The Chemistry of the "Insoluble Red" Woods. Part VI. Santalin and Santarubin.*

By Alexander Robertson and W. B. Whalley.

[Reprint Order No. 5250.]

The optically inactive colouring matters santalin, $C_{27}H_{15}O_6(OMe)_3$, and santarubin, $C_{27}H_{14}O_5(OMe)_4$, have been isolated from commercial camwood and barwood and shown to be quinonoid anhydrobenzopyranol bases, devoid of *C*-methyl or reactive carbonyl groups and forming salts by the addition of acids. Sandalwood contains santalin but no santarubin.

Methylation of santalin gave *O*-tetramethylsantalin, a quinonoid anhydro-base, forming salts additively, and *O*-pentamethylsantalin, a benzopyranol. Similarly, santarubin gave *O*-trimethylsantarubin, an anhydro-base, and *O*-tetramethylsantarubin, a benzopyranol. On hydrolytic fission *O*-tetramethylsantalin and *O*-trimethylsantarubin furnished 2 : 4-dihydroxy-5-methoxybenzaldehyde whilst on oxidation *O*-tetramethylsantalin gave rise to veratraldehyde, veratric acid, and 2 : 4-dimethoxybenzoic acid, and *O*-trimethylsantarubin to 2 : 4-dimethoxybenzaldehyde, 2 : 4-dimethoxybenzoic acid, and probably veratric acid. From this evidence provisional structures (VII) and (XI) have been deduced, respectively, for *O*-tetramethylsantalin and *O*-trimethylsantarubin, and it appears that santalin and santarubin are ethers of two isomeric quinonoid anhydro-bases.

The pigments present in commercial specimens of the "insoluble red" woods, sandalwood, camwood, and barwood, have been examined by various investigators, of whom Pelletier (*Annalen*, 1833, **6**, 28) appears to have been the first to obtained a crude preparation to which he assigned the empirical formula $C_{16}H_{16}O_3$ and the name, santalin. By various and often tedious and complicated processes a succession of later investigators (*inter al.*, Preisser, *Berz. Jahresber.*, 1845, **24**, 515; Meier, *Arch. Pharm.*, 1848, **55**, 285;

---

* Part V, *J.*, 1954, 1440.

1848, **56**, 41; Bolley, *Annalen*, 1847, **62**, 150; Weyermann and Häffely, *ibid.*, 1850, **74**, 226; Anderson, *J.*, 1876, **30**, 582; Franchimont, *Ber.*, 1879, **12**, 14; and Perkin, *J.*, 1899, **75**, 443) isolated crude amorphous pigment fractions, some of which may or may not have been identical with santalin. A crystalline santalin, m. p. 226°, appears to have been first isolated by Cain and Simonsen (*J.*, 1912, **101**, 1061) who obtained it by a complex procedure and ascribed to it the empirical formula $C_{14}H_{11}O_4{\cdot}OMe$, which, in collaboration with Smith (*J.*, 1914, **105**, 1335), they subsequently revised to $C_{28}H_{22}O_8(OMe)_2$. By methylation with potassium hydroxide solution and methyl sulphate these authors prepared an *O*-dimethylsantalin, m. p. 165—167° (Found: C, 67·9; H, 6·1; OMe, 31·6%), giving veratric and anisic acid on oxidation. O'Neill and Perkin (*J.*, 1918, **113**, 125) maintained, however, that their microcrystalline santalin had the formula $C_{22}H_{18}O_6(OMe)_2$, and also claimed to have isolated an *iso*santalin, $C_{24}H_{24}O_8$, as a chocolate-coloured powder, which furnished oxonium salts. This was the first indication that these pigments might be benzopyranols or anhydrobenzopyranols.

By the oxidation of santalin (a microcrystalline powder) with alkaline ferricyanide Dieterle and Stegemann (*Arch. Pharm.*, 1926, **264**, 1) claimed the production of homopterocarpin (Part I, *J.*, 1940, 787) but their results were inconclusive and it seems likely that, as the authors themselves appeared to suspect, the homopterocarpin was probably contained as an impurity in their so-called santalin. The first clear recognition of the benzopyranol, or anhydrobenzopyranol, character of santalin is due to Raudintz, Navratil, and Benda (*Ber.*, 1934, **67**, 1036) who proposed the empirical formula $C_{34}H_{23}O_{10}$ for the base.

