336. *The Chemistry of the "Insoluble Red" Woods. Part III. The Structure of Santal and a Note on Orobol.*

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An improved method has been devised for the isolation of santal, which has been found to have the empirical formula $C_{15}H_9O_5(OMe)$ originally suggested by O'Neill and Perkin and to form an *O*-triacetyl and an *O*-trimethyl derivative. By the degradation and synthesis of the latter derivative and of the corresponding triethyl ether it has been shown that santal is 5 : 3′ : 4′-trihydroxy-7-methoxy*iso*flavone (I; R = Me).

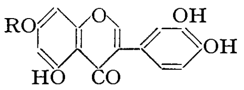
It seems reasonably certain that norsantal (I; R = H), formed by the demethylation of santal, is identical with orobol, the aglucone of oroboside (Bridel and Charaux).

The phenolic compound, santal, appears to have been first isolated in small yield from Sandelwood (syn. Red Sandelwood or Santalwood), *Pterocarpus santalinus* (Linn.), by Weidel (*Zeit. für Chem.*, 1870, **6**, 83) who assigned to it the empirical formula $C_8H_6O_5,0{\cdot}5H_2O$, but did not record a melting point. On fusing his substance with alkali, Weidel obtained piperonal and protocatechuic acid, remarking that, when kept for a long time in air, alkaline solutions of the compound became red and then green. In their examination of barwood, *Baphia nitida* (Lodd.), O'Neill and Perkin (*J.*, 1918, **113**, 125) isolated a compound, m. p. 223°, which gave the same analytical results as Weidel (*loc. cit.*) had obtained for santal, but which they, unlike Weidel who recorded a violet-black ferric reaction, found to give a wine-red ferric reaction in alcohol and to contain a methoxyl group; they proposed the empirical formula $C_{15}H_9O_5(OMe)$. It may well be that Weidel's material was largely composed of santal (compare Raudnitz and Perlmann, *Ber.*, 1935, **68**, 1862), although in the light of the results described in the present communication it is clear that the piperonal obtained from it by this author was derived from an impurity, in all probability pterocarpin (compare Part I, *J.*, 1940, 787). O'Neill and Perkin (*loc. cit.*) considered that their santal was very similar to baphic acid, one of the compounds isolated from barwood by Anderson (*Trans. Chem. Soc.*, 1876, **30**, 582), but the latter author did not define the properties of his product very clearly and the identity is not certain. Similarly, Raudnitz and Perlmann (*loc. cit.*) isolated, from sandelwood, a compound, m. p. 218°, which they considered to be santal and to have the empirical formula $C_{13}H_{10}O_5$; from their substance these authors prepared an *O*-diacetyl and an *O*-dimethyl derivative, m. p. 152° and 141°, respectively.

In the course of our examination of the colourless minor constituents of the "insoluble red" woods, sandelwood, barwood, and camwood, the formulæ of which we expect may be of some assistance in the elucidation of the structures of the more complex colouring matters, we have devised a suitable procedure for the isolation of santal, m. p. 223°, from commercial camwood which is stated to be a variety of barwood, and have also obtained the compound from sandelwood. Although at first considerable difficulty was experienced in obtaining consistent analytical results for santal and its derivatives, it finally became clear that the compound formed a *monohydrate* and that the anhydrous substance had the empirical formula $C_{15}H_9O_5(OMe)$ in agreement with that proposed by O'Neill and Perkin (*loc. cit.*). Through the kindness of Dr. Cross of the Department of Colour Chemistry, University of Leeds, we have been able to compare a specimen of O'Neill and Perkin's santal with our own material and found them to be identical.

Santal, which is devoid of a methylenedioxy- or an active keto-group, formed a *triacetate* and a *trimethyl ether*. On hydrogenation with a palladium–charcoal catalyst at 100° *O*-trimethylsantal gave rise to a compound which appears to have the formula $C_{19}H_{22}O_5$ and is devoid of a hydroxyl or carbonyl group, and which yielded a ketonic substance on oxidation with potassium permanganate. Ozonolysis of the trimethyl ether furnished a complex mixture, from which 2-hydroxy-4 : 6-dimethoxybenzoic acid was separated, together with a small amount of a crystalline compound, m. p. 77—78°, which, owing to lack of material, was not examined in detail. On being subjected to hydrolytic fission with hot aqueous or alcoholic potassium hydroxide, *O*-trimethylsantal yielded formic acid and a saturated phenolic *ketone*, $C_{14}H_8O_2(OMe)_4$ which exhibited an intense ferric reaction in alcohol and was characterised by the formation of a *methyl ether* and an *oxime*. Oxidised with potassium permanganate in acetone, this ketone gave veratric acid (characterised by the preparation of the p-*nitrobenzyl* ester) along with a ketonic *compound* which appears to have the formula $C_{14}H_8O_3(OMe)_4$. This second ketone, which was also formed in small amounts when *O*-trimethylsantal was oxidised directly with potassium permanganate in acetone, is phenolic, exhibiting a strong ferric reaction and forming (with difficulty) a *methyl ether* and a 2 : 4-*dinitrophenylhydrazone*. These properties are in keeping with the view that this substance also is an *o*-hydroxy-phenolic ketone.

