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Studies on the Chemistry of Lichens

VII *. Structure of Porphyrilic Acid **

CARL AXEL WACHTMEISTER

Institutionen för organisk kemi, Kungl. Tekniska Högskolan, Stockholm, Sweden

Porphyrilic acid, $C_{16}H_{10}O_7$, has been isolated from *Haematomma coccineum* (Dicks.). It contains two phenolic hydroxyl groups, one ether oxygen, one C-methyl group, one carboxyl group and one lactone group. The dimethyl ether has been oxidized by permanganate to a tetracarboxylic acid, which easily forms a yellow dianhydride. Accordingly, the carboxyl group is in *ortho*-position to the methyl group and the lactone group is of the phthalide type. On demethylation and decarboxylation the tetracarboxylic acid ultimately forms 1,7-dihydroxydibenzofuran (I) which has been synthetised. These results are in harmony with two alternative structures, V and VI, for porphyrilic acid.

Zopf [1], in his classical investigations on lichens, studied the grey, leprous species *Haematomma porphyrium* (Pers.), collected from rocks on the peninsula of Kullen, South Sweden. Among other substances, *e.g.* atranorin, he isolated a crystalline, colourless acid, which melted with decomposition at about 298° after darkening from 270°. A decomposition product, porphyrilin, crystallised as characteristic prisms from the melt. In ethanolic solution, porphyrilic acid gave an intense indigo-blue colour with ferric chloride. Crystals of porphyrilic acid gave a green colour with a solution of bleaching powder.

From the yellowish-green species *H. coccineum* (Dicks.), growing together with *H. porphyrium*, Zopf [2] isolated the same porphyrilic acid, atranorin and *l*-usnic acid.

H. coccineum var. *abortivum* (Hepp) was investigated by Hesse [3], who gave an incomplete description of a substance called coccinic acid (m.p. 262—264°), similar to porphyrilic acid. Zopf gave no analyses at all for porphyrilic acid, but in a single analysis of coccinic acid Hesse found: C 58.6; H 3.6 %.

A preliminary investigation of *H. coccineum* (Dicks.), carried out by H. Erdtman several years ago, indicated that the high melting, sparingly soluble

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substance isolated from this lichen by extraction with acetone in a Soxhlet-apparatus probably belonged to a new type of non-hydrolysable lichen acids.

The substance was very similar to Zopf's porphyrilic acid in properties and colour reactions, and this name was adopted for it. *H. coccineum* also contained atranorin and *l*-usnic acid, the latter substance in remarkably large amounts, up to 20 % of the dry weight.

For constitutional studies it was necessary to collect large amounts of lichen material. *H. coccineum* is a more or less pulverous, crustose lichen and is rather common on stone blocks and rocks in Sweden. Sometimes it covers large areas but it often grows together with other lichens, *e.g. H. porphyrium* and *Crocynia*-species, and it is difficult to collect large quantities of quite pure lichen. Our material was collected mainly in the vicinity of Stockholm and in Blekinge, South Sweden, and the greatest possible care was taken to avoid contamination by other species.

The acid was isolated by treating the crystallisate from the acetone extract with boiling benzene, whereby an undissolved residue of crude porphyrilic acid amounting to 2—6 % of the lichen material was obtained. It was further purified *via* its *cyclo*hexylamine salt and after crystallisation from ethanol was obtained as fine, colourless needles, m.p. 280—283°. (decomp.). After drying *in vacuo* at 180°, porphyrilic acid gave analytical values agreeing with the formula $C_{16}H_{10}O_7$. Preparations dried at lower temperatures retained water of crystallisation (1—2 molecules) and traces of ethanol and the analytical values were not quite satisfactory. The *cyclo*hexylamine salt had the composition $C_{16}H_{10}O_7$, $C_6H_{11}NH_2$, indicating that porphyrilic acid is a monobasic acid.

Porphyrilic acid is very sparingly soluble in most solvents but may be crystallised from ethanol or dioxan. The solutions in organic solvents and especially in alkali exhibited a bluish-white fluorescence in ultra-violet light. As found by Zopf [1] the alcoholic solution gave an intense indigo-blue colour with ferric chloride, indicating the occurrence of a phenolic hydroxyl in the *ortho*-position to a carbonyl function, probably a free or esterified carboxyl group [4].

The acid was recovered unchanged after boiling with 1 *N* sodium hydroxide solution as well as after treatment with cold concentrated sulphuric acid and hence is not a depside or a depsidone.

