product, m.p. 175°, thereby conclusively proving it to be 2′,6′-dihydroxy-4′-methoxydihydrochalcone (I).



I R = H

II R = OCH_3

The other compound, m.p. 145°, had the composition $C_{17}H_{18}O_5$ and contained two methoxyl groups. The colour reactions and the spectra were largely similar to those of the first dihydrochalcone. However in the infrared spectrum the absorptions due to the mono-substituted benzene ring were absent and a new band at 815 cm^{-1} indicated the presence of two adjacent hydrogen atoms on an aromatic ring. It seemed reasonable to assume the new compound to be a dimethyl ether of phloretin (2′,4,4′,6′-tetrahydroxydihydrochalcone). This was proved by methylation with diazomethane to give phloretin trimethyl ether. The positions of the methoxyl groups were established by hydrogenolysis of 5-hydroxy-4′,7-dimethoxyflavanone to give a compound identical with the natural product, which is therefore 2′,6′-dihydroxy-4,4′-dimethoxydihydrochalcone (II).

The problem of defining the position of the methoxyl groups in phloroacylophenone monomethyl ethers is a classical one, which in this case was easily solved by relating the products to known flavanones. In other cases it has been solved by more laborious procedures involving alternating methylation and ethylation [6] or ethylation followed by oxidation to quinones [7]. The infrared spectra of the present dihydrochalcones and some related compounds indicate that the choice between 2-O-methyl- and 4-O-methylphloroacylophenones can be made by a study of the 1500—1700 cm^{-1} region of the infrared spectra. The results indicated in Fig. 1 are selfexplanatory. Essentially analogous spectra were recorded for 2-O-methyl- and 4-O-methylphloroacetophenone and for the corresponding phloretin dimethyl ethers. Thus the 4-O-methylphloroacylophenones investigated show a fairly sharp chelate carbonyl absorption band at *ca.* 1 640 cm^{-1} whereas the 2-O-methylphloroacylophenones are characterised by a broad band near 1 620 cm^{-1}. Also in the 1 500—1 600 cm^{-1} region the absorption patterns are different and characteristic.

Dihydrochalcones are apparently not very widely spread in nature. In the bibliography of Karrer [9] only phloretin, asebogenin and 2′,6′-dihydroxy-4′-methoxydihydrochalcone are mentioned. Of these phloretin and asebogenin seem to occur in nature only as glucosides.

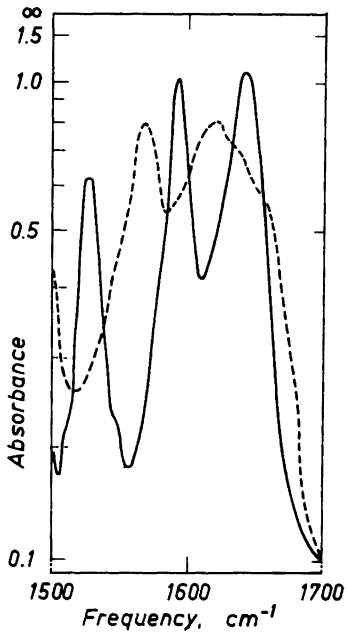


Fig. 1. Part of the infrared spectra for 2′,6′-dihydroxy-4′-methoxydihydrochalcone (I, ——) and 2′,4′-dihydroxy-6′-methoxydihydrochalcone (II, — —). Potassium bromide discs, 13 mm diam., 1 mg of sample.

As for the "calomelanene" mentioned in the introduction it seems that the composition $C_{17}H_{18}O_5$ would fit as well as that proposed by Zopf, who did not perform any determination of the molecular weight or methoxyl content. It is therefore very probable that calomelanene is identical with the 2′,6′-dihydroxy-4,4′-dimethoxydihydrochalcone.