From its empirical formula, its ferric reaction, and its oxidation with potassium permanganate to give veratric acid, in conjunction with the production of 2-hydroxy-4 : 6-dimethoxybenzoic acid by the ozonolysis of *O*-trimethylsantal, it appeared probable that the ketone $C_{14}H_8O_2(OMe)_4$ was 2-hydroxy-4 : 6 : 3′ : 4′-tetramethoxydeoxybenzoin (III), a conclusion which was supported by the conversion of the compound on methylation into 2 : 4 : 6 : 3′ : 4′-pentamethoxydeoxybenzoin (Freudenberg *et al.*, *Annalen*, 1925, **446**, 87). That the ketone (III) contained a hydroxyl in the *o*-position to a carbonyl group was confirmed by the fact that on vigorous acetylation with sodium acetate and acetic anhydride it underwent cyclisation giving rise to a product, $C_{20}H_{20}O_6$, which is clearly 5 : 7 : 3′ : 4′-*tetramethoxy*-2-*methyl*iso*flavone* (IV). Ultimately, the structure of this ketone (III) was established synthetically by two routes. Condensation of 3 : 4-dimethoxybenzyl cyanide and phloroglucinol monomethyl ether according to the method of Hoesch gave only one product which, from the known behaviour of phloroglucinol monomethyl ether with other cyanides, is clearly 2 : 4-dihydroxy-6 : 3′ : 4′-trimethoxydeoxybenzoin (V; R and R′ = Me) and which, by partial methylation, furnished the ketone (III) identical with the product from santal. When phloroglucinol monomethyl ether is replaced by the dimethyl ether in the Hoesch reaction, the ketone (III) is obtained directly along with smaller amounts of the isomeride 4-*hydroxy*-2 : 6 : 3′ : 4′-*tetramethoxydeoxybenzoin* (VI), which, as would be expected, is readily soluble in 1% aqueous sodium hydroxide and has a negative ferric reaction in alcohol.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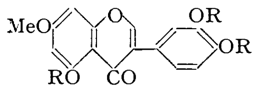
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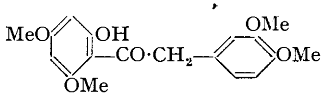
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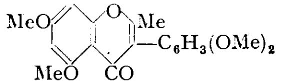
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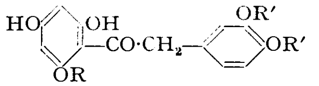
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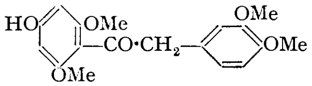
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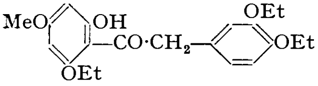
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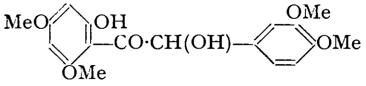
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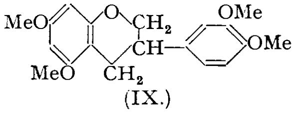
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In view of the production of formic acid along with the ketone (III) by hydrolytic fission, it seemed reasonably certain that *O*-trimethylsantal was 5 : 7 : 3′ : 4′-tetramethoxy*iso*flavone (II; R = Me), a conclusion which was confirmed by the synthesis of the compound from the ketone (III) (natural or synthetical) and ethyl formate in the presence of sodium according to the standard procedure. Consequently, it became clear that santal was a monomethyl ether of 5 : 7 : 3′ : 4′-tetrahydroxy*iso*flavone (I; R = H). In order to determine the position of the methyl group, santal was converted into the *triethyl ether*, and on hydrolytic fission this derivative gave rise to a methoxytriethoxydeoxybenzoin, the properties of which were very similar to those of the related ketone (III). On being oxidised with potassium permanganate, the methoxytriethoxy-ketone yielded 3 : 4-diethoxybenzoic acid in addition to a ketonic compound, $C_{21}H_{26}O_6$, having an intense ferric reaction in alcohol and corresponding to the oxidation product, $C_{14}H_8O_3(OMe)_4$, obtained from the analogue (III). The production of 3 : 4-diethoxybenzoic acid clearly showed that the *O*-methyl group was in the phloroglucinol residue of the methoxytriethoxy-ketone, *i.e.*, that this ketone was 2-*hydroxy*-4-*methoxy*-6 : 3′ : 4′-*triethoxy*- (VII) or 2-*hydroxy*-6-*methoxy*-4 : 3′ : 4′-*triethoxy-deoxybenzoin*. The condensation of 3 : 4-diethoxybenzyl cyanide with phloroglucinol monoethyl ether gave rise to 2 : 4-*dihydroxy*-6 : 3′ : 4′-*triethoxydeoxybenzoin* (V; R = R′ = Et) which on partial methylation furnished the ketone (VII), identical with the compound from *O*-triethylsantal. On the other hand, the condensation of the same cyanide with phloroglucinol monomethyl ether under the same conditions, followed by monoethylation of the resulting 2 : 4-*dihydroxy*-6-*methoxy*-3′ : 4′-*diethoxydeoxybenzoin* (V; R = Me; R′ = Et), furnished 2-hydroxy-6-methoxy-4 : 3′ : 4′-triethoxydeoxybenzoin. From the synthetic ketone (VII) and methyl formate *O*-triethylsantal was synthesised by the standard method and found to be identical with the natural derivative. In consequence it became clear that triethylsantal has formula (II; R = Et) and, therefore, that santal is 5 : 3′ : 4′-trihydroxy-7-methoxy*iso*flavone (I; R = Me). In the course of the determination of the orientation of triethylsantal the synthesis of the following *iso*flavones was undertaken simultaneously with the degradation and synthesis of *O*-triethylsantal, and their non-identity with the natural derivative serves to reinforce the arguments advanced for the structure of santal: (*a*) 5-*methoxy*-7 : 3′ : 4′-*triethoxy*iso*flavone* from 2-*hydroxy*-6-*methoxy*-4 : 3′ : 4′-*triethoxydeoxybenzoin* obtained by the partial ethylation of 2 : 4-*dihydroxy*-6-*methoxy*-3′ : 4′-*diethoxydeoxybenzoin,* (*b*) 4′-*methoxy*-5 : 7 : 3′-*triethoxy*iso*flavone* from 2-*hydroxy*-5′-*methoxy*-4 : 6 : 3′-*triethoxydeoxybenzoin,* and (*c*) 3′-methoxy-5 : 7 : 4′-*triethoxy*iso*flavone* from 2-*hydroxy*-3′-*methoxy*-4 : 6 : 4′-*triethoxydeoxybenzoin.* On the basis of the structure (II; R = Me) for *O*-trimethylsantal it seems reasonably certain that the neutral reduction product (deoxy-derivative), $C_{19}H_{22}O_5$, formed from this ether, is the *iso*flavan (IX), and hence its ketonic oxidation product is in all probability the corresponding 5 : 7 : 3′ : 4′-tetramethoxy*iso*flavanone.

It is not clear whether the diacetate and dimethyl ether of santal described by Raudnitz and Perlmann (*loc. cit.*) are impure forms of the triacetate and the trimethyl ether obtained in the present work, but it may be noted that the lower melting points observed by these authors may be due to the retention of solvents. We have observed that derivatives of santal occasionally show anomalous melting points unless precautions have been taken in those particular cases completely to remove the solvent by heating in a high vacuum. Nevertheless, for compounds having the type of structure (I) now established for santal it is well known that the hydroxyl group in the 5-position is somewhat inert towards methylating and acylating reagents under the usual conditions, and consequently it may well be that the derivatives described by Raudnitz and Perlmann are the *O*-3′ : 4′-dimethyl and the *O*-3′ : 4′-diacetyl derivatives of santal. From its method of preparation it would seem likely that their ether is the dimethyl derivative.

Whilst our investigations of the keto-phenolic oxidation product, $C_{14}H_8O_3(OMe)_4$, obtained from *O*-trimethylsantal and from 2-hydroxy-4 : 6 : 3′ : 4′-tetramethoxydeoxybenzoin (III) are not yet complete, it seems possible that this substance may be a benzoin derivative (VIII), but, as far as we are aware, the production of mixed benzoins in this way has not so far been described. The benzil structure is not excluded, but the failure of the compound to react with *o*-phenylenediamine makes this unlikely. Further, the alternative *p*-quinone type of structure, envisaged as being derived by oxidation of the phloroglucinol residue, is excluded because oxidation of 2 : 4 : 6 : 3′ : 4′-pentamethoxydeoxybenzoin with potassium permanganate gives small yields of a product having a negative ferric reaction and identical in every way with the *methyl ether* obtained by methylating the compound $C_{14}H_8O_3(OMe)_4$ with methyl iodide and potassium carbonate in boiling acetone. The oxidation of the analogous ketones, 2-hydroxy-4-methoxy-6 : 3′ : 4′-triethoxy-, 2-*hydroxy*-4 : 6 : 4′-*trimethoxy*- and 2-*hydroxy*-4 : 6-*dimethoxy*-*deoxybenzoin,* gave products having properties similar to the compound $C_{14}H_8O_3(OMe)_4$. Unlike benzoin, these oxidation products reduce Fehling's solution only very slowly and, whilst they give ketonic reactions, we have not so far succeeded in preparing functional derivatives establishing the presence of a secondary alcohol group, as required by formulæ of type (VIII). Further, the compounds do not appear to be readily oxidisable with chromic oxide in acetic acid.