The substance did not contain any methoxyl groups and exhibited no keto-function. Kuhn-Roth determination gave evidence for the presence of one C-methyl group.

With diazomethane, the acid yielded methyl O-dimethyl porphyrilate, $C_{15}H_7O_3(OCH_3)_2COOCH_3$, m.p. 270—272°, hydrolysed by alkali to O-dimethyl-porphyrilic acid, $C_{15}H_7O_3(OCH_3)_2COOH$, also obtained with dimethyl sulphate and alkali. These derivatives were very sparingly soluble in organic solvents.

Hydrolytic titration of the dimethyl ether revealed the presence of a lactone group in addition to the free carboxyl group.

With acetic anhydride and pyridine porphyrilic acid afforded a diacetate, $C_{15}H_7O_3(OCOCH_3)_2COOH$, m.p. 262—265° (decomp.), transformed into a methyl ester, $C_{15}H_7O_3(OCOCH_3)_2COOCH_3$, by diazomethane. Acetylation with acetic anhydride alone yielded another acetate, m.p. 197—199°, which analysed approximately for $C_{15}H_7O_3(OCOCH_3)_2COOCOCH_3$. It gave acetanilide by treatment with aniline in the cold and was obviously a mixed anhydride.

When heated to the melting point, porphyrilic acid lost one molecule of carbon dioxide, yielding a characteristic decomposition product, porphyrilin, $C_{15}H_{10}O_5$, m.p. about 295—300° with sublimation, which like porphyrilic acid exhibited the blue ferric chloride reaction, the green colour with bleaching powder and the strong fluorescence in ultra-violet light. Porphyrilin contained one C-methyl group. On prolonged treatment with diazomethane it furnished a dimethyl ether, $C_{15}H_8O_3(OCH_3)_2$, and acetylation afforded a diacetate, $C_{15}H_8O_3(OCOCH_3)_2$. Hydrolytic titration showed the presence of a lactone group.

In carbonate buffer, O-dimethyl-porphyrilic acid could be oxidized with potassium permanganate to a tetracarboxylic acid (A), $C_{12}H_2O(OCH_3)_2(COOH)_4$, characterized by its tetramethylester. On heating, the acid (A) lost two molecules of water, yielding a yellow dianhydride (B), $C_{12}H_2O(OCH_3)_2(C_2O_3)_2$, m.p. about 330—335° with sublimation.

These results show that porphyrilic acid contains two phenolic hydroxyl groups, one carboxyl group in *ortho*-position to a C-methyl group and one lactone group of the phthalide type. With the exception of the carboxyl group, porphyrilin contains the same functional groups as porphyrilic acid and is obviously formed by a simple decarboxylation. One oxygen atom is unaccounted for in both compounds and is probably present as an ether bridge. The empirical formula for porphyrilic acid, $C_{16}H_{10}O_7$, may therefore be resolved into $(CH_3)(COOH)(OH)_2$ $(—CH_2—O—CO—)C_{12}H_2O$. The $C_{12}H_2O$-residue, due to its composition, appeared to contain a dibenzofuran structure, porphyrilic acid being a hexasubstituted dibenzofuran.

When boiled with hydrobromic acid, the anhydride (B) underwent demethylation and partial decarboxylation to a dihydroxy-dicarboxylic acid (C), $C_{12}H_4O(OH)_2(COOH)_2$, characterized as the tetramethylderivative, $C_{12}H_4O(OCH_3)_2(COOCH_3)_2$.

