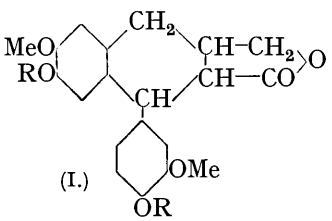
142. *The Constituents of Natural Phenolic Resins. Part II. "Sulphite-liquors Lactone."*

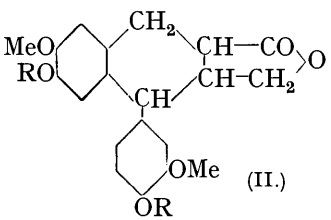
By Robert D. Haworth and George Sheldrick.

In view of the wide occurrence of compounds of the diarylbutane and phenylnaphthalene types (see preceding paper) methods for their preparation have been investigated. This communication concerns the synthesis of some substances of importance in connexion with the constitution of matairesinol and " sulphite-liquors lactone " (see Part I for the more important references).

Holmberg (*loc. cit.*) formulated " sulphite-liquors lactone " as a *cyclo*butane derivative, but the later investigations of Erdtman (*loc. cit.*) led to formula (I; R = H) or (II; R = H). Emde and Schartner (*loc. cit.*) identified " sulphite-liquors lactone " with the main constituent of the resin of *Picea excelsa*, and also with tsugaresinol which had been isolated previously by Kawamura (*loc. cit.*) from the wood of *Tsuga Sieboldii*, Carr. As a result of their analytical figures, Emde and Schartner suggest structure (III; R = H) for " sulphite-liquors lactone." Erdtman's conclusions are largely based on the isolation of veratroylveratric acid and 6 : 7-*dimethoxy*-1-(3′ : 4′-*dimethoxyphenyl*)*naphthalene*-2 : 3-*dicarboxylic acid* (IV) as oxidation products of the dimethyl ether of the lactone. The formation of (IV) established the carbon skeleton of the dimethyl ether, and the positions of



(I.)



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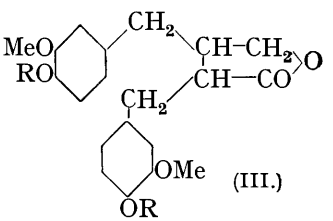


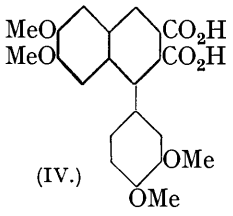
(III.)

the phenolic hydroxyl groups were assumed from biogenetic relationships. The structure assigned to the acid (IV) depended on its identity with a synthetic acid, prepared by one of us and Dr. C. R. Mavin in May, 1932, by the dimerisation of 3 : 4-dimethoxyphenylpropiolic acid with acetic anhydride. The evidence in support of the structure rested entirely on analogy; phenylpropiolic acid is converted into 1-phenylnaphthalene-2 : 3-dicarboxylic acid (Michael, *Ber.*, 1912, **39**, 1909; Stobbe, *ibid.*, 1913, **40**, 3373) under similar conditions. During the present work conclusive evidence has been obtained for the structure of the acid (IV), the positions of the phenolic hydroxyl groups of " sulphite-liquors lactone " have been established, and a decision between (I), (II), and (III) has been made in favour of (II).

The *anhydride* of the dicarboxylic acid (IV) was decarboxylated by heating with quinoline and copper bronze to 6 : 7-*dimethoxy*-1-(3′ : 4′-*dimethoxyphenyl*)*naphthalene* (V), but in very small yield. Fortunately, two additional methods were discovered for the preparation of (V), and its structure has been confirmed by demethylation, and distillation of the tetrahydroxy-compound with zinc dust, 1-phenylnaphthalene being obtained.

The first synthetical experiments were made with β-3 : 4-*dimethoxybenzoyl*-α-3′ : 4′-

dimethoxybenzylidenepropionic acid (VI), the *γ-lactone* of which was obtained from veratraldehyde and sodium β-3 : 4-dimethoxybenzoylpropionate by the method of Borsche (*Ber.*,



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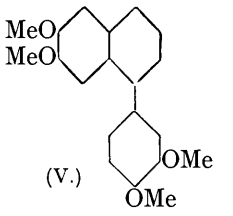

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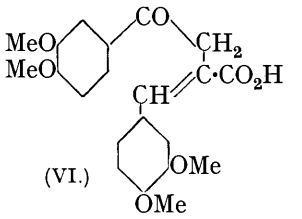
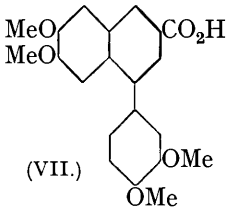


(VI.)

1914, **47**, 1108), the modifications introduced by Haq, Kapur, and Ray (J., 1933, 1087) giving inferior results. When the acid (VI) was heated with methyl-alcoholic hydrogen chloride, it was converted into the *methyl* ester of 6 : 7-*dimethoxy*-1-(3′ : 4′-*dimethoxyphenyl*)-*naphthalene*-3-*carboxylic acid*, from which the corresponding *acid* (VII) was prepared. This acid was also obtained by the action of alcoholic iodine on the lactone of (VI). The acid (VII) was converted into (V) in good yield by heating with quinoline and copper bronze. The difficulty experienced in attempts to esterify or reduce the acid (VI) has led to the examination of other routes to compounds of the diarylbutane and phenylnaphthalene types.