Orobol.—In their examination of the glucoside, oroboside, which they isolated from the vetch, *Orobus tuberosus* (L), Bridel and Charaux (*Compt. rend.*, 1930, **190**, 387) obtained from it a flavone-like aglucone, orobol, m. p. 270·5°; subsequently, Charaux and Rabate (*Bull. Soc. Chim. biol.*, 1939, **21**, 1330), prepared, from orobol, an acetyl derivative, m. p. 211° (bloc Maquenne), and obtained phloroglucinol and homoprotocatechuic acid on fusing it with potassium hydroxide, concluding that the compound was probably 5 : 7 : 3′ : 4′-tetrahydroxy*iso*flavone (I; R = H). In view of the constitution now allocated to santal it seemed likely that orobol was identical with norsantal, m. p. 270—273°, which O'Neill and Perkin (*loc. cit.*) had obtained by the demethylation of santal. We have now found that norsantal, prepared by the demethylation of santal, has m. p. 270°, and forms a tetra-acetate, m. p. 207·5°.

The following is a comparative summary of the properties of orobol as described by the French authors and of norsantal which we have observed :

	Orobol.	Norsantal.
Crystalline form	Pale-yellow, bent needles	Pale-yellow, rhombic plates
Melting point	270·5°	270°
Ferric reaction	Green, " becoming colour of diluted wine "	Green, becoming purplish brown
Sulphuric acid reaction	Yellow-green solution, becoming blood-red on addition of a few drops of concentrated nitric acid	Same as orobol
Nitric acid reaction	Brown-red solution becoming yellow	Same as orobol
Ammoniacal silver nitrate	Reduces	Reduces
Acetyl derivative	M. p. 211° (bloc Maquenne)	207·5° (tube)

Subject to a direct comparison, when a specimen of orobol becomes available, we therefore consider that the two compounds are identical.

EXPERIMENTAL.

Santal (I; R = Me).—Commercial " camwood " (600 g.) was heated under reflux with carbon tetrachloride (3 l.) for 6 hours, filtered, dried, and then continuously extracted in a Soxhlet apparatus with chloroform for 16 hours. After 2 further charges had been extracted, the chloroform liquor was kept for 48 hours, and the dark-red pigment (*A*) (50—80 g.) which had separated was removed by filtration. The residue left on evaporation of the chloroform filtrate in a vacuum was dissolved in ethyl acetate (1 l.) and the solution divided into 5 equal portions. Into each portion a rapid stream of dry hydrogen chloride was passed for about 10 seconds and the red slurry (*B*), which separated, was collected immediately by filtration, washed with a little ethyl acetate and then thoroughly with ether, dried, and stored for further investigation. The condition of the pigment (*B*) depended largely on the dexterity with which the operations were performed. The optimum conditions appeared to depend on the use of a dilute ethyl acetate solution of the chloroform residue, careful adjustment of the time and rate of passage of the hydrogen chloride which can only be achieved by trial, and thorough and rapid washing and drying of the solid pigment (*B*) with ether. Exposure of this solid, while moist with solvent, to the air generally resulted in the formation of dark sticky material.

The ethyl acetate filtrate and washings from the pigment (*B*) were combined, washed with a little aqueous sodium hydrogen carbonate to remove hydrogen chloride, evaporated to approximately 25 ml., and kept. In the course of 3 weeks a small amount of reddish-brown pigment (*C*) (1—1·5 g.) separated, and, after its removal, the liquor was further concentrated to about 10 ml. When kept, this concentrate gradually (about 2 weeks) deposited santal as a reddish crystalline solid; the yield of crude compound was approximately 2 g. from 1800 g. of wood, and a further quantity (0·5 g.) separated from the residues after several months. The crude material was triturated with a little cold alcohol, dried, and then purified by recrystallisation from alcohol or ethyl acetate, giving santal, as a monohydrate, in lustrous yellow plates (1·2 g. from 2 g. of crude product), m. p. 223°, unchanged on sublimation at 190—200°/0·0005 mm. [Found (in specimen dried in air or in a vacuum-desiccator at room temperature): C, 60·5; H, 4·5; OMe, 8·8; $C_{15}H_9O_5(OMe),H_2O$ requires C, 60·4; H, 4·4; OMe, 9·8%. Found (in material sublimed in a high vacuum): C, 63·9; H, 4·0; OMe, 9·7. Calc. for $C_{15}H_9O_5(OMe)$: C, 63·9; H, 4·0; OMe, 10·3%]. Santal gives an intense brownish-red ferric reaction in alcohol. When kept, colourless aqueous alkaline solutions of the compound slowly became green. Acetylation of santal (0·5 g.) with boiling acetic anhydride (10 ml.) and sodium acetate (0·5 g.) gave rise to O-*triacetylsantal* (0·6 g.) which separated from methanol or acetic acid in colourless needles, m. p. 170°, after sintering at 152°, having a negative ferric reaction (Found: C, 62·4; H, 4·4. $C_{22}H_{18}O_9$ requires C, 62·0; H, 4·2%). These analytical results are in close agreement with those given by Raudnitz and Perlmann for their so-called diacetyl derivative.

O-*Trimethylsantal* (II; R = Me).*—Santal (1 g.) was methylated with methyl iodide (2 ml.) and potassium carbonate (10 g.) in boiling acetone (75 ml.) during 12 hours, with the addition of further portions of iodide (1·5 g.) and carbonate (3 g.) after 4 hours and then after 8 hours. After isolation from the acetone liquor, O-*trimethylsantal* crystallised from warm alcohol in colourless needles (0·9 g.), m. p. 155—156°, which after repeated purification from alcohol or ethyl acetate had m. p. 166° [Found: C, 66·5; H, 5·5; OMe, 33·5. $C_{15}H_6O_2(OMe)_4$ requires C, 66·7; H, 5·3; OMe, 36·3%]. It seems hardly likely that this ether is the same compound as the so-called dimethyl ether, m. p. 142°, described by Raudnitz and Perlmann (*loc. cit.*). *O*-Trimethylsantal which has a negative ferric reaction and does not react with 2 : 4-dinitrophenylhydrazine, is readily soluble in acetone, moderately soluble in benzene, and insoluble in light petroleum or aqueous sodium hydroxide. On being warmed the deep green solution of the ether in concentrated sulphuric acid becomes yellow.