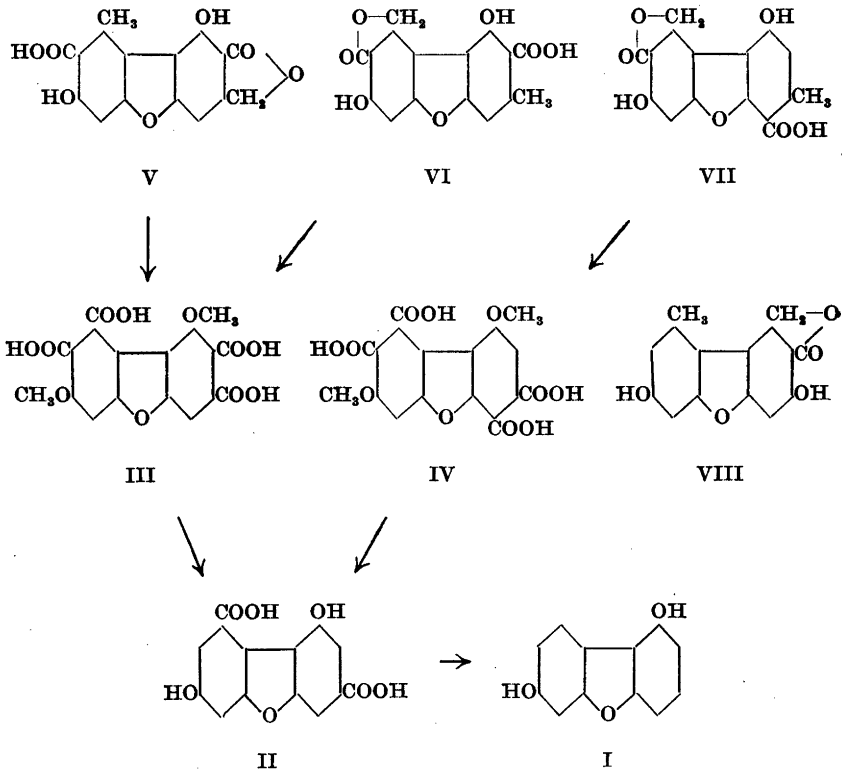
The acid (C) was further decarboxylated by heating with quinoline and a copper chromite catalyst, whereby a phenol (D), $C_{12}H_6O(OH)_2$, m.p. 162.5—164°, was obtained in 70 % yield. It yielded a diacetate, $C_{12}H_6O(OCOCH_3)_2$, m.p. 141—142°. If the above deduction is correct this phenol should be a dihydroxy-dibenzofuran.

In view of the dominating role of orcinol in lichen chemistry it seemed to be most probable that the phenol (D) was related to the dihydroxy-dibenzofuranes derived from a dehydro-diresorcinol. The symmetrical 3,7-dihydroxy- and 1,9-dihydroxy-dibenzofuranes are known [5,6], having m.p. 241° and 215° respectively. The unsymmetrical 1,7-dihydroxy-dibenzofuran, (I), m.p. 163.5—164.5°, has now been prepared. A mixed Ullmann coupling of 2-iodo-resorcinol dimethyl ether and excess of 4-iodo-resorcinol dimethyl ether yielded 2,4,2′,4′-tetramethoxy-biphenyl, m.p. 92—93° (lit.[7] m.p. 93°), 2,6,2′,6′-tetramethoxy-biphenyl, m.p. 174—175° (lit.[8] m.p. 175—176°) and the unknown unsymmetrical isomeride, 2,6,2′,4′-tetramethoxy-biphenyl, m.p. 106—107°. When boiled with hydrobromic acid, the last compound underwent simultaneous demethylation and ring closure to 1,7-dihydroxy-dibenzofuran (I) which was found to be identical with substance (D) by mixed melting point determinations carried out with the free phenols and with the acetates.

Acid (C), from which the phenol (D) (I) is obtained, must have structure (II), as it is decarboxylated only with difficulty, a property characteristic of aromatic *meta*-hydroxy-carboxylic acids. The absence of carboxyl groups in *ortho*-position to a hydroxyl group is further supported by the reddish-brown ferric chloride reaction of this acid.

For the tetracarboxylic acid (A) two structures, (III) and (IV), are probable alternatives. Both should give dianhydrides on heating and loose two molecules of carbon dioxide on demethylation with hydrobromic acid.

From the formulae (III) and (IV) several structures for porphyrilic acid may be derived. An acceptable alternative, however, must explain the smooth decarboxylation of porphyrilic acid to porphyrilin and also the blue ferric reaction of both these substances. These requirements are fulfilled by structures (V), (VI) and (VII), all of which embody the structure of orsellinic acid. In structures (V) and (VI), the free carboxyl group occupies an *ortho*-position but in structure (VII) a *para*-position to a free hydroxyl group. Compounds of the former type are known to form borate complexes, which may be detected by paper chromatographic methods [9]. The R_F values of porphyrilic acid on borate- and phosphate-impregnated paper of pH 8.7 were 0.03 and 0.15 respectively, a clear indication of the formation of a borate complex, and hence structure (VII) may be eliminated. Consequently, porphyrilic acid must be



represented by either of formulae (V) and (VI) and the structure of the acid (A) is (III).