3 : 4 : 3′ : 4′-Tetramethoxybenzophenone reacted with ethyl succinate in the presence of potassium ethoxide to give *γ-di*-(3 : 4-*dimethoxyphenyl*)*itaconic acid* (VIII), the *anhydride* of which was converted into 1-*keto*-5 : 6-*dimethoxy*-3-(3′ : 4′-*dimethoxyphenyl*)*indene*-2-*acetic acid* (IX) by treatment with aluminium chloride. Stobbe and Vieweg (*Ber.*, 1902, **35**, 1727) showed that diphenylitaconic acid was converted into an orange indone derivative on treatment with cold sulphuric acid, and the bright red colour of (IX) is consistent with the suggested structure. Catalytic reduction of the indone (IX) gave an unusual result; both the keto-group and the ethylenic linkage were reduced and 5 : 6-*dimethoxy*-3-(3′ : 4′-*dimethoxyphenyl*)*hydrindene*-2-*acetic acid* was obtained. The substituted diphenylitaconic acid (VIII) was reduced catalytically to *bis*-(3 : 4-*dimethoxyphenyl*)*methylsuccinic acid* (X), but almost quantitative yields of this acid were obtained by condensing two molecular proportions of veratrole with ethyl hydroxymethylenesuccinate in cold acetic acid–sulphuric acid solution. The anhydride of (X), when treated with aluminium chloride in nitrobenzene, was converted in 90% yield into 4-*keto*-6 : 7-*dimethoxy*-1-(3′ : 4′-*dimethoxyphenyl*)-1 : 2 : 3 : 4-*tetrahydronaphthalene*-2-*carboxylic acid* (XI). The constitution was established by reducing the acid (XI), or better its *ethyl* ester, by Clemmensen's method to 6 : 7-*dimethoxy*-1-(3′ : 4′-*dimethoxyphenyl*)-1 : 2 : 3 : 4-*tetrahydronaphthalene*-2-*carboxylic acid*, which was converted into 6 : 7-dimethoxy-1-(3′ : 4′-dimethoxyphenyl)naphthalene (V) by heating with selenium at 280°.



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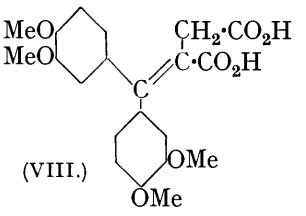

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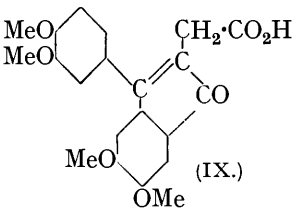
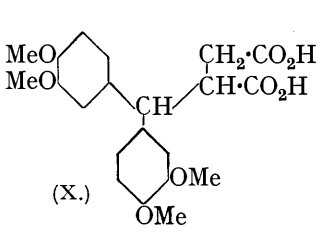


(IX.)

The accessibility of the acid (XI) rendered it extremely promising for the synthesis of compounds of type (I; R = Me). A dibromo-compound, probably *ethyl* 3-*bromo*-4-*keto*-6 : 7-*dimethoxy*-1-(6′-*bromo*-3′ : 4′-*dimethoxyphenyl*)-1 : 2 : 3 : 4-*tetrahydronaphthalene*-2-*carboxylate*, was prepared by the action of bromine on the ethyl ester of (XI). The dibromo-compound was heated with diethylaniline and converted into *ethyl* 4-*hydroxy*-6 : 7-*dimethoxy*-1-(6′-*bromo*-3′ : 4′-*dimethoxyphenyl*)*naphthalene*-2-*carboxylate* (XII), which reacted with formaldehyde to give the *lactone* of 4-*hydroxy*-6 : 7-*dimethoxy*-1-(6′-*bromo*-3′ : 4′-*dimethoxyphenyl*)-3-*hydroxymethylnaphthalene*-2-*carboxylic acid* (XIII), but the

difficulty experienced in the removal of the bromine from both the ester (XII) and the lactone (XIII) led to the temporary abandonment of this method.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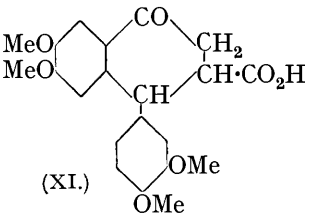
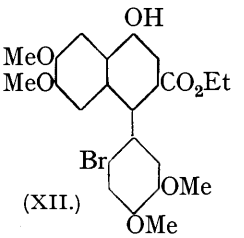
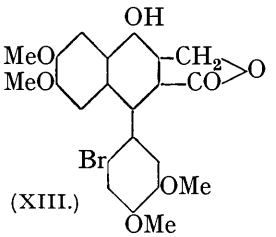

(XI.)


(XII.)

The ethyl ester of the acid (XI) reacted with ethyl formate in presence of sodium to give an almost quantitative yield of *ethyl* 3-*aldehydo*-4-*keto*-6 : 7-*dimethoxy*-1-(3′ : 4′-*dimethoxyphenyl*)-1 : 2 : 3 : 4-*tetrahydronaphthalene*-2-*carboxylate* (XIV), which was reduced with sodium amalgam to an acid, $C_{22}H_{26}O_8$, which is provisionally regarded as 4-*hydroxy*-6 : 7-*dimethoxy*-1-(3′ : 4′-*dimethoxyphenyl*)-3-*hydroxymethyl*-1 : 2 : 3 : 4-*tetrahydronaphthalene*-2-*carboxylic acid* (XV). The analytical figures obtained were in accordance with the suggested structure, but boiling with 10% sulphuric acid or heating at 200° converted the acid (XV), in 45% yield, into the α-form of the *lactone* of 6 : 7-*dimethoxy*-1-(3′ : 4′-*dimethoxyphenyl*)-3-*hydroxymethyl*-1 : 2 : 3 : 4-*tetrahydronaphthalene*-2-*carboxylic acid* (I; R = Me), m. p. 187°. This lactone can exist in a number of stereoisomeric forms, and the compound, m. p. 187°, is referred to as the α-form in order to distinguish it from a stereoisomeride which is described below. The explanation of this reductive lactonisation of (XV) into (I; R = Me) must be deferred until more data are available, but the structure of the product is consistent with the properties. The lactone (I; R = Me) reacted as a saturated compound towards both hydrogen and cold dilute potassium permanganate solution, and it was dehydrogenated by lead tetra-acetate, but not by heating with palladium-black, to give the lactone of 6 : 7-dimethoxy-1-(3′ : 4′-dimethoxyphenyl)-3-hydroxymethylnaphthalene-2-carboxylic acid (XVI), m. p. 255°, which on oxidation with sodium hypobromite was converted into the dicarboxylic acid (IV).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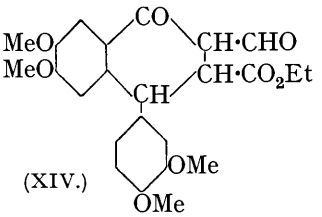
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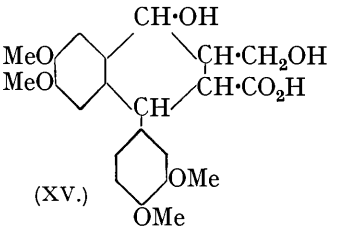
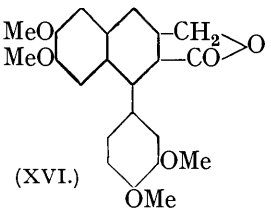
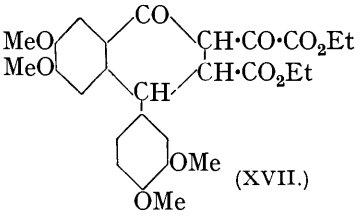