The hydrogenation of *O*-trimethylsantal (0·9 g.) in acetic acid (110 ml.) at 100° with a palladium–charcoal catalyst (from 2 g. of charcoal and 0·2 g. of palladium chloride) and hydrogen at atmospheric pressure appeared to be complete in about 25 minutes. The resulting 5 : 7 : 3′ : 4′-*tetramethoxy*iso*flavan* (IX) was crystallised from alcohol, forming colourless silky needles (0·55 g.), m. p. 134°, insoluble in aqueous sodium hydroxide and having a negative ferric reaction [Found: C, 68·7; H, 6·6; OMe, 33·9. $C_{15}H_{10}O(OMe)_4$ requires C, 69·1; H, 6·7; OMe, 37·6. $C_{15}H_8O_2(OMe)_4$ requires C, 66·3; H, 5·8; OMe, 36·0%]. This substance, which is readily soluble in acetone, ethyl acetate, and benzene, and insoluble in light petroleum, gives a pale yellow solution in sulphuric acid which on being warmed becomes green and then ruby-red. For an unknown reason it was not always possible to effect this hydrogenation, and then only unchanged *O*-trimethylsantal was obtained.

A saturated solution of potassium permanganate (100 ml.) was added dropwise during 3 hours to the foregoing *iso*flavan (1 g.), dissolved in acetone (150 ml.), and next day the mixture was cleared with sulphur dioxide, warmed with a little 2N-sulphuric acid, cooled, and diluted with water. Unchanged compound (0·6 g.), m. p. 133°, quickly separated, and, after the isolation of this substance and spontaneous evaporation of the acetone, the liquor slowly (2 weeks) deposited a product (0·1 g.), m. p. 151—156°, which is probably 5 : 7 : 3′ : 4′-tetramethoxy*iso*flavanone. Recrystallised from alcohol or a little ethyl acetate, this compound formed white needles, m. p. 158·5°, which had a negative ferric reaction and

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* A small specimen of santal, m. p. 218°, was isolated by H. W. Jones in collaboration with one of us (A. R.) during 1939—1940 from an ethereal extract of sandelwood which had been exhausted with carbon tetrachloride. This material gave analytical figures agreeing reasonably well with those now obtained for the monohydrate of santal (Found: C, 60·2; H, 4·6; OMe, 11·5%), and formed the trimethyl ether, m. p. 166° (Found: OMe, 35·8%) and an acetyl derivative (? *O*-diacetate), m. p. 152°. These results were embodied in a Thesis submitted by H. W. Jones for the degree of Master of Science of the University of Liverpool in May, 1941.—A. R.

readily reacted with 2 : 4-dinitrophenylhydrazine. Attempts to improve the yield of this *iso*flavanone by varying the conditions of oxidation, *e.g.*, elevated temperatures or presence of potassium carbonate, failed.

Ozonolysis of O-*Trimethylsantal.*—Ozone and oxygen were passed for ½ hour into a solution of the ether (1 g.) in chloroform (100 ml.) at 0°, and the solvent was then removed in a vacuum. On treatment with water the combined brown oily products from two experiments set to a hard glass which was disintegrated by being triturated with 2N-sodium hydroxide. The insoluble material (0·09 g.), consisting of unchanged *O*-trimethylsantal, was separated by filtration, and the filtrate acidified with hydrochloric acid and extracted with ether. Crystallised from alcohol and then ethyl acetate, the residue left on evaporation of the ethereal extracts gave 2-hydroxy-4 : 6-dimethoxybenzoic acid in colourless needles (0·4 g.), m. p. 156°, identical in every way with an authentic sample prepared according to Herzig *et al.* (*Monatsh.*, 1902, **23**, 95) (Found : C, 54·8; H, 5·2. Calc. for $C_9H_{10}O_5$; C, 54·5; H, 5·5%). Prepared by means of diazomethane, the methyl ester of this acid from either source had m. p. and mixed m. p. 109°. Evaporation of the alcoholic liquors from the purification of 2-hydroxy-4 : 6-dimethoxybenzoic acid left a semi-solid mass, part of which did not dissolve on being triturated with aqueous sodium hydrogen carbonate. Recrystallised from a little alcohol, this non-acidic compound formed colourless needles (0·2 g.), m. p. 77—78°, giving an amethyst colour with alcoholic ferric chloride (Found : C, 58·2; H, 6·1; OMe, 40·9%).

Hydrolysis of O-*Trimethylsantal.*—A solution of this ether (1 g.) in alcohol (47·5 ml.), containing potassium hydroxide (2·5 g.) and water (2·5 ml.), was boiled under reflux for 1 hour, cooled, diluted with water (150 ml.), and acidified (Congo-red) with 2N-hydrochloric acid. The resulting precipitate (0·8 g.) was dried and crystallised from alcohol, giving 2-*hydroxy*-4 : 6 : 3′ : 4′-*tetramethoxydeoxybenzoin* (III) in white needles, m. p. 117°, which had a reddish-brown ferric reaction in alcohol and were soluble in cold 2N-sodium hydroxide [Found : C, 64·9; H, 6·2; OMe, 35·4. $C_{14}H_8O_2(OMe)_4$ requires C, 65·1; H, 6·0; OMe, 37·3%]. The compound is readily soluble in acetone, chloroform, or ethyl acetate, and moderately soluble in benzene or ether.

Hydrolysis of *O*-trimethylsantal (2 g.) with 5% boiling potassium hydroxide (100 ml.) for 1 hour and acidification, after cooling, with 2N-sulphuric acid, yielded a slightly sticky precipitate. Crystallised from alcohol, this gave 2-hydroxy-4 : 6 : 3′ : 4′-tetramethoxydeoxybenzoin, m. p. and mixed m. p. 117°. Distillation of the aqueous liquor and subsequent neutralisation of the distillate, followed by evaporation to dryness and heating the residue with aniline (5 ml.) and aniline hydrochloride (2 g.), gave rise to *NN′*-diphenylformamidine hydrochloride (0·2 g.), identified by comparison with authentic material.

Oximation of 2-hydroxy-4 : 6 : 3′ : 4′-tetramethoxydeoxybenzoin (0·5 g.) in methanol (20 ml.) and water (6 ml.) was effected with hydroxylamine hydrochloride (0·5 g.) and sodium acetate (1·0 g.) on the steam-bath for 8 hours; shorter reaction periods gave unchanged ketone. After the addition of water (25 ml.) to the cooled mixture the *oxime* slowly separated in white needles (0·5 g.), m. p. 134—135°, and on being recrystallised from alcohol or ethyl acetate formed colourless prisms, m. p. 150° (Found : N, 3·9. $C_{18}H_{21}O_6N$ requires N, 4·0%).

Methylation of 2-hydroxy-4 : 6 : 3′ : 4′-tetramethoxydeoxybenzoin (1 g.) with methyl iodide (3 ml.) and potassium carbonate (10 g.) in boiling acetone (100 ml.) during 8 hours, with the addition of more iodide (3 ml.) and carbonate (5 g.) after 3 hours, gave rise to 2 : 4 : 6 : 3′ : 4′-pentamethoxydeoxybenzoin (0·8 g.), m. p. 97—99°, which on purification from alcohol formed white needles, m. p. 110°, having a negative ferric reaction (Found : C, 65·8; H, 6·2. $C_{19}H_{22}O_6$ requires C, 65·9; H, 6·4%). This compound was identical with a specimen prepared according to Freudenberg *et al.* (*Annalen*, 1925, **446**, 87).