A decision between the alternatives (V) and (VI) requires partial oxidation of O-dimethyl-porphyrilic acid to a tricarboxylic acid, decarboxylation of this acid to the dihydroxy-methyldibenzofuran and synthesis of this compound. The degradations have been accomplished and the synthetic work is in progress.

An isomer of porphyrilin is known among the lichen acids: Strepsilin, m.p. 324°, which has been isolated by Zopf[10] from *Cladonia strepsilis* Wain. According to Shibata [11] it is a derivative of 3,7-dihydroxy-dibenzofuran (VIII). The two substances show great similarities in properties and colour reactions.

EXPERIMENTAL *

Isolation of porphyrilic acid. Extraction of the lichen material with acetone for 2—3 days in a Soxhlet apparatus yielded an acetone extract, worked up as here described for a single run on air-dry *H. coccineum* (160 g, corresponding to 120 g dry, ash-free material). The acetone-solution (2 000 ml) deposited a greyish crystallisate A (7.4 g) which was collected. Evaporation of the filtrate to dryness and extraction of the residue with warm ethanol (250 ml) yielded a yellow crystallisate B (15.6 g), insoluble in ethanol. The mother liquor on evaporation yielded an oil (28 g) containing crystals. It was not further investigated.

Fraction B was dissolved by warming with a saturated solution of sodium acetate in 50 % ethanol (500 ml). The undissolved residue (0.7 g) was crystallised from chloroform (m. p. 195—196°) and identified as atranorin by hydrolysis with 100 % sulphuric acid and subsequent paper chromatography [12].

The solution on dilution with water yielded *l*-usnic acid (11.4 g), m. p. 198—199°, $[\alpha]_D^{20} = -488°$ (Chloroform, $c = 0.266$) after crystallisation from chloroform-ethanol.

Fraction A was extracted with boiling benzene, dissolved in boiling ethanol (1 500 ml) and filtered. Excess *cyclo*hexylamine (4 ml) was added, the *cyclo*hexylamine salt (6.7 g) collected after one night in the refrigerator and washed with ethanol. It was suspended in 50 % ethanol, decomposed with 2 *N* hydrochloric acid and the porphyrilic acid (4.9 g) collected and washed with water. The substance was finally crystallised from ethanol (2 500 ml), yielding fine needles (3.5 g). The analytical sample was purified *via* the *cyclo*hexylamine salt and crystallised several times from ethanol; m. p. 280—283° (decomp.) after darkening from 270°. The substance was analysed after drying to constant weight *in vacuo* at 180° (*prep. I*), at 120° (*prep. II*) and at 70° (*prep. III*). It titrates in the cold as a dibasic acid (thymolphtalein) or as a monobasic acid (bromothymol blue); the end points are not very sharp. (Found: *Prep. I* C 61.1; H 3.31; Equiv. weight 158 ± 5; 323 ± 10. $C_{16}H_{10}O_7$ requires C 61.2; H 3.21; Equiv. weight 157.1; 314.2. *Prep. II* C 57.5; H 3.76; C—CH_3 3.9; 4.0. $C_{16}H_{10}O_7$, H_2O requires C 57.8; H 3.64; C—CH_3 4.5. *Prep. III* C 56.7; H 4.06. $C_{16}H_{10}O_7$, 1.5 H_2O requires C 56.3; H 3.84.)

Colour reactions: Ferric chloride-ethanol, indigo blue; bleaching powder, green; 2,6-dichlorquinone-chlorimide (Gibbs reagent), blue; diazotised benzidine, red. Cold concentrated sulphuric acid dissolved porphyrilic acid, giving a colourless solution, from which it was recovered unchanged on addition of water. The acid is scarcely soluble in sodium bicarbonate solution, but is soluble in sodium carbonate and sodium hydroxide solutions. The solutions are colourless. Boiling with 1 *N* sodium hydroxide for one hour did not affect the acid. Alkaline permanganate was reduced rapidly in the cold, but ammoniacal silver nitrate solution only on heating.

The *cyclo*hexylamine salt was analysed after crystallisation from 50 % ethanol and drying *in vacuo* at 90°. M. p. 274—278° (decomp.). (Found: C 63.7; H 5.64; N 3.16. $C_{16}H_{10}O_7$, $C_6H_{11}NH_2$ requires C 63.9; H 5.61; N 3.38.)

* All melting points uncorrected.