(XV.)

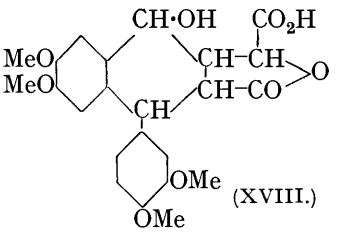
A reaction similar to that observed during the conversion of (XV) into (I; R = Me) was encountered in another series of experiments. The ethyl ester of the keto-acid (XI) reacted almost quantitatively with ethyl oxalate in the presence of potassium ethoxide, giving a yellow product, probably (XVII). This was reduced with aluminium amalgam in moist ethereal solution to a colourless compound, which was hydrolysed and converted into a lactonic acid, provisionally formulated as the *lactone* of 4-*hydroxy*-6 : 7-*dimethoxy*-2-*carboxy*-1-(3′ : 4′-*dimethoxyphenyl*)-1 : 2 : 3 : 4-*tetrahydronaphthalene*-3-*glycollic acid* (XVIII).* This substance crystallises with one molecule of water of crystallisation which cannot be removed without profound decomposition, but the lactonic nature of the compound was established by titration with alkali. When the lactone was heated at 200°, a 25% yield of the β-form of the *lactone* of 6 : 7-*dimethoxy*-1-(3′ : 4′-*dimethoxyphenyl*)-3-*hydroxymethyl*-1 : 2 : 3 : 4-*tetrahydronaphthalene*-2-*carboxylic acid* (I; R = Me), m. p. 208°, was obtained. The formation of this reduced decarboxylation product is obviously analogous to the conversion of (XV) into (I; R = Me) and is equally difficult to understand. A

* Two alternative formulæ can be derived by including the nuclear CH·OH group in the γ-lactone ring.

further study of (XV), (XVIII), and related compounds is contemplated. The lactone, m. p. 208°, was unaffected by hydrogen in the presence of palladium, but it was de-

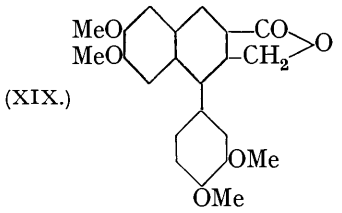

(XVI.)

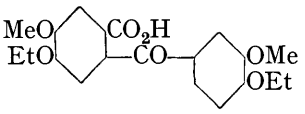

(XVII.)


(XVIII.)

hydrogenated more readily than the α-form described above. Either heating with palladium-black at 250° or treatment with lead tetra-acetate at 70° converted it into the lactone (XVI), m. p. 255°, identical with the substance obtained from the α-form of the lactone (I; R = Me).

It has now been found that " sulphite-liquors lactone " dimethyl ether can be converted into a dehydrolactone, $C_{22}H_{20}O_6$, m. p. 215—216°,* either by heating with selenium or by means of lead tetra-acetate. The dehydrolactone was unattacked by hydrogen in the presence of palladium. Although it differed from the lactone (XVI), m. p. 255°, on oxidation with potassium permanganate, it was converted into the dicarboxylic acid (IV). It must be concluded from these observations that the dehydrolactone, m. p. 215—216°, is the lactone of 6 : 7-dimethoxy-1-(3′ : 4′-dimethoxyphenyl)-2-hydroxymethylnaphthalene-3-carboxylic acid (XIX) and that " sulphite-liquors lactone " dimethyl ether must have the structure (II; R = Me). A synthesis of (XIX) is in progress, but the above conclusions are substantiated by the conversion of matairesinol dimethyl ether into a mixture of the lactones (XVI) and (XIX) (see previous communication).


(XIX.)


(XX.)

The positions of the phenolic hydroxyl groups in " sulphite-liquors lactone " have been established by preparing the diethyl ether and oxidising this with permanganate to 5-methoxy-4-ethoxy-2-(3′-methoxy-4′-ethoxybenzoyl)benzoic acid (XX), identical with the acid prepared by Vanzetti and Dreyfuss (*loc. cit.*) from *iso*livil. Consequently " sulphite-liquors lactone " must be represented by formula (II; R = H).

The formation of a dibromo-substitution product from " sulphite-liquors lactone " dimethyl ether (Erdtman, *loc. cit.*) may be used as an argument against formula (II; R = Me) and in favour of (III; R = Me). However, it has now been shown that phenylnaphthalene derivatives, such as the acid (VII) and 6 : 7-dimethoxy-1-(3′ : 4′-dimethoxyphenyl)-1 : 2 : 3 : 4-tetrahydronaphthalene-3-carboxylic acid, readily yield dibromo-substitution products by the action of bromine in cold acetic acid solution. Although the positions of the bromine atoms have not been established, the formation of a dibromo-derivative can no longer be regarded as an objection to formula (II; R = Me) for " sulphite-liquors lactone " dimethyl ether. Formula (III) can be excluded; it is shown in the previous communication that this formula is required to account for the properties of matairesinol dimethyl ether.