When potassium permanganate (1·25 g.) in water (50 ml.) was gradually added to 2-hydroxy-4 : 6 : 3′ : 4′-tetramethoxydeoxybenzoin (0·5 g.) in acetone (75 ml.), a slow oxidation ensued which became somewhat more rapid after a time. Next day the solutions from three experiments were combined, cleared with sulphur dioxide, saturated with ammonium sulphate, and extracted with ether (50 ml. × 5). The residue left on evaporation of the dried extracts was redissolved in ether (100 ml.) and agitated with four successive portions of 2N-sodium hydrogen carbonate (20 ml., each). Acidification of the combined sodium hydrogen carbonate extracts gave veratric acid which was isolated with ether and purified by crystallisation from warm water and then alcohol, forming needles (0·15 g.), m. p. and mixed m. p. 180°, identified by comparison with an authentic sample [Found : C, 59·6; H, 5·7; OMe, 33·2. Calc. for $C_7H_4O_2(OMe)_2$: C, 59·3; H, 5·5; OMe, 34·1%]. The p-*nitrobenzyl* ester was prepared by heating under reflux a mixture of the sodium salt of veratric acid (0·3 g.) in a little water, and *p*-nitrobenzyl bromide (0·1 g.) in alcohol (5 ml.) for 45 minutes. On cooling the mixture, the precipitated ester (0·5 g.) was collected and crystallised from alcohol, forming silky needles, m. p. 144° (Found : N, 4·4. $C_{16}H_{15}O_6N$ requires N, 4·4%), identical with an authentic specimen, m. p. 144°, prepared in the same way (Found : N, 4·4%).

Evaporation of the washed and dried ethereal liquors remaining after the separation of veratric acid gave a product which crystallised from alcohol in pale yellow rhombic prisms (0·8 g.), m. p. 160·5°, having a reddish-brown ferric reaction in alcohol and dissolving in cold 2N-sodium hydroxide [Found: C, 62·2; H, 5·3; OMe, 35·7; *M* (Rast), 331, 303. $C_{14}H_8O_3(OMe)_4$ requires C, 62·1; H, 5·7; OMe, 35·7%; *M*, 348]. This substance, which has solubilities similar to those of the parent ketone and was also formed in poor yield when *O*-trimethylsantal was oxidised by means of potassium permanganate, gave a 2 : 4-*dinitrophenylhydrazone* forming red prisms, m. p. 206°, from ethyl acetate [Found : C, 54·7; H, 4·5; N, 11·2; OMe, 22·6. $C_{20}H_{12}O_6N_4(OMe)_4$ requires C, 54·5; H, 4·5; N, 10·6; OMe, 23·5%]. Methylation of this oxidation product (0·7 g.) by the procedure employed for the parent ketone gave rise to a *monomethyl ether* (*D*) which formed large yellow rhombic tablets (0·6 g.), m. p. 174·5°, insoluble in aqueous sodium hydroxide and having a negative ferric reaction [Found : C, 62·9; H, 6·3; OMe, 43·7. $C_{14}H_7O_2(OMe)_5$ requires C, 63·0; H, 6·1; OMe, 42·8%]. The same ether was obtained when 2 : 4 : 6 : 3′ : 4′-pentamethoxydeoxybenzoin (0·5 g.) in boiling acetone (60 ml.) was oxidised with aqueous potassium permanganate (15 ml. of a solution of 1·25 g. of permanganate in 60 ml. of water) and the solution subsequently cleared with sulphur dioxide and extracted with ether. Crystallised from aqueous alcohol and then from ethyl acetate, this specimen had m. p. and mixed m. p. 174—175°. From the alcoholic liquors unchanged ketone (0·3 g.) was obtained by evaporation and purified by repeated crystallisation; m. p. 110°.

Interaction of the ether (*D*), with phenylhydrazine under the usual conditions employed for the preparation of phenylhydrazones gave rise to a product which separated from alcohol in pale-yellow hexagonal plates, m. p. 201°, the analytical results for which do not agree with those required for the expected hydrazone $C_{25}H_{28}O_6N_2$ (Found: C, 68·3, 68·4; H, 5·9, 5·8; N, 6·8. Calc. for $C_{25}H_{28}O_6N_2$: C, 66·4; H, 6·2; N, 6·2. Calc. for $C_{25}H_{26}O_5N_2$: C, 69·1; H, 6·0; N, 6·5%).

5 : 7 : 3′ : 4′-*Tetramethoxy*-2-*methyl*iso*flavone* (IV).—Vigorous acetylation of 2-hydroxy-4 : 5 : 3′ : 4′-tetramethoxydeoxybenzoin (1·5 g.) with boiling acetic anhydride (10 ml.) and sodium acetate (1 g.) for 33 hours gave the 2-*methyl*iso*flavone* (1 g.) which formed colourless needles, m. p. 215—216°, from alcohol or ethyl acetate [Found: C, 67·2; H, 5·6; OMe, 30·7. $C_{16}H_8O_2(OMe)_4$ requires C, 67·4; H, 5·6; OMe, 34·8%].

O-*Triethylsantal* (II; R = Et).—A mixture of santal (2 g.), acetone (150 ml.), ethyl iodide (5 ml.), and potassium carbonate (8 g.) was heated under reflux for 24 hours with the addition of further portions of iodide (2 ml. each time) and carbonate (2 g. each time) at intervals of 8, 12, and 18 hours. The *triethyl ether* crystallised from alcohol and then ethyl acetate in colourless needles (2·1 g.), m. p. 111—112°, insoluble in cold aqueous sodium hydroxide, having a negative ferric reaction in alcohol (Found: C, 68·9; H, 6·5. $C_{22}H_{24}O_6$ requires C, 68·8; H, 6·3%), and readily soluble in acetone and moderately soluble in benzene.

O-Triethylsantal (1 g.) was boiled under reflux in a solution of potassium hydroxide (25 g.) in water (25 ml.) and alcohol (25 ml.) for 1·5 hours, and after the addition of water (15 ml.) the cooled solution was acidified with 2N-hydrochloric acid. Next day the precipitate was collected, washed, dried, and crystallised from alcohol and then from a little ethyl acetate, giving 2-*hydroxy*-4-*methoxy*-6 : 3′ : 4′-*triethoxydeoxybenzoin* (VII) in colourless hexagonal prisms (0·65 g.), m. p. 99°, soluble in acetone, chloroform, or in cold aqueous sodium hydroxide, and having a brownish-red ferric reaction in alcohol (Found: C, 67·5; H, 7·0. $C_{21}H_{26}O_6$ requires C, 67·4; H, 7·0%). The *oxime* separated from aqueous alcohol in colourless needles, m. p. 138° (Found: N, 3·5. $C_{21}H_{27}O_6N$ requires N, 3·6%). Oxidation of the ketone (0·6 g.) in acetone (75 ml.) was effected with a solution of potassium permanganate (1·5 g.) in water (50 ml.), added drop-wise, and next day the reaction mixture was cleared with sulphur dioxide, boiled with a little dilute sulphuric acid for two minutes, cooled, saturated with ammonium sulphate, and extracted with ether (50 ml. × 5). The combined extracts were evaporated, and a solution of the residue in ether was extracted with 2N-sodium hydrogen carbonate (20 ml. × 4). Acidification of the combined carbonate washings gave 3 : 4-diethoxybenzoic acid (0·3 g.), m. p. 156—163°, which on recrystallisation from aqueous acetone or alcohol had m. p. 165—166°, undepressed on admixture with an authentic specimen prepared by the oxidation of 3 : 4-diethoxybenzaldehyde (Herzig, *Monatsh.*, 1884, **5**, 78) [Found: C, 62·7; H, 6·8; equiv. (by titration), 216. $C_{11}H_{14}O_4$ requires C, 62·9; H, 6·7%; equiv., 210]. A specimen of the p-*nitrobenzyl* ester of the acid from natural sources was prepared by the method employed in the case of veratric acid and formed silky needles, m. p. 100°, from alcohol (Found: N, 4·0. $C_{18}H_{19}O_6N$ requires N, 4·1%); it was identified by comparison with a specimen, m. p. 100°, prepared from an authentic sample of 3 : 4-diethoxybenzoic acid (Found: N, 4·3%).