Paper chromatography. The purity of porphyrilic acid and many of its derivatives and degradation products was conveniently controlled by chromatography on buffered paper with *n*-butanol-water as solvent system [9,12]. On paper (Whatman no. 1) impregnated with phosphate buffer of pH 8.7 and 11.7 the R_F values of porphyrilic acid were 0.15 and 0.02 respectively, whereas the R_F value of porphyrilic acid on paper impregnated with borate buffer of pH 8.7 was only 0.03. The spots showed a bluish-white fluorescence in ultraviolet light and could also be detected by spraying with a solution of diazotised benzidine or with Gibbs reagent.

Acetylation of porphyrilic acid. a) *Diacetoxy-porphyrilic acid.* Porphyrilic acid (0.30 g) was briefly boiled with acetic anhydride (5 ml) and pyridine (5 ml). The solution was evaporated to dryness *in vacuo*, giving a quantitative yield of the diacetate, crystallising from acetone or ethanol in needles, m. p. 262—265° (decomp.). (Found: C 60.6; H 3.58; CH_3CO 21.1, 22.1; Equiv. weight 399. $C_{20}H_{14}O_9$ requires C 60.3; H 3.54; CH_3CO 21.7; Equiv. weight 398.3.)

b) *Methyl diacetoxy-porphyrilate.* A small excess of ethereal diazomethane was added to a solution of the diacetate (250 mg) in acetone (150 ml), followed after 0.5 minutes by a few drops of acetic acid. The methyl ester crystallised from acetone in fine needles, m. p. 241—243°. (Found: C 61.5; H 3.97; OCH_3 7.60, 7.42. $C_{21}H_{16}O_9$ requires C 61.2; H 3.91; OCH_3 7.53.)

c) *Mixed anhydride of diacetoxy-porphyrilic acid and acetic acid.* Porphyrilic acid (450 mg) was boiled for 30 minutes with acetic anhydride (10 ml) and the solution evaporated to dryness *in vacuo*. The product crystallised from dry acetone in needles, m. p. 197—199°, then solidifying and decomposing gradually from 250°. (Found: C 60.2; H 3.66; CH_3CO 27.1. $C_{22}H_{16}O_{10}$ requires C 60.0; H 3.66; CH_3CO 29.3.)

d) *Reaction of the mixed anhydride with aniline.* Aniline (0.1 ml) was added to a solution of the above acetate (140 mg) in dry acetone (60 ml). After standing over-night at room-temperature, the solution was evaporated to dryness *in vacuo* and the residue treated with ether (100 ml). The ethereal solution was washed with 2 *N* hydrochloric acid, sodium carbonate solution and water and evaporated to dryness. Acetanilide (25 mg), m. p. 110—111°, was obtained and identified by direct comparison with an authentic specimen (m. p. 113—114°).

Methylation of porphyrilic acid. a) *Methyl O-dimethyl porphyrilate.* Porphyrilic acid (1 g) was suspended in acetone containing a trace of methanol and treated with an excess of ethereal diazomethane for several days, until a sample gave no colour with ferric chloride. After several crystallisations from pyridine and pyridine-ethanol the product formed fine needles, m. p. 270—272°, sparingly soluble in most organic solvents. The substance showed a very intense white fluorescence in ultraviolet light. For analysis the sample was dried *in vacuo* at 120°. (Found: C 64.1; H 4.53; OCH_3 25.8. $C_{19}H_{16}O_7$ requires C 64.0; H 4.53; OCH_3 26.1.)

b) *O-Dimethyl-porphyrilic acid.* The above ester (500 mg) in 1 *N* sodium hydroxide (20 ml) and ethanol (20 ml) was boiled under reflux for one hour, and the solution acidified with hydrochloric acid. The voluminous precipitate was collected, dried and crystallised from pyridine (50 ml), yielding small needles (400 mg). Before analysis it was recrystallised twice from pyridine and finally washed with glacial acetic acid and methanol and dried *in vacuo* at 130°. The acid gradually decomposed from about 320°. On phosphate-impregnated papers of pH 8.7 and 11.7, the acid showed R_F values 0.45 and 0.30 respectively (*n*-butanol-water). The spots were detected by means of their bluish-white fluorescence in ultra-violet light.