* Dr. Erdtman (private communication) informs us that he had previously prepared this dehydrolactone by the tetra-acetate method. The amount obtained was insufficient to enable him to crystallise the product to constant m. p., and no analyses were made.

Experimental.

6 : 7-*Dimethoxy*-1-(3′ : 4′-*dimethoxyphenyl*)*naphthalene*-2 : 3-*dicarboxylic Acid* (IV).—(With C. R. Mavin) 3 : 4-Dimethoxyphenylpropiolic acid (3·2 g.) (Perkin and Schiess, J., 1904, **85**, 164) was dissolved in boiling acetic anhydride (20 c.c.), and the solution heated at 100° for 4 hours. After cooling, the solid was collected; it crystallised from nitrobenzene (carbon) in pale yellow prisms (2·4 g.), m. p. 305—306° (Found: C, 66·8; H, 4·7. $C_{22}H_{18}O_7$ requires C, 67·0; H, 4·6%). This *anhydride*, which was sparingly soluble in the usual organic solvents, dissolved slowly in boiling 10% sodium hydroxide solution; acidification of the cold alkaline solution precipitated the dibasic *acid* (IV), which crystallised from methyl alcohol–chloroform in slender colourless needles, m. p. 232—234° (Found: C, 64·2; H, 5·0. $C_{22}H_{20}O_8$ requires C, 64·1; H, 4·9%). When the acid is heated above its m. p., it is rapidly converted into the yellow anhydride. The *dimethyl* ester, obtained by boiling the anhydride with methyl-alcoholic hydrogen chloride, crystallised from methyl alcohol in colourless prisms, m. p. 166° (Found: C, 65·4; H, 5·6. $C_{24}H_{24}O_8$ requires C, 65·5; H, 5·5%). The *diethyl* ester crystallised from methyl alcohol in colourless prisms, m. p. 127—128° (Found: C, 66·9; H, 5·9. $C_{26}H_{28}O_8$ requires C, 66·7; H, 6·0%).

β-3 : 4-*Dimethoxybenzoyl*-α-(3′ : 4′-*dimethoxybenzylidene*)*propionic Acid* (VI).—Sodium β-(3 : 4-dimethoxybenzoyl)propionate (35 g.), veratraldehyde (40 g.), and acetic anhydride (80 c.c.) were heated at 100° for 12 hours. Water was added and after 4 hours the solid was collected and washed with sodium carbonate solution and then with methyl alcohol. Crystallisation from alcohol containing a little chloroform yielded the *lactone* of (VI) as greenish-yellow plates (34 g.), which melt at 140—147°, resolidify, and melt again at 153°. The lactone can also be crystallised from benzene or acetic acid and the same behaviour was observed on heating (Found: C, 68·5; H, 5·6. $C_{21}H_{20}O_6$ requires C, 68·5; H, 5·4%). The lactone (1·8 g.) was shaken with a solution of sodium (0·12 g.) in methyl alcohol (15 c.c.). When solution was complete, water was added, the alcohol removed, the filtered solution acidified, and the precipitate collected. Crystallisation from either methyl alcohol or benzene yielded the *acid* (VI) in colourless needles (1·5 g.), m. p. 175° (Found: C, 65·4; H, 5·8. $C_{21}H_{22}O_7$ requires C, 65·3; H, 5·7%).

6 : 7-*Dimethoxy*-1-(3′ : 4′-*dimethoxyphenyl*)*naphthalene*-3-*carboxylic Acid* (VII).—(a) The acid (VI) (20 g.) was refluxed for 4 hours with methyl alcohol (100 c.c.) saturated with hydrogen chloride. On cooling, the *methyl* ester of (VII) (17 g.) separated; it yielded the *acid* (VII) (15 g.) on hydrolysis with alcoholic potassium hydroxide. (b) The lactone of acid (VI) (3·6 g.) was kept for 3 days with iodine (3 g.) in chloroform (30 c.c.). Shaking with sodium thiosulphate solution decomposed the greenish-brown solid which had separated, and subsequent removal of the chloroform yielded the acid (VII) (1·5 g.). The acid (VII) crystallised from methyl alcohol containing a little chloroform in colourless slender needles, m. p. 222—223° (Found: C, 68·7; H, 5·4. $C_{21}H_{20}O_6$ requires C, 68·5; H, 5·4%). The methyl ester, obtained as described above or by esterification of the acid, crystallised from methyl alcohol in colourless needles, m. p. 177—178° (Found: C, 68·9; H, 6·0. $C_{22}H_{22}O_6$ requires C, 69·1; H, 5·8%). Acetic acid solutions of the acid (VII) were kept over-night (i) with 1 mol. and (ii) with 4 mols. of bromine. The product from (i) crystallised from 50% acetic acid in slender colourless needles, shrinking at about 280—285° and melting at 295—296°, and gave analytical figures in agreement with an impure *monobromo*-derivative (Found: Br, 14·8; equiv., 459. $C_{21}H_{19}O_6Br$ requires Br, 17·9%; equiv., 447). The product from (ii) crystallised from methyl alcohol–chloroform in colourless prisms, m. p. 260°, having the composition of a *dibromo*-derivative of (VII) (Found: C, 47·6; H, 3·5; Br, 30·9; equiv., 524. $C_{21}H_{18}O_6Br_2$ requires C, 47·9; H, 3·4; Br, 30·4%; equiv., 526).