The ethereal solution left after the separation of 3 : 4-diethoxybenzoic acid was dried and evaporated; the residue, on crystallisation from alcohol and then from ethyl acetate–light petroleum (b. p. 60—80°) gave a *compound* (1·2 g.) in needles, m. p. 114—115°, slowly soluble in cooled 2N-sodium hydroxide and having a reddish-brown ferric reaction in alcohol (Found: C, 64·9; H, 6·2. $C_{21}H_{26}O_7$ requires C, 64·6; H, 6·7%). A solution of this substance in concentrated sulphuric acid had a deep puce colour, unchanged on gentle warming, whilst the blue solution in concentrated nitric acid changed to scarlet on being gently warmed.

2 : 4-*Dihydroxy*-6 : 3′ : 4′-*trimethoxydeoxybenzoin* (V; R = R′ = Me).—A mixture of phloroglucinol monomethyl ether (5 g.), powdered zinc chloride (2 g.), and 3 : 4-dimethoxybenzyl cyanide (6 g.) in ether (200 ml.) was saturated with hydrogen chloride in the course of 3 hours. Next day the crystalline ketimine derivative was well washed with ether and hydrolysed with water (100 ml.) on the steam-bath for ¾ hour, giving 2 : 4-*dihydroxy*-6 : 3′ : 4′-*trimethoxydeoxybenzoin*, which separated from the cooled hydrolysate. Recrystallised from alcohol, this ketone formed minute rhombic prisms (2·2 g.), m. p. 180° (Found: C, 63·8; H, 5·7. $C_{17}H_{18}O_6$ requires C, 64·2; H, 5·7%).

2-*Hydroxy*-4 : 6 : 3′ : 4′-*tetramethoxydeoxybenzoin* (III).—(*a*) Prepared from a mixture of *O*-dimethylphloroglucinol (6 g.), 3 : 4-dimethoxybenzyl cyanide (6 g.), and zinc chloride (2 g.) in ether (100 ml.) saturated with hydrogen chloride, the oily ketimine derivative was well washed with ether and dissolved in water (100 ml.). After having been almost neutralised with aqueous sodium hydrogen carbonate, this solution was heated on the steam-bath for 90 minutes, and the product which separated from the cooled mixture was collected, washed, and recrystallised several times from alcohol, giving 2-hydroxy-4 : 6 : 3′ : 4′-tetramethoxydeoxybenzoin in characteristic rosettes of colourless needles (1·5 g.), m. p. 117°, identical with the ketone obtained by the alkaline hydrolysis of *O*-trimethylsantal (Found: C, 65·0; H, 6·3%). Concentration of the alcoholic liquors from the purification of this ketone gave 4-*hydroxy*-2 : 6 : 3′ : 4′-*tetramethoxydeoxybenzoin* (VI) which separated from dilute alcohol in colourless prisms (0·3 g.), m. p. 140°, readily soluble in dilute aqueous sodium hydroxide and having a negative ferric reaction in alcohol (Found: C, 64·8; H, 6·2%). Alternatively, the ketones were separated as follows: a chloroform extract of the hydrolysate was extracted with 1% aqueous sodium hydroxide, and the chloroform solution washed, dried, and evaporated, leaving (III), m. p. 117° (after purification). Acidification of the alkaline extract gave the isomeric 4-hydroxy-ketone, m. p. 140°.

(*b*) A solution of 2 : 4-dihydroxy-6 : 3′ : 4′-trimethoxydeoxybenzoin (1·8 g.) in acetone (50 ml.) containing potassium carbonate (5 g.) and methyl iodide (2 ml.) was boiled for 1 hour; the product was crystallised from alcohol, giving 2-hydroxy-4 : 6 : 3′ : 4′-tetramethoxyphenacetophenone in colourless needles (1·5 g.), m. p. and mixed m. p. 117°.

Methylation of 2-hydroxy-4 : 6 : 3′ : 4′-tetramethoxydeoxybenzoin (2 g.) by potassium carbonate (15 g.) and methyl iodide (15 ml.) in boiling acetone during 11 hours gave 2 : 4 : 6 : 3′ : 4′-pentamethoxydeoxybenzoin (1·8 g.), m. p. 109—110°, undepressed on admixture of a specimen prepared by the method of Freudenberg *et al.* (*Annalen*, 1924, **446**, 87) (Found : C, 65·6; H, 6·4. Calc. for $C_{19}H_{22}O_6$: C, 65·9; H, 6·4%).

Oxidation of synthetic 2-hydroxy-4 : 6 : 3′ : 4′-tetramethoxydeoxybenzoin by the method employed for the compound obtained from *O*-trimethylsantal gave the same product, m. p. and mixed m. p. 160·5°.

5 : 7 : 3′ : 4′-*Tetramethoxy*iso*flavone* (II; R = Me).—2-Hydroxy-4 : 6 : 3′ : 4′-tetramethoxydeoxybenzoin (1 g.), ethyl formate (1·5 ml.), and pulverised sodium (1 g.) were mixed at −10° and then kept at −5° for 2 days. After addition of ice the mixture was extracted with ether (50 ml. × 4), and the combined extracts were washed, dried, and evaporated, leaving the *iso*flavone as an oil which, on crystallisation from alcohol and then from ethyl acetate, formed colourless needles, m. p. 164—166°, identical with *O*-trimethylsantal (Found : C, 66·9; H, 5·5%).

2 : 4-*Dihydroxy*-6 : 3′ : 4′-*triethoxydeoxybenzoin* (V; R = Et).—The condensation of phloroglucinol monoethyl ether (4 g.) and 3 : 4-diethoxybenzyl cyanide (4 g.) in ether (20 ml.) by means of zinc chloride (2 g.) and excess of hydrogen chloride gave a brown viscous oil, which was well washed with ether and dissolved in water (100 ml.). This solution was almost neutralised with saturated aqueous sodium hydrogen carbonate and then heated on the steam-bath for 90 minutes. After the mixture cooled, the precipitated brownish oily product gradually solidified, and on crystallisation from alcohol and then ethyl acetate gave the 2 : 4-*dihydroxy*-6 : 3′ : 4′-*triethoxydeoxybenzoin* (V; R = R′ = Et) in spherical clusters of rhombic prisms (1·1 g.) which had a reddish-brown ferric reaction in alcohol (Found : C, 66·7; H, 6·8. $C_{20}H_{24}O_6$ requires C, 66·7; 6·7%). This substance is readily soluble in acetone, moderately soluble in benzene, and almost insoluble in light petroleum.