The pyridine solution of O-dimethyl-porphyrilic acid titrates with 0.05 *N* sodium hydroxide as a monobasic acid (bromothymol blue). After hydrolysis with excess boiling 0.05 *N* sodium hydroxide (20 minutes) and back-titration of the cold solution with 0.02 *N* hydrochloric acid, it consumed two moles of alkali (thymol blue). (Found: C 62.6, 62.9; H 4.19, 4.26; OCH_3 18.2; Equiv. weight 344; 172. $C_{18}H_{14}O_7$ requires C 63.2; H 4.12; OCH_3 18.1; Equiv. weight 342.3; 171.2.)

The same compound was obtained by methylation with dimethyl sulphate: Sodium hydroxide solution (5 ml, 40 %) was added to a suspension of porphyrilic acid (5.1 g) in water (100 ml) and methanol (50 ml), whereupon the acid passed into solution. Dimethyl sulphate (50 ml) and sodium hydroxide solution (50 ml, 40 %) were added in small portions with continuous shaking. At the end of the reaction a crystalline precipitate appeared consisting of methyl O-dimethyl porphyrilate. The reaction mixture was acidified with

hydrochloric acid, the precipitate collected and boiled for one hour with 1 *N* sodium hydroxide (150 ml) and ethanol (150 ml) to hydrolyse the ester. Acidification with hydrochloric acid yielded crude O-dimethylporphyrilic acid (5.0 g), identified by paper chromatography as described above. It was used without further purification to the oxidative degradations.

Porphyrilin. Porphyrilic acid was heated in a test tube to about 300° and the gas evolved taken up in barium hydroxide solution and identified as carbon dioxide. The decomposition product, porphyrilin, sublimed as long yellowish-white needles on the wall of the tube. Preparatively, porphyrilic acid (300—500 mg) was rapidly distilled in a test tube *in vacuo* over a free flame. Porphyrilin sublimed in 70—80 % of the theoretical yield and crystallised from methyl ethyl ketone or glacial acetic acid as white needles, m.p. 295—300° with sublimation from about 250°. It was sparingly soluble in the common solvents and gave a green colour with bleaching powder, an indigo-blue colour with ferric chloride and a blue colour with Gibbs reagent. Sodium hydroxide solution dissolved the substance giving a yellowish solution, but it was only slightly soluble in sodium carbonate solution.

On phosphate-buffered paper of pH 8.7 and 11.7, porphyrilin showed R_F values of 0.72 and 0.50 respectively. On borate-buffered paper of pH 8.7 it showed R_F = 0.69. (*n*-butanol-water.) The spots were detected in ultra-violet light (bluish-white fluorescence) and gave a redbrown colour with a solution of diazotised benzidine. Crude preparations of porphyrilin gave a second spot (R_F = 0.08, pH 11.7), having an intense yellowish fluorescence in ultra-violet light. This unknown impurity prooved very difficult to remove completely.

The analytical sample was crystallised from methyl ethyl ketone and dried *in vacuo* at 50° (*prep. I*) and at 150° (*prep. II*). The equivalent weight was determined by boiling for one hour with 0.05 *N* sodium hydroxide and back-titrating with 0.02 N hydrochloric acid (thymol blue). (Found: *prep. I.* C 62.4; H 4.40. $C_{15}H_{10}O_5$, H_2O requires C 62.5; H 4.20. *Prep. II.* C 65.9; H 3.74; equiv. weight 270 ± 10. $C_{15}H_{10}O_5$ requires C 66.7; H 3.73; equiv. weight 270.2.)

Porphyrilin dimethyl ether. Porphyrilin (300 mg) was dissolved in acetone (350 ml) containing a trace of methanol and treated with an excess of ethereal diazomethane for about two weeks until a sample gave only a faint colour with ferric chloride. The crude dimethyl ether was distilled *in vacuo* and crystallised from glacial acetic acid in needles, m.p. 267—269°. (Found: C 68.4; H 4.66; OCH_3 20.2; C—CH_3 4.4. $C_{17}H_{14}O_5$ requires C 68.5; H 4.73; OCH_3 20.8; C—CH_3 5.0.)

Porphyrilin diacetate. Porphyrilin (130 mg) was boiled briefly with acetic anhydride (3 ml) and pyridine (2 ml) and allowed to stand over night. The product (140 mg) was collected and crystallised from acetone in long needles, m.p. 235—237°. (Found: C 64.4; H 3.78; CH_3CO 24.0. $C_{19}H_{14}O_7$ requires C 64.4; H 3.98; CH_3CO 24.3.)