In our investigations on the colouring matters of the "insoluble-red" woods we extracted the sawdusts of the commercial woods with boiling carbon tetrachloride (cf. Part I, *loc. cit.*) to remove homopterocarpin, pterocarpin, traces of santal (Part III, *J.*, 1949, 1571), and vegetable oils. On subsequent concentration the extracts from camwood and barwood deposited small quantities of a pigment which on purification was obtained in chocolate-coloured prisms. Although this colouring matter, which does not appear to occur in our specimen of sandalwood, resembles somewhat the *iso*santalin of O'Neill and Perkin (*loc. cit.*) we propose, for the sake of clarity, to name the compound santarubin.

After the separation of the santarubin-containing fraction the residual wood was exhausted with ether or chloroform and ultimately a vermilion-coloured pigment was isolated which possibly is identical with the product previously designated santalin and for which we propose to retain this name.

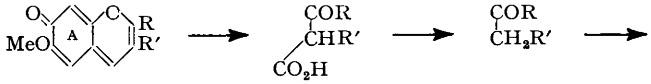
Thus isolated, santalin, m. p. 305° (decomp.), has the properties of an anhydrobenzopyranol base, $C_{27}H_{15}O_6(OMe)_3$, of the quinonoid type, derived from the carbinol base for which we propose the name santalanol. Whilst closely allied empirical formulations cannot be excluded at this stage, the formula $C_{27}H_{15}O_6(OMe)_3$ is in the closest accord with the numerous analytical results obtained with santalin and the derivatives described in this paper and will be used for the present as a basis for discussion. Santalin appears to retain water rather tenaciously and if not dried rigorously before analysis gives results more nearly in accord with the formula $C_{30}H_{26}O_{10}$, which is in close agreement with the formulation $C_{30}H_{28}O_{10}$ of Cain, Simonsen, and Smith (*loc. cit.*). This quinonoid base, which is devoid of *C*-methyl groups, forms salts by the addition of acids, *e.g.*, with hydrochloric acid it gives a hydrochloride of type (IX), a chloride derived from the pyranol base santalanol, which we propose to call santalylium chloride and which upon treatment with sodium acetate regenerates santalin without the intermediate formation of santalanol (cf. Irvine and Robinson, *J.*, 1927, 2086). Contrary to the expected conversion of an anhydrobenzopyranol into the methyl ether of hydroxybenzopyranol (cf., *e.g.*, Pratt and Robinson, *J.*, 1923, 739; Armit and Robinson, *J.*, 1925, 1604) the methylation of santalin with an excess of methyl sulphate and aqueous-methanolic sodium hydroxide or by the methyl iodide–potassium carbonate method gave rise to *O*-tetramethylsantalin $C_{27}H_{11}O_2(OMe)_7$, which retains the properties of a quinonoid anhydrobenzopyranol base and gives rise to the expected salts; the melting point and analytical results of *O*-tetramethylsantalin are in close agreement with those recorded for *O*-dimethylsantalin by Cain, Simonsen, and Smith (*loc. cit.*), and the molecular-weight determinations in boiling benzene are in accord with the empirical formula now proposed. Further, methylation of *O*-tetramethylsantalin with methyl sulphate and potassium carbonate in boiling benzene (cf. Armit and Robinson, *loc. cit.*) furnished the optically inactive, colourless *O*-pentamethylsantalanol which readily gave rise to *O*-pentamethylsantalylium picrate and perchlorate.