EXPERIMENTAL

The melting points were determined on a Kofler block. The infrared spectra were recorded on a Perkin Elmer No. 21 instrument (sodium chloride prism and potassium bromide discs) and the ultraviolet spectra on a Beckman DK-2 spectrophotometer (solvent ethanol).

Isolation procedures. Air-dried fronds and stems of *Pityrogramma chrysophylla* var. *marginata* collected and identified in the Royal Botanic Gardens, Kew, Richmond, Surrey, England, during the autumn 1958 (7.1 g) were rapidly extracted with ether. The extract was filtered and on evaporation afforded a somewhat waxy material (1.04 g), which melted with some decomposition at 147—165°. Recrystallisation from benzene gave a crystalline material, m.p. 166—170° (0.35 g).

The material in the mother liquors was partitioned between light petroleum (b.p. 40—60°) and dimethyl sulphoxide. The petroleum phase on evaporation gave a colourless wax, m.p. 50—66° (0.1 g), the infrared spectrum of which indicated the presence of hydrocarbons and small amounts of ketones and alcohols. The benzidine test indicated that no phenolic material was present in this fraction. The dimethyl sulphoxide solution was poured into a large excess of water and the mixture was exhaustively extracted with ether. The ether extract after washing and drying was evaporated to give a solid (0.5 g).

Chromatography on paper impregnated with an ethylenediaminetetraacetic acid buffer using dimethyl sulphoxide as the stationary and *iso*propyl ether as the mobile phase according to Wachtmeister and Wickberg [10] showed the presence of the compound isolated

above (R_F 0.20) and another phenolic component (R_F 0.13). There was also a minor component (R_F 0.08).

The mixture was separated by chromatography on a silica gel column impregnated with dimethyl sulphoxide using *iso*propyl ether as the eluant [11]. It was also found advantageous to treat the silica gel with EDTA-buffer. The silica gel was pretreated with nitric acid (*d* 1.42), washed with water and then with a buffer containing 0.015 M disodium-EDTA and 0.005 M EDTA and dried at 120° without any additional washing with water. This chromatography gave a further amount of the compound, m.p. *ca.* 170°, and the compound, R_F 0.13 (60 mg, m.p. *ca.* 140°).

Investigation of the compound m.p. ca. *170°.* Recrystallisation from benzene and sublimation (0.005 mm) gave the pure compound as plates, m.p. 173—175°. (Found: C 70.5; H 5.9; O 23.3; CH_3O 11.1. Calc. for $C_{16}H_{16}O_4$: C 70.6; H 5.9; O 23.5; CH_3O (one) 11.4.)

Infrared spectrum: 3 240 m, 3 050 w, 3 000 w, 2 960 w, 2 930 w, 2 850 w, 2 800—2 400 w, 1 640 s, 1 590 s, 1 525 m, 1 500 w, 1 470 w, 1 435 m, 1 430 m, 1 385 m, 1 360 m, 1 330 w, 1 300 m, 1 230 m, 1 215 s, 1 160 m, 1 080 m, 1 065 w, 1 040 w, 1 030 w, 980 w, 960 m, 905 w, 845 w, 810 s, 765 w, 750 m, 725 w, and 700 cm^{-1} m.

Ultraviolet absorptions: $\lambda_{shoulder}$ 330 mμ (log ε 3.5), λ_{max} 285 (4.37), 226 (4.29) and 210 (4.38).

Compound m.p. ca. *140°.* Recrystallisation from benzene and sublimation gave plates, m.p. 142—145°. (Found: C 66.8; H 6.0; CH_3O 19.8. Calc. for $C_{17}H_{18}O_5$: C 67.5; H 6.0; CH_3O (two) 20.5.)

Infrared spectrum: 3 220 m, 3 020 w, 2 980 w, 2 920 w, 2 810 w, 2 800—2 400 w, 1 640 s, 1 610 m, 1 590 s, 1 525 m, 1 510 s, 1 465 m, 1 440 s, 1 425 m, 1 390 m, 1 360 m, 1 295 m, 1 245 s, 1 220 m, 1 210 s, 1 175 m, 1 160 m, 1 100 w, 1 075 m, 1 060 w, 1 030 m, 975 w, 960 m, 905 w, 855 w, 815 m, 805 s, 790 w and 720 cm^{-1} w.