Partial methylation of this ketone (1·2 g.) was effected with methyl iodide (0·8 g.) and potassium carbonate (2 g.) in boiling acetone (50 ml.) during 1 hour with the addition of more iodide (0·4 ml.) after 30 minutes. The product was crystallised from 95% alcohol, giving 2-hydroxy-4-methoxy-6 : 3′ : 4′-triethoxydeoxybenzoin (VII) in colourless needles, m. p. 99°, identical in every way with a specimen obtained by the hydrolytic fission of *O*-triethylsantal (Found : C, 65·4; H, 7·2%).

7-*Methoxy*-5 : 3′ : 4′-*triethoxy*iso*flavone* (*O-Triethylsantal*) (II; R = Et).—The condensation of methyl formate (25 ml.) and 2-hydroxy-4-methoxy-6 : 3′ : 4′-triethoxydeoxybenzoin (0·7 g.) by means of sodium (0·7 g.) at −15° and then at −5° for 3 days gave an oily product which did not solidify and which may have been the formyl derivative of the ketone. A solution of this in acetic acid (5 ml.) was heated under reflux for 30 minutes, diluted with water (30 ml.), neutralised with sodium hydrogen carbonate, and extracted with ether (30 ml. × 4). Crystallised from ethyl acetate, the residue obtained on evaporation of the dried extracts gave the *iso*flavone (0·5 g.) in colourless needles, m. p. 111—112°, identical with a specimen of *O*-triethylsantal (Found : C, 68·6; H, 6·1%).

2 : 4-*Dihydroxy*-6-*methoxy*-3′ : 4′-*diethoxydeoxybenzoin* (V; R = Me; R′ = Et).—From the interaction of phloroglucinol monomethyl ether (4 g.) and 3 : 4-diethoxybenzyl cyanide (4 g.), zinc chloride (2 g.), and excess of hydrogen chloride in ether (200 ml.) during 4 days, a viscous olive-brown product was obtained which was dissolved in water (200 ml.). After having been almost neutralised with sodium hydrogen carbonate and then heated on the steam-bath for 90 minutes, this solution gave 2 : 4-*dihydroxy*-6-*methoxy*-3′ : 4′-*diethoxydeoxybenzoin* as a brown oil which slowly solidified and separated from alcohol and then ethyl acetate in elongated rhombic tablets (1·6 g.), m. p. 129—130°, having a reddish-brown ferric reaction in alcohol (Found : C, 65·9; H, 6·5. $C_{19}H_{22}O_6$ requires C, 65·9; H, 6·4%). Recrystallisation of the pure ketone from 95% alcohol gave material of a slightly lower and somewhat variable melting point, a result apparently due to solvation since on being dried in a high vacuum at 80° this product then melted at 129—130°. The compound is readily soluble in dilute aqueous sodium hydroxide or acetone, and sparingly soluble in benzene or ether.

Monoethylation of this ketone (1·2 g.) with ethyl iodide (0·6 ml.) and potassium carbonate (1·5 g.) in boiling acetone (22 ml.) during 2 hours gave 2-*hydroxy*-4 : 6 : 3′ : 4′-*tetraethoxydeoxybenzoin* which formed colourless needles (1·0 g.), m. p. 111—112°, from alcohol or ethyl acetate, having a reddish-brown ferric reaction in alcohol (Found : C, 67·2; H, 6·8. $C_{21}H_{26}O_6$ required C, 67·4; H, 7·0%). This ketone is slowly soluble in 2N-sodium hydroxide and, on being warmed, its pale green solution in concentrated sulphuric acid becomes lilac and then brown, whilst the green solution of the substance in concentrated nitric acid quickly becomes blue and then orange.

5-*Methoxy*-7 : 3′ : 4′-*triethoxy*iso*flavone* (II; R = Et).—2-Hydroxy-6-methoxy-4 : 3′ : 4′-triethoxydeoxybenzoin (0·7 g.), methyl formate (15 ml.), and pulverised sodium were mixed at −10° and then kept at −5° for 3 days. After the addition of ice the iso*flavone* was isolated by repeated extraction with ether and then crystallised from ethyl acetate, forming thin parallelepipeds (0·4 g.), m. p. 129—130°, readily soluble in acetone and moderately soluble in alcohol (Found : C, 69·0; H, 6·4. $C_{22}H_{24}O_6$ requires C, 68·8; H, 6·3%).

2-*Hydroxy*-3′-*methoxy*-4 : 6 : 4′-*triethoxydeoxybenzoin*.—The reddish oil obtained from the interaction of phloroglucinol diethyl ether (4 g.), 3-methoxy-4-ethoxybenzyl cyanide (4 g.), zinc chloride (2 g.), and excess of hydrogen chloride in ether (150 ml.) was dissolved in water (200 ml.), and after having been almost neutralised with sodium hydrogen carbonate the solution was heated on the steam-bath for 1½ hours. A solution of the resulting oily product in chloroform was washed once with water and then extracted with 1% aqueous sodium hydroxide (20 ml. × 5), dried, and evaporated. Crystallisation of the residue from a little alcohol gave 2-*hydroxy*-3′-*methoxy*-4 : 6 : 4′-*triethoxydeoxybenzoin* (1·25 g.) which on recrystallisation from alcohol or ethyl acetate formed colourless needles, m. p. 138°, slowly soluble in 2N-sodium hydroxide and having a reddish-brown ferric reaction in alcohol (Found : C, 67·2; H, 7·3. $C_{21}H_{26}O_6$ requires C, 67·4; H, 7·0%). Acidification of the 1% aqueous sodium hydroxide extracts gave a small amount of an oil which did not solidify and may have contained the isomeric 4-hydroxy-ketone along with unchanged phloroglucinol diethyl ether.

3′-*Methoxy*-5 : 7 : 4′-*triethoxy*iso*flavone*.—Condensation of the foregoing ketone (1·2 g.) with methyl formate (50 ml.) by means of sodium (1·2 g.) at −5° for 3 days gave rise to the iso*flavone* (0·4 g.) which on repeated crystallisation from ethyl acetate was obtained in colourless needles, m. p. 134°, changing to 150° after having been dried in a high vacuum at 80° for 2 hours [Found (in dried material): C, 68·9; H, 6·4. $C_{22}H_{24}O_6$ requires C, 68·8; H, 6·3%].