In extensive studies on the degradation of santalin and its methyl ethers it was found that ozonolysis (in a variety of solvents), oxidation with hydrogen peroxide in acetic acid, methanol, or methanolic sodium hydroxide, or oxidation with chromic acid gave intractable products. *O*-Pentamethylsantalanol was surprisingly resistant to hot alkalis but *O*-tetramethylsantalin on degradation with concentrated aqueous-methanolic potassium hydroxide furnished 2 : 4-dihydroxy-5-methoxybenzaldehyde (I) in very low yield together with a complex mixture from which there were isolated by careful chromatography two colourless resinous products, (*a*) with an intense green and (*b*) with a deep brown ferric reaction. From the fraction (*a*) a semicarbazone $C_{28}H_{16}O_3N_3(OMe)_7$ and a 2 : 4-dinitrophenylhydrazone $C_{33}H_{17}O_6N_4(OMe)_7$ were prepared, which appear to retain the original carbon skeleton and thus correspond to derivatives of a styryl ketone derived from *O*-tetramethylsantalin. The second fraction, (*b*), from the hydrolysate furnished a semicarbazone and a 2 : 4-dinitrophenylhydrazone, the analytical results of which could not be satisfactorily equated with an empirical formula.

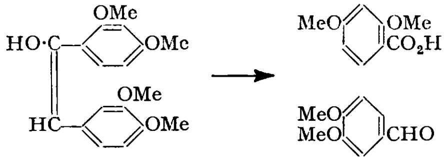
Oxidation of *O*-tetramethylsantalin with potassium permanganate under a variety of conditions gave rise to a complex mixture from which ultimately there were isolated veratraldehyde, veratric acid, and 2 : 4-dimethoxybenzoic acid. Despite a careful search *p*-anisic acid (cf. Cain, Simonsen, and Smith, *loc. cit.*) could not be detected among the acidic degradation products and it may well be that the pigment described by these authors, whilst similar in some respects, is not identical with the compound now described.

From the results of the foregoing degradation experiments it may reasonably be assumed that the 2 : 4-dihydroxy-5-methoxybenzaldehyde residue (I) is derived from an anhydrobenzopyrylium system in *O*-tetramethylsantalin where the hydroxyl group in the 2-position of the aldehyde arises from the oxonium ring and that in the 4-position is derived from the hemiquinone system, *i.e.*, the aldehyde (I) is derived from the residue (II) which cannot have a substituent in the 4-position. Further, if it is assumed that the veratraldehyde and veratric acid are derived from the same part of the molecule, the isolation of (I) along with the veratrole unit, together with the 2 : 4-dimethoxybenzoic acid, account for five of the seven methoxyl groups in *O*-tetramethylsantalin and, in conjunction with the unit (II), for seven of the nine oxygen atoms. Thus the remaining two oxygen atoms are present as methoxyl groups and, in agreement with the empirical formula

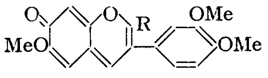
(I)



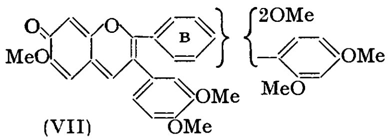
(II) (III) (IV)



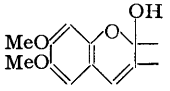
(V)



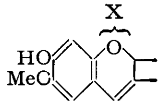
(VI)



(VII)



(VIII)

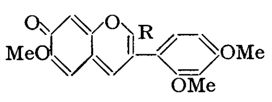


(IX)

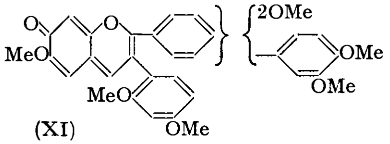
imply the presence of a fourth benzenoid system. Moreover, it is also reasonable to assume that the veratraldehyde residue, formed during the oxidation of *O*-tetramethylsantalin, probably arises from the oxidation of the enolic form of a deoxybenzoin system resulting from the destruction of ring (A) of the residue (II), *i.e.*, the oxidative degradation proceeds by way of (III), (IV), (V). That the initial seat of oxidation in *O*-tetramethylsantalin is in ring (A) of (II) finds support in the extreme resistance of *O*-pentamethylsantalanol to hydrolysis or oxidation under comparable conditions. The oxidation route proposed to account for the production of veratraldehyde is supported by the results obtained in the oxidation of deoxybenzoins which can be best explained on the assumption that it is the enolic form which reacts with potassium permanganate (Part IV, *J.*, 1950, 2961; cf. Part V, *J.*, 1954, 1440). Therefore, if these views are correct the veratraldehyde and the veratric acid arise from a veratrole residue in the 3-position of the system (II) in *O*-tetramethylsantalin which may therefore be expanded to formula (VI). Since the *O*-dimethylresorcinol nucleus appears only as 2 : 4-dimethoxybenzoic acid, therefore to accommodate the dimethoxybenzene unit which apparently is destroyed in the oxidation, the residue R in (VI) may be expanded to a diphenyl system where the resorcinol unit is terminal as in (VII). Thus the quinonoid anhydropyranol base, *O*-tetramethylsantalin and the pyranol, *O*-pentamethylsantalanol, may be provisionally represented by the structures (VII) and (VIII) respectively where the position of the two methoxyl groups in ring (B) of the diphenyl system remains to be determined.