Ultraviolet absorptions: $\lambda_{shoulder}$ 330 mμ (log ε 3.5), λ_{max} 286 (4.34), 225 (4.40) and 210 (4.33).

Houben-Hoesch acylations. A mixture of phloroglucinol monomethyl ether [12] (0.01 mole), β-phenylpropionitrile [13] or β-(*p*-methoxyphenyl)-propionitrile [15] (0.01 mole) and freshly fused zinc chloride (*ca.* 1 g) in dry ether (50 ml) was saturated with dry hydrogen chloride at 0° and left in the refrigerator for 2—4 days. The supernatant was discarded, the remaining oil or crystalline mixture was washed with small portions of ether and then boiled with water (100 ml) for 1 h and left to cool. The phloroacylophenones crystallised in a fairly pure state in ca 60 % yield. Water of crystallisation was present but was readily removed by drying at 100°.

2′,4′-Dihydroxy-6′-methoxydihydrochalcone was obtained as needles from benzene, m.p. 194—197° (strong sublimation). (Found: C 70.9; H 6.1; CH_3O 11.3. Calc. for $C_{16}H_{16}O_4$: C 70.6; H 5.9; CH_3O 11.4). (Lit. m.p. 189° [15]).

2′,4′-Dihydroxy-4,6′-dimethoxydihydrochalcone crystallised as needles from benzene, m.p. 175—177°. (Found: C 67.8; H 6.0; CH_3O 20.3. Calc. for $C_{17}H_{18}O_5$: C 67.5; H 6.0; CH_3O 20.5).

Methylations. Treatment of 2′,4′-dihydroxy-6′-methoxydihydrochalcone with excess diazomethane in methanol-ether overnight afforded a quantitative yield of 2′-hydroxy-4′,6′-dimethoxydihydrochalcone, which was recrystallised from methanol and from *cyclo*hexane to give prisms, m.p. 106—108°. (Found: C 71.4; H 6.4; CH_3O 21.3. Calc. for $C_{17}H_{18}O_4$: C 71.3; H 6.3; CH_3O 21.7.) It gave a strong brownish red colour with iron(III)-chloride.

Methylation of the phenol, m.p. 173—175°, afforded the same compound, m.p. and mixed m.p. 105—107°. The infrared spectra were identical.

Similarly methylations of 2′,4′-dihydroxy-4,6′-dimethoxydihydrochalcone and the phenol, m.p. 143—145°, afforded phloretin trimethyl ether, m.p. and mixed m.p. 108—110°

Hydrogenations. 5,7-Dihydroxyflavanone was prepared according to Rosenmund's method and was methylated with diazomethane to give 5-hydroxy-7- methoxyflavanone, m.p. 100—102°.

The flavanone (20 mg), palladised charcoal (20 mg, 10 %) and ethanol (10 ml) were shaken in a hydrogen atmosphere for 48 h. Paper chromatography then indicated that most of the starting material had been consumed and that a compound with the same R_F-value as the phenol, m.p. 173—175°, had been formed. The hydrogen consumption was not measured. After filtering the solvent was evaporated and the residue recrys-

tallised from benzene and sublimed to afford a product, m.p. 172—174°, alone or in admixture with the natural product. The infrared spectra were identical.

Naringenin was prepared by acid hydrolysis of commercial naringin (Eastman) and was methylated with diazomethane to 5-hydroxy-4′,7-dimethoxyflavanone, m.p. 119—120°. Hydrogenation as above furnished a product with the same R_F value as the phenol, m.p. 143—145°, and after recrystallisation from benzene and sublimation the identity of the two products was proved by mixed melting point determination and comparison of the infrared spectra.

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