6 : 7-*Dimethoxy*-1-(3′ : 4′ -*dimethoxyphenyl*)*naphthalene* (V).—The acid (VII) or the anhydride of (IV) (1 g.) was boiled with quinoline (10 c.c.) and copper powder (0·2 g.) for 2 hours. Ether was added and the quinoline and unchanged acids were removed by washing first with dilute hydrochloric acid and then with sodium hydroxide solution. The ethereal solution was dried, and the solvent removed; the residue crystallised from methyl alcohol in colourless plates, m. p. 159—160° (Found: C, 73·8; H, 6·2. $C_{20}H_{20}O_4$ requires C, 74·1; H, 6·1%). When the anhydride of (IV) was employed, the yield of (V) was about 2%, but a 50% conversion of the acid (VII) was obtained. The naphthalene derivative (V) (4 g.) was boiled with hydriodic acid (10 c.c., *d* 1·7) and acetic acid (20 c.c.) for 4 hours. The solvents were removed under reduced pressure and the residue was mixed with zinc dust (10 g.) and distilled. The oily distillate was washed with dilute hydrochloric acid and with sodium hydroxide solution and dried in ether, and the solvent removed. The residue was distilled and the fraction (1·0 g.), b. p. 160—170°/

0·1 mm., was identified as 1-phenylnaphthalene by conversion into the 4-bromo- and the 4-nitro-derivative, m. p.'s 69° and 132° respectively, which were identical with the substances prepared by Weiss and Woidich's method (*Monatsh.*, 1925, **46**, 453).

γ-Di-(3 : 4-dimethoxyphenyl)itaconic Acid (VIII).—A mixture of 3 : 4 : 3′ : 4′-tetramethoxybenzophenone (4 g.) (Perkin and Weizmann, J., 1906, **89**, 1661) and ethyl succinate (2·4 g.) was boiled for 12 hours with a suspension of potassium ethoxide (from 1 g. of potassium) in benzene (40 c.c.). Ether and water were added, the aqueous layer was mixed with 5% sodium hydroxide solution (10 c.c.) and boiled for 1 hour to complete the hydrolysis of the half ester of (VIII). Acidification precipitated the *acid* (VIII), which, collected after 12 hours, crystallised from acetone–benzene in small needles (3·3 g.), m. p. 128—130° with slight previous softening (Found : C, 59·6; H, 5·8; equiv., 207. $C_{21}H_{22}O_8,H_2O$ requires C, 60·0; H, 5·7%; equiv., 210). The acid can be recrystallised from hot water or glacial acetic acid, but it is sparingly soluble in ether, light petroleum, and benzene. The *anhydride*, obtained by heating the acid (VIII) with acetyl chloride (4 parts) for 2 hours, crystallised from benzene in colourless needles, m. p. 147—148° (Found : C, 65·5; H, 5·3. $C_{21}H_{20}O_7$ requires C, 65·6; H, 5·2%).

1-Keto-5 : 6-dimethoxy-3-(3′ : 4′-dimethoxyphenyl)indene-2-acetic Acid (IX).—The anhydride of the acid (VIII) (1 g.) was kept for 24 hours with a solution of aluminium chloride (1 g.) in nitrobenzene (20 c.c.). After the addition of dilute hydrochloric acid, the nitrobenzene was removed in steam; the red solid which separated from the residue crystallised from methyl alcohol or benzene in red plates (0·7 g.), m. p. 216—217° (Found : C, 65·8; H, 5·4. $C_{21}H_{20}O_7$ requires C, 65·6; H, 5·2%). This compound was soluble in sodium bicarbonate solution, and gave a semicarbazone, which crystallised from alcohol in pale yellow nodules, m. p. 254° (decomp.).

5 : 6-Dimethoxy-3-(3′ : 4′-dimethoxyphenyl)hydrindene-2-acetic Acid.—The ketone (IX) (0·3 g.) in acetic acid (50 c.c.) was reduced with hydrogen in the presence of palladised charcoal (0·2 g. of 0·5%) during 6 hours. The colourless solution was filtered, and evaporated under reduced pressure; the residue crystallised from methyl alcohol in colourless needles (0·2 g.), m. p. 169—170° (Found : C, 67·6; H, 6·4. $C_{21}H_{24}O_6$ requires C, 67·7; H, 6·5%). This *acid* did not decolorise potassium permanganate in sodium carbonate solution and it could not be converted into a semicarbazone.

Bis-(3 : 4-dimethoxyphenyl)methylsuccinic Acid (X).—This could be prepared by catalytic reduction of the itaconic acid (VIII), but an active platinic oxide catalyst was necessary and the following method was adopted for the preparation of large quantities of the acid. A mixture of acetic acid (150 c.c.) and concentrated sulphuric acid (150 c.c.) was added with stirring to a solution of ethyl hydroxymethylenesuccinate (41 g.) and veratrole (57 g.) in acetic acid (100 c.c.), the temperature being maintained below 15°. After 12 hours, water was added, and the product extracted with chloroform. The solvent was removed and, after being heated at 100° under diminished pressure to remove acetic acid, the oily residue was hydrolysed by boiling with 10% methyl-alcoholic potassium hydroxide (250 c.c.) for 2 hours. The methyl alcohol was removed, water (150 c.c.) added, and the boiling continued for another 2 hours. The *acid* (X), liberated by the addition of hydrochloric acid and isolated with chloroform, crystallised from benzene in colourless needles (72 g.), m. p. 177—178°; a further yield (7 g.) was obtained from the benzene liquors (Found : C, 62·5; H, 6·2. $C_{21}H_{24}O_8$ requires C, 62·4; H, 6·0%).