In agreement with numerous analytical results of the compound and its derivatives santarubin is best represented by the empirical formula $C_{27}H_{14}O_5(OMe)_4$. This quinonoid anhydro-base, which is devoid of *C*-methyl groups, closely resembles santalin, forming a well-defined hydrochloride, santarubylium chloride, and, on methylation by the methyl iodide–potassium carbonate method, an *O*-trimethyl ether, isomeric with *O*-tetramethylsantalin. Like this compound, *O*-trimethylsantarubin is a quinonoid anhydro-base, forming a well-crystallised picrate and giving by the methyl sulphate–benzene–potassium carbonate method, a benzopyranol, *O*-tetramethylsantarubanol, characterised by the formation of a picrate and perchlorate.

In its behaviour towards hydrolytic and oxidising agents *O*-trimethylsantarubin is practically identical with *O*-tetramethylsantalin. With hot concentrated alkali it gave 2 : 4-dihydroxy-5-methoxybenzaldehyde (I), implying the presence of the residue (II) in the molecule. In addition a complex resinous product was formed from which there was prepared a 2 : 4-dinitrophenylhydrazone $C_{33}H_{17}O_8N_4(OMe)_7$, isomeric with the corresponding product from *O*-tetramethylsantalin. On oxidation with potassium permanganate *O*-trimethylsantarubin furnished 2 : 4-dimethoxybenzaldehyde, 2 : 4-dimethoxybenzoic acid, and an acid, in all probability veratric acid. Consequently, since *O*-tetramethylsantalin and *O*-trimethylsantarubin are isomeric and have the common unit (I) present in a residue of type (II), by the same chain of reasoning *O*-trimethylsantarubin contains the unit (X) which can be expanded to type (XI) as representing the structure of this compound. The production of 2 : 4-dimethoxybenzaldehyde from *O*-trimethylsantarubin in place of veratraldehyde, as in the case of *O*-tetramethylsantalin, indicates the presence of the *O*-dimethylresorcinol residue in the 3-position of *O*-trimethylsantarubin.



(X)



(XI)

Thus santalin and santarubin are regarded as partially methylated derivatives of two isomeric, similarly constituted, quinonoid heptahydroxyanhydro-bases with tetrahydroxydiphenyl substituents in the 2-position, the orientations of which are unknown. In agreement with this it was found that the ultra-violet absorption curves of santalin and santarubin are typical of quinonoid anhydro-benzopyranols. Although for the present the structures assigned to these compounds are regarded as provisional we believe that they contain the main essential features of the molecules and it is of interest that these formulæ are in a general way related to the structures of other constituents isolated from these woods, *viz.*, pterocarpin and homopterocarpin (Part I, *J.*, 1940, 787), and santal (Part III, *J.*, 1949, 1571).

In view of the exceptional difficulties encountered in the isolation of large amounts of the pigments and in the degradation studies, experiments on the preparation of type compounds have been initiated with a view to the ultimate synthesis of the methyl ethers of santalin and santarubin.