*4′-Methoxy-5 : 7 : 3′-triethoxy*iso*flavone.*—The crude product formed by the condensation of phloroglucinol diethyl ether (3·1 g.) and 4-methoxy-3-ethoxybenzyl cyanide (3·1 g.) according to the method of Hoesch was dissolved in chloroform, and the solution extracted with 1% aqueous sodium hydroxide, dried, and evaporated, leaving *2-hydroxy-5′-methoxy-4 : 6 : 3′-triethoxydeoxybenzoin* (1 g.) which formed colourless rectangular tablets, m. p. 117°, from alcohol or ethyl acetate (Found: C, 67·4; H, 7·0. $C_{21}H_{26}O_6$ requires C, 67·4; H, 7·0%). This compound has a reddish-brown ferric reaction in alcohol, and on being warmed the pale green solution in concentrated sulphuric acid becomes deep green and then amber. From this ketone *4′-methoxy-5 : 7 : 3′-triethoxy*iso*flavone* was prepared in the same manner as 3′-methoxy-5 : 7 : 4′-triethoxy*iso*flavone and on crystallisation from alcohol formed colourless needles, m. p. 114° [Found (in specimen dried in a high vacuum at 80°): C, 68·7; H, 6·1. $C_{22}H_{24}O_6$ requires C, 68·8; H, 6·3%].

1-3′ : *4′-Dimethoxyphenyl-2-2″ : 4″ : 6″-trimethoxybenzoylethylene oxide* was prepared in the course of attempts to define the oxidation product of 2-hydroxy-4 : 6 : 3′ : 4′-tetramethoxyphenacetophenone. A solution of 2 : 4 : 6-trimethoxyacetophenone (4 g.) and veratraldehyde (4 g.) in the minimum amount of alcohol was mixed with aqueous sodium hydroxide (8 g. in 16 ml. of water), boiled under reflux for 1 hour, and poured on ice. The resulting styryl ketone separated from ethyl acetate in yellow prisms (5·5 g.), m. p. 117° (compare Tutin and Caton, *J.*, 1910, **97**, 2062). It (5·8 g.) was oxidised in methanol (30 ml.) at 25° with a mixture of 15% hydrogen peroxide (5 ml.) and 2N-sodium hydroxide during 2 hours, and the clear solution then diluted with water. Crystallised from ethyl acetate–light petroleum (b. p. 60—80°) and then from alcohol or ethyl acetate, the resulting precipitate gave the oxide in colourless silky needles (4·5 g.), m. p. 117—118°, readily soluble in acetone (Found: C, 64·2; H, 6·0. $C_{20}H_{22}O_7$ requires C, 64·2; H, 5·9%).

2-Hydroxy-4 : 6-dimethoxy- and *2-Hydroxy-4 : 6 : 4′-trimethoxy-deoxybenzoin.*—The condensation of benzyl cyanide (5 g.) and phloroglucinol dimethyl ether (5 g.) by the method of Hoesch gave an oily product which was dissolved in chloroform; the solution was then extracted with 1% aqueous sodium hydroxide to remove unchanged phloroglucinol dimethyl ether and any 4-hydroxy-2 : 6-dimethoxydeoxybenzoin. Evaporation of the chloroform solution left the required *2-hydroxy-4 : 6-dimethoxydeoxybenzoin*, which separated from 95% alcohol and then ethyl acetate in large aggregates of colourless rhombic plates (2·5 g.), m. p. 117°, having a reddish-brown ferric reaction in alcohol (Found: C, 70·3; H, 6·0. $C_{16}H_{16}O_4$ requires C, 70·6; H, 5·9%).

Potassium permanganate (2·5 g.), dissolved in water (100 ml.), was added gradually in 20-ml. portions to a solution of 2-hydroxy-4 : 6-dimethoxydeoxybenzoin (1 g.) in acetone (75 ml.). Next day the mixture was cleared with sulphur dioxide; in the course of 24 hours a *product* (0·8 g.) separated in silky needles, insoluble in aqueous sodium hydrogen carbonate but readily soluble in aqueous sodium hydroxide. Recrystallised from ethyl acetate–light petroleum (b. p. 80—100°), the compound had m. p. 110—111° and on admixture with the parent ketone melted at 98° (Found: C, 66·7; H, 5·5. $C_{16}H_{16}O_5$ requires C, 66·7; H, 5·6%); it is slowly soluble in aqueous sodium carbonate, and gives a reddish-brown ferric reaction in alcohol. Benzoic acid appears not to have been formed in appreciable quantity in this oxidation.

In a similar manner *2-hydroxy-4 : 6 : 4′-trimethoxydeoxybenzoin* (1·64 g.) was prepared from phloroglucinol dimethyl ether (4·5 g.) and 4-methoxybenzyl cyanide (4·5 g.) and on crystallisation from alcohol formed white needles, m. p. 88—89°, slowly soluble in 2N-sodium hydroxide and having a reddish-brown ferric reaction (Found: C, 67·8; H, 6·1. $C_{17}H_{18}O_5$ requires C, 67·6; H, 6·0%). Oxidation of this ketone (1 g.) in acetone (75 ml.) was effected with potassium permanganate (2·5 g.) in water (100 ml.) added in portions of about 20 ml. To initiate the reaction after the addition of the first portion of permanganate solution it was necessary to warm the mixture gently on the steam-bath for a few minutes, but subsequently the mixture was cooled in tap-water before each fresh addition of the reagent. After having been cleared with sulphur dioxide, the reaction mixture was saturated with ammonium sulphate and extracted with ether (30 ml. × 4). The residue left on evaporation of the combined ethereal extracts which had contained acetone was dissolved in fresh ether and then extracted with saturated aqueous sodium hydrogen carbonate (25 ml. × 4). Acidification of the latter combined extracts gave anisic acid (0·75 g.), m. p. and mixed m. p. 183° (after purification). Evaporation of the dried ethereal solution left after the separation of anisic acid gave an oil which was dissolved in a mixture of boiling ethyl acetate and light petroleum (b. p. 80—100°). On cooling this solution deposited a *compound* in pale yellow needles (0·7 g.), m. p. 122°, soluble in cold 2N-sodium carbonate, and having a reddish-brown ferric reaction in alcohol (Found: C, 64·1; H, 5·7. $C_{17}H_{18}O_6$ requires C, 64·2; H, 5·7%).

Demethylation of Santal.—Acetic anhydride (20 ml.) was carefully added to hydriodic acid (5 ml., sp. gr. 1·7) with cooling. Santal (1 g.) was then introduced, and the mixture heated under reflux (oil-bath at 150°) for 30 minutes, cooled, mixed with saturated aqueous sodium sulphite (50 ml.), and saturated with ammonium sulphate. Next day the yellow precipitate (0·8 g.) was collected, well washed with water, and crystallised from 50% acetic acid, giving 5 : 7 : 3′ : 4′-tetrahydroxy*iso*flavone (norsantal) (I; R = H) in cream-coloured, globular clusters of minute tablets which, on being sublimed at 230°/0·005 mm., formed a mass of pale yellow, elongated, rhombic plates, m. p. 270° (Found: C, 63·1; H, 3·6. Calc. for $C_{15}H_{10}O_6$: C, 63·0; H, 3·5%). Acetylation of this compound (0·3 g.) with boiling acetic anhydride (5 ml.) and sodium acetate (0·2 g.) gave rise to 5 : 7 : 3′ : 4′-tetra-acetoxy*iso*flavone (0·3 g.) which on recrystallisation from acetic acid formed colourless needles, m. p. 207·5°, unchanged on further purification from alcohol and ethyl acetate (Found: C, 60·5; H, 4·1. Calc. for $C_{23}H_{18}O_{10}$: C, 60·8; H, 4·0%).

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