4-Keto-6 : 7-dimethoxy-1-(3′ : 4′-dimethoxyphenyl)-1 : 2 : 3 : 4-tetrahydronaphthalene-2-carboxylic Acid (XI).—The acid (X) (30 g.) was refluxed with acetyl chloride (60 c.c.) for 2 hours. The excess of acetyl chloride was removed and the residue, after being heated at 100° under reduced pressure for 1 hour, was dissolved in nitrobenzene (30 c.c.) and added gradually with stirring to an ice-cold solution of aluminium chloride (21 g.) in nitrobenzene (100 c.c.). After 12 hours, dilute hydrochloric acid was added, the nitrobenzene removed in steam, the residue cooled, and the *acid* (XI) collected, dried at 100°, and crystallised from methyl alcohol containing a little chloroform, colourless needles (26 g.), m. p. 200—201°, being obtained (Found : C, 64·9; H, 5·7. $C_{21}H_{22}O_7$ requires C, 65·3; H, 5·7%). The *semicarbazone* crystallised from acetic acid in slender needles, m. p. 244—245° (decomp.) (Found : N, 9·7. $C_{22}H_{25}O_7N_3$ requires N, 9·5%). The *ethyl* ester, prepared by refluxing the finely powdered acid (XI) with alcoholic hydrogen chloride (10 parts) for 6 hours, crystallised from alcohol in colourless needles, m. p. 130—131° (Found : C, 66·9; H, 6·4. $C_{23}H_{26}O_7$ requires C, 66·7; H, 6·5%).

6 : 7-Dimethoxy-1-(3′ : 4′-dimethoxyphenyl)-1 : 2 : 3 : 4-tetrahydronaphthalene-2-carboxylic Acid.—This can be prepared by reducing the acid (XI), but the best results were obtained with the ethyl ester. The ethyl ester (1 g.) was gently boiled for 12 hours with amalgamated zinc (5 g.) and concentrated hydrochloric acid (10 c.c.). After dilution and cooling, the product

was isolated with chloroform; it crystallised from methyl alcohol in tufts of slender needles, m. p. 184—185° (Found: C, 67·8; H, 6·7. $C_{21}H_{24}O_6$ requires C, 67·7; H, 6·5%). The structure of this *acid* was confirmed by heating with selenium (2 parts) at 280° for 12 hours. The product, isolated with chloroform, crystallised from methyl alcohol (carbon) in colourless plates, m. p. 159—160°, identical with 6 : 7-dimethoxy-1-(3′ : 4′-dimethoxyphenyl)naphthalene (V) (p. 640). A *dibromo-acid* was obtained by the action of bromine (4 mols.) on a chloroform solution of the above carboxylic acid; it crystallised from alcohol in clusters of small colourless prisms, m. p. 190—191° (Found: Br, 30·6. $C_{21}H_{22}O_6Br_2$ requires Br, 30·2%).

Ethyl 3-Bromo-4-keto-6 : 7-dimethoxy-1-(6′-bromo-3′ : 4′-dimethoxyphenyl)-1 : 2 : 3 : 4-tetrahydronaphthalene-2-carboxylate.—A solution of bromine (1 g.) in chloroform (10 c.c.) was added to the ester (XI) (1 g.) in chloroform (10 c.c.). After 12 hours, the hydrogen bromide was removed in a current of dry air, the chloroform evaporated, and the residue crystallised from methyl alcohol; colourless prisms (1·7 g.), m. p. 146—147°, were obtained (Found: Br, 28·6. $C_{23}H_{24}O_7Br_2$ requires Br, 28·0%).

Ethyl 4-Hydroxy-6 : 7-dimethoxy-1-(6′-bromo-3′ : 4′-dimethoxyphenyl)naphthalene-2-carboxylate (XII).—The above dibromo-ester (2 g.) was heated with diethylaniline (10 c.c.) at 180—190° for 3 hours. The base was removed in steam; the product, isolated with ether, crystallised from aqueous acetic acid in almost colourless plates (1·5 g.), m. p. 193—195° (Found: C, 56·6; H, 4·8; Br, 16·2. $C_{23}H_{23}O_7Br$ requires C, 56·2; H, 4·7; Br, 16·3%). This *compound* was insoluble in sodium bicarbonate solution but soluble in sodium hydroxide and a red azo-dye was precipitated by the addition of diazotised aniline to its alkaline solution. A stream of hydrogen was passed through a boiling alcoholic solution of (XII) in the presence of a palladised charcoal catalyst. The product, probably *ethyl 4-hydroxy-6 : 7-dimethoxy-1-(3′ : 4′-dimethoxyphenyl)naphthalene-2-carboxylate*, crystallised from methyl alcohol in colourless prisms, m. p. 228° (Found: C, 66·4; H, 5·7. $C_{23}H_{24}O_7$ requires C, 67·0; H, 5·8%), but numerous attempts to repeat this experiment were unsuccessful.

Lactone of 4-Hydroxy-6 : 7-dimethoxy-1-(6′-bromo-3′ : 4′-dimethoxyphenyl)-3-hydroxymethylnaphthalene-2-carboxylic Acid (XIII).—The bromophenol (XII) (0·5 g.), 40% formalin (1 c.c.), concentrated hydrochloric acid (2 c.c.), and glacial acetic acid (5 c.c.) were heated at 100° for 3 hours. The brown powder which separated crystallised from nitrobenzene in small buff-coloured prisms, m. p. 319—320° (Found: C, 55·3; H, 4·1. $C_{22}H_{19}O_7Br$ requires C, 55·6; H, 4·0%). This *lactone* was insoluble in sodium bicarbonate solution, but no precipitation occurred when solutions of this compound in sodium hydroxide were saturated with carbon dioxide. Diazonium compounds did not couple with the lactone in alkaline solution.