Permanganate oxidation of O-dimethyl porphyrilic acid. A solution of O-dimethyl porphyrilic acid (1.14 g = 3.35 mmoles) in water (200 ml) containing sodium carbonate (1.5 g) was heated on the boiling water-bath and powdered potassium permanganate (2.10 g = 13.3 mmoles) was added in small portions with stirring over 7 hours. After addition of a few drops of methanol, the manganese sludge was removed by filtration and washed with hot water. The combined filtrates were concentrated to 40 ml and acidified with conc. hydrochloric acid (5 ml). The crude acid (A) was collected, dissolved in 0.2 *N* sodium hydroxide (40 ml), the solution filtered and the acid precipitated in the cold with 2 *N* hydrochloric acid (5 ml). The compound (830 mg, yield 60 %) formed a yellowish white powder and was analysed after drying *in vacuo* at room temperature. The acid is sparingly soluble in most common solvents and possesses no sharp melting point. It easily looses water on heating, forming a yellow dianhydride (see below). (Found: OCH_3 15.3; equiv. weight 102. $C_{18}H_{12}O_{11}$ requires OCH_3 15.4; equiv. weight 101.1.)

Treatment of the acid (A) in acetone suspension with ethereal diazomethane furnished a tetramethyl ester, crystallising from acetone in prisms, m.p. 221.5—223°. (Found: C 57.5; H 4.40; OCH_3 39.8. $C_{22}H_{30}O_{11}$ requires C 57.4; H 4.38; OCH_3 40.5.)

Dianhydride of acid A. The acid (A) (980 mg) was heated *in vacuo* at 150° (loss of weight: found 8.9, calc. 9.6 %) and then sublimed *in vacuo* (1 mm) over a free flame; yield 850 mg. A small sample was resublimed (bath-temp. 270—290°, 0.05 mm) and analysed. The anhydride formed a micro-crystalline, yellow powder, m.p. 330—335° with sublimation. It was hydrolysed with boiling aqueous pyridine and the resulting solution

titrated with 0.05 *N* sodium hydroxide (bromothymol blue). (Found: C 58.5; H 2.29; OCH_3 17.0; equiv. weight 92. $C_{18}H_8O_9$ requires C 58.7; H 2.19; OCH_3 16. 9; equiv. weight 92.1.)

Demethylation and decarboxylation of acid (A). The dianhydride (B) (920 mg) of the acid (A) was heated under reflux for 3 days with hydrobromic acid (25 ml, $d = 1.5$). After cooling, the precipitate of the crude acid (C) (750 mg) was collected and crystallised from dioxan until pure, as shown by paper chromatography. The acid formed yellow needles, which gradually decomposed from about 250°. It had an R_F value of 0.55 on phosphate-buffered paper of pH 4.5 (*n*-butanol-water). The spot showed a yellowish fluorescence in ultra-violet light and gave a brown colour with diazotised benzidine. In ethanol, the acid gave a reddish brown colour with ferric chloride. It crystallised with 2 molecules of dioxan, removed completely only after drying *in vacuo* at 180°. (Loss of weight: 38.2 %. $C_{14}H_8O_7$, 2 $C_4H_8O_2$ requires 38.0 %. Found: C 57.8; H 2.74; $C_{14}H_8O_7$ requires C 58.3; H 2.80).

With ethereal diazomethane, the acid yielded a tetramethylderivative, crystallising from ethanol or acetic acid in light brownish needles, m.p. 149.5—150.5°. (Found: C 62.8; H 4.72; OCH_3 35.25. $C_{18}H_{16}O_7$ requires C 62.8; H 4.68; OCH_3 36.05).

Decarboxylation of acid (C). The acid (C) (300 mg) in quinoline (5 ml) was boiled with a copper chromite catalyst (60 mg) for 3 hours in a nitrogen atomsphere. The reaction mixture was taken up in ether, filtered and the insoluble material washed thoroughly with ether. The ethereal solution was shaken with 2 *N* sulphuric acid and water, dried with sodium sulphate and evaporated to dryness. On distillation *in vacuo* the resulting brownish oil (200 mg) yielded the crude phenol (D) (160 mg) as yellowish crystals, m.p. 150—153°. Crystallisation from benzene afforded needles, m.p. 162.5—164°, undepressed on admixture with synthetic 1,7-dihydroxy-dibenzofuran, m.p. 163.5—164.5°, described below. Colour reactions: ferric chloride, no colour: Gibbs reagent, blue; diazotised benzidine, red. The two phenols also proved chromatographically indistinguishable ($R_F = 0.14$, solvent system benzene-water) and clearly distinguished from 3,7-dihydroxy-dibenzofuran [5] (m.p. 241°, $R_F = 0.07$) and 1,9-dihydroxy-dibenzofuran [6] (m.p. 215°, $R_F = 0.75$). (Found: C 71.3; H 3.94. $C_{12}H_8O_3$ requires C 72.0; H 4.03.)

