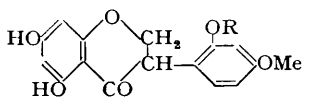
693. *The Synthesis of Homoferreirin.*

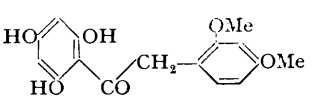
By K. G. Neill.

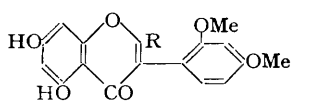
This paper describes the unambiguous synthesis of 5 : 7-dihydroxy-2′ : 4′-dimethoxy*iso*flavanone which is identical with homoferreirin.

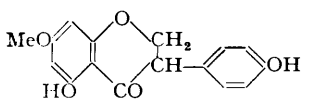
Two phenols, ferreirin and homoferreirin, were isolated from the heartwood of *Ferreirea spectabilis* (King, Grundon, and Neill, *J.*, 1952, 4580) and from degradation studies were assigned the *iso*flavanone structures (I; R = H) and (I; R = Me), respectively (King and Neill, *J.*, 1952, 4752). The synthesis of 5 : 7-dihydroxy-2′ : 4′-dimethoxy*iso*flavanone confirms the structure of homoferreirin.

The 2 : 4-dimethoxyphenylacetonitrile required for the conversion into the deoxybenzoin (II) was prepared in low yield from ethyl 2 : 4-dimethoxyphenylacetate, *via* the amide; but the azlactone method (Mitter and Maitra, *J. Chem. Soc., India*, 1936, **13**, 236) was found to be more convenient. Although the deoxybenzoin failed to condense with ethyl formate in the presence of sodium (cf. *idem, loc. cit.*, Baker, Chadderton, Harborne, and Ollis, *J.*, 1953, 1852), it was readily converted into the *iso*flavone ester (III; R = CO_2Et) in good yield by ethoxalyl chloride (Baker and Ollis, *Nature*, 1952, **169**, 706). On

(I) 

 (II)

(III) 

 (IV)

hydrolysis with cold dilute sodium hydroxide, the acid (III; R = CO_2H) was obtained and this when heated above its melting point gave 5 : 7-dihydroxy-2′ : 4′-dimethoxy*iso*flavone (III; R = H). Although this *iso*flavone was not sufficiently soluble for it to be hydrogenated at room temperature and pressure its diacetate was readily hydrogenated with palladium–charcoal catalyst to the *iso*flavanone diacetate. The latter on mild alkaline hydrolysis gave 5 : 7-dihydroxy-2′ : 4′-dimethoxy*iso*flavanone which was identical with natural homoferreirin.

The isolation from the bark of *Prunus puddum* of another *iso*flavanone, padmakastein (dihydroprunetin) (IV) by Narasimhachar and Seshadri (*Proc. Indian Acad. Sci.*, 1952, **35**, *A*, 202) suggests that this hitherto undiscovered class of compound may be more widely spread in Nature than has been realised.

Experimental

Microanalyses are by Mrs. S. M. Bark, B.Sc., of Nottingham.

2 : 4-*Dimethoxyphenylacetonitrile*.—Ethyl 2 : 4-dimethoxyphenylacetate (10·3 g.) (Pschorr and Knoffer, *Annalen*, 1911, **382**, 56) was heated in a sealed tube with ammonia solution (25 ml.; *d* 0·88) for 3 hr. On cooling, the *amide* separated and crystallised from benzene–light petroleum (b. p. 60—80°) as rectangular plates (7·2 g.), m. p. 130—131° (Found: C, 61·8; H, 7·0; N, 7·2. $C_{10}H_{13}O_3N$ requires C, 61·5; H, 6·7; N, 7·2%). 2 : 4-Dimethoxyphenylacetic acid (2·1 g.) was recovered by acidifying the filtrate. The amide (7·0 g.) was heated under reflux with phosphorus oxychloride (100 ml.) for 1 hr. The residue obtained after removal of excess of phosphorus oxychloride was dissolved in chloroform, the solution washed, the solvent evaporated, and the product chromatographed in benzene on alumina. Concentration of the eluate gave the nitrile (1·9 g.) as needles, m. p. 76° (Found: C, 67·5; H, 6·2; N, 8·0. Calc. for $C_{10}H_{11}O_2N$: C, 67·8; H, 6·3; N, 7·9%) (Mitter and Maitra, *loc. cit.*, give m. p. 76°).

2 : 4-*Dimethoxybenzyl* 2 : 4 : 6-*Trihydroxyphenyl Ketone* (II).—This was prepared from the above nitrile by Mitter and Maitra's method (*loc. cit.*). The ketone (2·76 g.) separated from

aqueous methanol as needles, m. p. 178° (Found: C, 63·1; H, 5·7; OMe, 20·2. Calc. for $C_{16}H_{16}O_6$: C, 63·1; H, 5·3; 2OMe, 20·4%).