Ethyl 3-Aldehydo-4-keto-6 : 7-dimethoxy-1-(3′ : 4′-dimethoxyphenyl)-1 : 2 : 3 : 4-tetrahydronaphthalene-2-carboxylate (XIV).—The ethyl ester of the tetralonecarboxylic acid (XI) (8 g.), ethyl formate (4 c.c.), and sodium wire (1 g.) were allowed to react in benzene (40 c.c.) for 12 hours. Water was added, the aqueous layer acidified, and the product extracted with ether and dried. Removal of the ether gave a compound, which crystallised from methyl alcohol containing a little chloroform in large prisms (7·3 g.), m. p. 165° (Found: C, 65·0; H, 6·1. $C_{24}H_{26}O_8$ requires C, 65·2; H, 5·9%). This *hydroxymethylene* compound was soluble in sodium hydroxide solution, and addition of ferric chloride to a solution of (XIV) in alcohol produced a deep green coloration. Boiling with alcoholic potassium hydroxide converted the hydroxymethylene compound into the tetralonecarboxylic acid (XI), m. p. 205°.

4-Hydroxy-6 : 7-dimethoxy-1-(3′ : 4′-dimethoxyphenyl)-3-hydroxymethyl-1 : 2 : 3 : 4-tetrahydronaphthalene-2-carboxylic Acid (XV).—4% Sodium amalgam (50 g.) was gradually added to a solution of the above hydroxymethylene compound (1 g.) in 0·2% sodium hydroxide solution (50 c.c.) at 100°; excessive alkalinity was prevented by a continuous stream of carbon dioxide. When the amalgam was exhausted, the clear solution was acidified; the product, isolated with chloroform, crystallised slowly from a small amount of methyl alcohol in small plates (0·2 g.), m. p. 195—197°, raised to 200° by a further crystallisation (Found: C, 63·4, 63·3; H, 6·5, 6·3; equiv., 420. $C_{22}H_{26}O_8$ requires C, 63·2; H, 6·2%; equiv., 418). The methyl-alcoholic liquors gave 0·2 g. of the lactone when treated with acids as described below.

α-Form of the Lactone of 6 : 7-Dimethoxy-1-(3′ : 4′-dimethoxyphenyl)-3-hydroxymethyl-1 : 2 : 3 : 4-tetrahydronaphthalene-2-carboxylate (I; R = Me).—This was prepared either (a) by heating the acid (XV) at 200° for 10 minutes or (b) by boiling the acid with 10% sulphuric acid (20 parts) for 2 hours. The product was washed in chloroform with sodium bicarbonate solution, and the chloroform removed. The residue separated from methyl alcohol, containing a little chloroform, in a gelatinous form, which was converted into a crystalline powder (yield, 70%), m. p. 170—175°, by drying at 100°. Repeated crystallisation either from the same solvent or

from 60% formic acid gave colourless nodules (yield, 40%), m. p. 186—187° (Found : C, 68·7, 68·6; H, 6·3, 6·4. $C_{22}H_{24}O_6$ requires C, 68·7; H, 6·3%). Attempts to reduce this *lactone* were unsuccessful. It sublimed when heated to 250°/0·1 mm. and could not be dehydrogenated by heating with palladium-black.

Lactone of 4-*Hydroxy*-6 : 7-*dimethoxy*-2-*carboxy*-1-(3′ : 4′-*dimethoxyphenyl*)-1 : 2 : 3 : 4-*tetrahydronaphthalene*-3-*glycollic Acid* (XVIII).—A mixture of ethyl oxalate (1·2 c.c.) and the ethyl ester of the tetralonecarboxylic acid (XI) (2 g.) in benzene (7 c.c.) was poured into a suspension of potassium ethoxide (from 0·3 g. of potassium and 0·5 c.c. of alcohol) in ether (30 c.c.). After 2 hours, water (70 c.c.) was added, and the yellow aqueous layer was separated and acidified. The caseous yellow precipitate, which gave a violet colour with ferric chloride, was extracted with ether and the moist ethereal extract (100 c.c.) was poured on aluminium amalgam (from 5 g. of aluminium). After 12 hours, the colourless solution was removed from the hydroxide, which was washed with ether. The combined ethereal extracts were evaporated, and aqueous sodium hydroxide was gradually added to a boiling solution of the residual oil (1·8 g.) in a little methyl alcohol, until permanent alkalinity was obtained. Water was added, the methyl alcohol removed, and the residue acidified and boiled for 10 minutes. The precipitate, after being dried, crystallised from methyl alcohol in colourless needles (0·8 g.), m. p. 212—213° (decomp.) [Found : C, 59·8, 59·5; H, 5·6, 5·6; equiv. (by titration), 456; (by back titration), 231. $C_{23}H_{26}O_{10}$ requires C, 59·7; H, 5·6%; equivs., 462 and 231]. These figures agree with a monohydrate, but we have been unable to prepare the anhydrous form of (XVIII). Several reactions of this lactone are difficult to explain. When refluxed with ethyl-alcoholic hydrogen chloride, it was converted into a *diethyl* ester, which crystallised from benzene–light petroleum in slender needles, m. p. 145—146° (Found : C, 64·8, 65·1; H, 6·5, 6·6. $C_{27}H_{32}O_9$ requires C, 64·8; H, 6·4%). Hydrolysis with methyl-alcoholic potassium hydroxide converted this ester into a *carboxylic acid*, which crystallised from methyl alcohol in colourless prisms, m. p. 212—213° (Found : C, 61·4; H, 5·5. $C_{23}H_{24}O_9$ requires C, 62·1; H, 5·4%), and depressed the m. p. of the hydrated form described above. When the hydrated lactone was heated for 10 minutes at 215°/12 mm., it was converted into an acidic *compound*, which was sparingly soluble in chloroform and methyl alcohol, but crystallised from acetic acid in red-orange plates, m. p. 285° (Found : C, 67·1, 67·1; H, 5·1, 4·9. $C_{22}H_{20}O_7$ requires C, 66·7; H, 5·1%).