The diacetate, obtained from the crude phenol with acetic anhydride and pyridine, crystallised from methanol in needles, m.p. 141—142°, undepressed when mixed with synthetic 1,7-diacetoxy-dibenzofuran, m.p. 142—143°. (Found: C 66.7; H 4.27; $C_{16}H_{12}O_5$ requires C 67.6; H 4.26.)

2,6,2',4'-tetramethoxy-biphenyl. 4-Iodo-resorcinol dimethyl ether was prepared as described by Kauffmann and Kieser [13]. 2-Iodo-resorcinol dimethyl ether was obtained from 2-nitroresorcinol as described by Adams *et al.*[8]. 4-Iodo-resorcinol dimethyl ether (27 g), 2-iodo-resorcinol dimethyl ether (3 g) and copper bronze (90 g) was mixed thoroughly and warmed in a saltbath to 190—200°. As soon as the reaction started, the temperature in the reaction vessel rapidly rose to 260—280° and the heating was interrupted. After 10 minutes, the reaction was completed by warming to 250° for 20 minutes. The reaction mixture was extracted with acetone and the solution concentrated to an oil, which was distilled *in vacuo*. The main fraction, 10.7 g (200—220°, 1 mm), on crystallisation from methanol (40 ml) yielded a fraction A (8.2 g), m.p. 85—88°. The motherliquor on slow evaporation in the air yielded a fraction B (0.9 g), m.p. 90—100°, from which by repeated crystallisation from methanol pure 2,6,2',4'-tetramethoxy-biphenyl (0.1 g), m.p. 106—107°, was obtained. (Found: C 69.2; H 6.59; OCH_3 44.9. $C_{16}H_{18}O_4$ requires C 70.1; H 6.61; OCH_3 45.25.)

Crystallisation from methanol of fraction A gave minute amounts of 2,6,2',6'-tetramethoxy-biphenyl [8], m.p. 174—175° and 2,4,2',4'-tetramethoxy-biphenyl [7] (6 g), m.p. 92—93°.

A more convenient separation of the isomeric biphenyls was achieved by chromatography on alumina, using the method of fractional elution [14]. The column was constructed in light petroleum (b.p. 40—60°). The biphenyl-mixture (1 g, from fraction B and its mother-liquor) in benzene-petrol (100 ml; 7—93) was adsorbed on alumina (30 g). The 2,4,2',4'-tetramethoxy-biphenyl was eluted by the same solvent, and the 2,6,2',4'-tetramethoxy-biphenyl by gradually increasing the benzene-content to 30 vol. %. Yield 0.3 g, m.p. 102—104° after one crystallisation from methanol.

1,7-dihydroxy-dibenzofuran. 2,6,2',4'-tetramethoxy-biphenyl (0.47 g) and hydrobromic acid (10 ml, $d = 1.5$) were boiled under reflux in an atmosphere of carbon dioxide

for 10 hours. On cooling, the dark solution deposited greyish needles, which were collected, dried and distilled *in vacuo*, yielding a rapidly crystallising oil (0.27 g). The substance crystallised from benzene in colourless needles, m. p. 163.5—164.5°; it was also observed in a lower-melting form, m. p. 156—157°. The colour reactions were identical with those described above for the phenol (D). (Found: C 70.8; H 3.94. $C_{12}H_8O_3$ requires C 72.0; H 4.03.)

1,7-diacetoxy-dibenzofuran. This compound was obtained from the phenol with acetic anhydride and pyridine. It crystallised from methanol in needles, m. p. 142—143°. (Found: C 67.6; H 4.20. $C_{16}H_{12}O_5$ requires C 67.6; H 4.26.)

1,7-dimethoxy-dibenzofuran. Treatment of the phenol with ethereal diazomethane for two days furnished an oil which was distilled *in vacuo* and then crystallised from 50 % acetic acid. Needles, m. p. 67—68°. (Found: OCH_3 27.8. $C_{14}H_{12}O_3$ requires OCH_3 27.2.)

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