5 : 7-*Dihydroxy*-2′ : 4′-*dimethoxy*iso*flavone*-2-*carboxylic Acid* (III; R = CO_2H).—The deoxybenzoin (0·5 g.) in pyridine (1 ml.) was treated with ethoxalyl chloride (1 ml.), and after 1 hr. the mixture was treated with water and extracted with ether. The ethereal solution was washed with 2N-hydrochloric acid and the *ethyl* 5 : 7-*dihydroxy*-2′ : 4′-*dimethoxy*iso*flavone*-2-*carboxylate*, obtained on evaporation crystallised from methanol, forming yellow leaflets (0·48 g.), m. p. 204—206° (Found: C, 60·9; H, 5·1; OMe, 23·0; loss at 150°, 2·2. $C_{20}H_{18}O_8$,0·5H_2O requires C, 60·7; H, 4·8; 3OMe, 23·5; loss, 2·3%). It gave a purple colour with ferric chloride and a red precipitate on acidification after reduction with sodium amalgam. The ester (1·1 g.) in 2N-sodium hydroxide (20 ml.) was kept at room temperature for 24 hr. Acidification precipitated the *acid* which crystallised from methanol in yellow plates (0·9 g.), m. p. 266—268° (decomp.) (Found: C, 57·8; H, 4·0; loss at 150°, 4·8. $C_{18}H_{14}O_8$,H_2O requires C, 57·5; H, 4·3; loss, 4·8%).

5 : 7-*Dihydroxy*-2′ : 4′-*dimethoxy*iso*flavone* (III; R = H).—The acid (0·5 g.) and copper bronze (10 mg.) were heated in three portions at 300—330° until effervescence ceased. Extraction of the residues with acetone gave 5 : 7-*dihydroxy*-2′ : 4′-*dimethoxy*iso*flavone* which crystallised from methanol as cream needles (0·27 g.), m. p. 219—220° (Found: C, 64·9; H, 4·6; OMe, 19·3. $C_{17}H_{14}O_6$ requires C, 65·0; H, 4·5; 2OMe, 19·7%). The *diacetate*, prepared with acetic anhydride and anhydrous sodium acetate, crystallised from ethyl acetate–light petroleum (b. p. 60—80°) as needles, m. p. 200—201° (Found: C, 63·1; H, 4·3; OAc, 30·1. $C_{21}H_{18}O_8$ requires C, 63·3; H, 4·6; 3OAc, 32·4%. The total volatile acid is calculated as acetyl; this includes the molecule of formic acid liberated by the alkaline hydrolysis of the *iso*flavone). This acetate (0·2 g.) was heated under reflux for 24 hr. in acetone (25 ml.) with anhydrous potassium carbonate (1 g.) and methyl sulphate (0·14 ml.), yielding 5 : 7 : 2′ : 4′-tetramethoxy*iso*flavone (0·15 g.) which separated from methanol in rhombs, m. p. and mixed m. p. with a specimen prepared from homoferreirin 204° (Found: C, 66·2; H, 5·3. Calc. for $C_{19}H_{18}O_6$: C, 66·7; H, 5·3%).

5 : 7-*Dihydroxy*-2′ : 4′-*dimethoxy*iso*flavanone* (I; R = Me) (*Homoferreirin*).—5 : 7-Diacetoxy-2′ : 4′-dimethoxy*iso*flavone (0·7 g.) in acetic acid was hydrogenated over palladised charcoal; the 5 : 7-*diacetoxy*-2′ : 4′-*dimethoxy*iso*flavanone* (0·3 g.) crystallised from methanol in needles, m. p. 144° (Found: C, 62·6; H, 4·9; OMe, 15·4. $C_{21}H_{20}O_8$ requires C, 63·0; H, 5·1; 2OMe, 15·5%). The *iso*flavanone (0·3 g.) was shaken intermittently with 2N-sodium hydroxide (30 ml.) for 24 hr. Acidification gave 5 : 7-*dihydroxy*-2′ : 4′-*dimethoxy*iso*flavanone* which crystallised from aqueous methanol in rectangular plates (0·22 g.), m. p. and mixed m. p. with a natural specimen of homoferreirin 168—169° (Found: C, 64·2; H, 5·0; OMe, 18·9. $C_{17}H_{16}O_6$ requires C, 64·6; H, 5·1; 2OMe, 19·4%). The *iso*flavanone (0·15 g.) was heated under reflux for 24 hr. in acetone (20 ml.) with anhydrous potassium carbonate (2 g.) and methyl sulphate (0·20 ml.) yielding 5 : 7 : 2′ : 4′-tetramethoxy*iso*flavanone (0·13 g.) which crystallised from benzene–light petroleum (b. p. 60—80°) in needles, m. p. and mixed m. p. with dimethylhomoferreirin 163°.

The author thanks Professor F. E. King for his continued interest, and gratefully acknowledges a Research Studentship from British Celanese Limited.

THE UNIVERSITY, NOTTINGHAM. [*Received, July 18th,* 1953.]