β-*Form of the Lactone of* 6 : 7-*Dimethoxy*-1-(3′ : 4′-*dimethoxyphenyl*)-3-*hydroxymethyl*-1 : 2 : 3 : 4-*tetrahydronaphthalene*-2-*carboxylic Acid* (I; R = Me).—The lactonic acid (XVIII) (0·1 g.) was heated in an oil-bath at 215° for 10 minutes; the product hardened on trituration with methyl alcohol and crystallised from methyl alcohol–chloroform in cream-coloured prisms (0·045 g.), m. p. 209—210°. Colourless prisms, m. p. 209—210°, were obtained by sublimation at 0·1 mm. (Found : C, 68·6, 68·4, 68·8; H, 6·3, 6·0, 6·1. $C_{22}H_{24}O_6$ requires C, 68·7; H, 6·3%). This *compound* was insoluble in sodium bicarbonate solution, slowly soluble in boiling aqueous sodium hydroxide, and rapidly dissolved by warm alcoholic alkali, subsequent addition of water producing no precipitate.

Lactone of 6 : 7-*Dimethoxy*-1-(3′ : 4′-*dimethoxyphenyl*)-3-*hydroxymethylnaphthalene*-2-*carboxylic Acid* (XVI).—(a) Either the α- or the β-form of the lactone (I; R = Me) (0·2 g.) and lead tetra-acetate (0·4 g.) in acetic acid (10 c.c.) were heated at 70° for 10 minutes. Water was added, the product extracted with chloroform and washed with water and sodium bicarbonate solution, and the solvent removed. The residue rapidly hardened on boiling with methyl alcohol. The conversion of the β-form was almost quantitative, but dehydrogenation of the α-form occurred to an extent of 10% only and a large amount of unchanged material was recovered. (b) The β-form of the lactone (I; R = Me) (0·1 g.) and palladium-black (0·02 g.) were intimately mixed and heated at 220—230° for ½ hour. The pressure was then reduced to 0·1 mm., and the temperature raised to 255° for ½ hour. The sublimate (0·07 g.) was collected. The α-form of the lactone (I; R = Me) was recovered after similar treatment. The products from experiments (a) and (b) were identical, and crystallised from methyl alcohol–chloroform in stout colourless prisms, m. p. 254—255° (Found : C, 69·2, 69·4; H, 5·4, 5·3. Calc. for $C_{22}H_{20}O_6$: C, 69·5; H, 5·3%). This lactone dissolved to a pale yellow solution in concentrated sulphuric acid, which gradually became red. Concentrated nitric acid gave a deep brownish-red colour. The lactone was hydrolysed slowly with boiling sodium hydroxide solution, but rapid hydrolysis occurred with alcoholic alkali. The lactone (0·2 g.) was dissolved in 1% methyl-alcoholic sodium hydroxide (10 c.c.) by boiling for 1 hour. Water (10 c.c.) was added, the methyl alcohol removed, and a solution of bromine (0·25 c.c.) in 10% sodium hydroxide solution (6 c.c.) added. After heating at 100° for 3 hours, the solution was filtered, acidified, and extracted with chloroform. The solvent was removed, and the residue heated for 1 hour on the water-bath with

excess of acetyl chloride. The solid which separated crystallised from nitrobenzene in pale yellow prisms, m. p. 304—306°, identical with the anhydride of the dibasic acid (IV).

Lactone of 6 : 7-*Dimethoxy*-1-(3′ : 4′-*dimethoxyphenyl*)-2-*hydroxymethylnaphthalene*-3-*carboxylic Acid* (XIX).—α-" Sulphite-liquors lactone " dimethyl ether was not dehydrogenated by heating with palladium-black, but (XIX) was obtained in 70% yield by dehydrogenation with lead tetra-acetate as described above in the preparation of the lactone of (XVI). Also α-" sulphite-liquors lactone " dimethyl ether (0·5 g.) was heated with selenium (0·5 g.) at 255—260° for 1 hour and then at 275° for 6 hours. The product, isolated with chloroform, was crystallised several times from methyl alcohol, yielding (XIX) (0·1 g.). The lactone (XIX) crystallised from methyl alcohol, containing a little chloroform, in slender prisms, m. p. 215—216° (Found : 69·4; H, 5·4. Calc. for $C_{22}H_{20}O_6$: C, 69·5; H, 5·3%). This lactone dissolved in concentrated sulphuric acid to a cherry-red solution, which became brown on addition of a drop of concentrated nitric acid. The behaviour of this lactone to alkalis was similar to that of the isomeric lactone of (XVI), but it could not be oxidised with sodium hypobromite.*

An alkaline solution of the lactone (XIX) (0·25 g.) was prepared as described above in the case of the isomeric lactone (XVI). The cold solution was saturated with carbon dioxide, and finely powdered potassium permanganate (0·3 g.) added during 3 hours. The liquid was filtered and acidified, and the product, isolated with chloroform, was converted into the anhydride of the dibasic acid (IV), m. p. 305—306°.

" *Sulphite-liquors lactone* " *Diethyl Ether.*—Ethyl sulphate (2 c.c.) was added to a solution of " sulphite-liquors lactone " (1 g.) in 2·7% aqueous sodium hydroxide (30 c.c.). After being stirred for 1 hour at 100°, the solution was cooled to 15°, 1% aqueous sodium hydroxide (30 c.c.) added, and the stirring continued for another hour at 15°. The solution was acidified and heated at 100° for 3 hours. The product crystallised from alcohol in slender felted needles (1·1 g.), m. p. 178—179° (Found : C, 69·7; H, 7·0. $C_{24}H_{28}O_6$ requires C, 69·9; H, 7·0%). This *diethyl* ether (2 g.) was oxidised with potassium permanganate as described by Erdtman (*loc. cit.*) in the case of the corresponding dimethyl ether. 5-Methoxy-4-ethoxy-2-(3′-methoxy-4′-ethoxybenzoyl)benzoic acid (0·08 g.), m. p. 213—214°, was obtained, and converted into the corresponding anthraquinone, m. p. 288° (Vanzetti and Dreyfuss give 214° and 288° respectively).

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