EXPERIMENTAL

Extraction of Santalin.—After having been twice digested with boiling carbon tetrachloride, powdered commercial red sandalwood (Part I, *loc. cit.*) (6 kg.) was exhaustively extracted with ether in a Soxhlet apparatus, and the very viscous resin (*ca.* 360 g.), which separated in the Soxhlet boiler, was dissolved in ethyl acetate (1 l.). On being kept this solution gradually deposited a red crystalline solid which was repeatedly recrystallised from alcohol, giving *santalin* in salmon-pink needles (20—30 g.), m. p. 305° (decomp.) with previous darkening from *ca.* 290°, $\lambda_{\text{max.}}$ 506, 355, 316 mμ ($E_{1\,\text{cm.}}^{1\%}$ 430, 129, 272) [Found in specimen dried in a vacuum at 200° for 16 hr.: C, 67·5; H, 4·7; OMe, 16·4. $C_{27}H_{15}O_6(OMe)_3$ requires C, 68·2; H, 4·6; OMe, 17·0%]. The pigment, which is sparingly soluble in the usual organic solvents, has an intense violet ferric reaction in alcohol, and is readily soluble in 2N-aqueous sodium hydroxide from which it is precipitated unchanged by carbon dioxide.

Addition of concentrated hydrochloric acid (3 ml.) to a suspension of santalin (1 g.) in alcohol (10 ml.) initially furnished a clear solution which then slowly deposited santalylium chloride in deep red prisms, with a green reflex. Recrystallised from aqueous-alcoholic hydrochloric acid, this salt separated as a *dihydrate* in deep red prisms, m. p. 294° (decomp.) [Found: C, 59·6, 60·2, 60·0; H, 4·7, 4·9, 5·4; Cl, 6·2; OMe, 17·0, 13·3, 13·0. $C_{27}H_{16}O_6Cl(OMe)_3,2H_2O$ requires C, 60·0; H, 4·8; Cl, 5·8; OMe, 15·5%]. Addition of much water or aqueous sodium acetate to an alcoholic solution of this chloride furnished the parent anhydro-base.

When saturated aqueous-alcoholic (1 : 1) picric acid (5 ml.) was added to a suspension of santalin (0·5 g.) in alcohol (2 ml.), the clear solution initially formed slowly deposited *santalylium picrate* in rosettes of dark crimson, rhombic prisms, m. p. 208—211° (decomp.) after purification from aqueous alcohol containing 2% of picric acid [Found: C, 56·6, 57·1, 56·6; H, 4·1, 4·4, 4·1; N, 5·8; OMe, 11·0, 10·8. $C_{33}H_{18}O_{13}N_3(OMe)_3$ requires C, 57·0; H, 3·6; N, 5·6; OMe, 12·3%].

On saturation with hydrogen chloride the ethyl acetate mother-liquors remaining from the purification of santalin furnished a red amorphous precipitate (460 g.) which rapidly darkened in contact with air whilst moist with solvent. After drying rapidly in a desiccator the product was a friable red powder, stable to air; it is reserved for further investigation.

Santalin was also isolated by a similar process from commercial camwood or barwood, which had been previously extracted with boiling carbon tetrachloride, but the yield of the pure compound was usually lower than that from sandalwood and the purification was rather more difficult. With some consignments of camwood and barwood, the use of chloroform in place of ether gave better results. Barwood and camwood also furnished the red amorphous pigment from the ethyl acetate mother-liquors remaining after removal of santalin.

O-*Tetramethylsantalin.*—A vigorously agitated solution of santalin (1 g.) in a mixture of 20% aqueous sodium hydroxide (10 ml.) and methanol (25 ml.) was treated with methyl sulphate (50 ml.) and 20% aqueous sodium hydroxide (100 ml.) alternately, with the addition of more methanol as required to maintain a homogeneous mixture; if the reaction tended to become too violent the mixture was occasionally cooled. The colour ultimately changed from intense red to pale orange and simultaneously a red, alkali-insoluble solid separated. After the addition of water (100 ml.) to complete the separation of the product, this was collected, washed, and dissolved in methanol, and the solution was poured into an excess of saturated aqueous sodium acetate (agitate). The well-washed and dried precipitate (1 g.) was crystallised from methanol or from benzene–light petroleum (b. p. 60—80°) containing 1% of methanol, giving *O*-tetramethylsantalin as a *hydrate* in slender, pale orange needles (0·7 g.), m. p. 154—155° (decomp.), which had a negative ferric reaction in alcohol and were insoluble in 2N-aqueous sodium hydroxide [Found: C, 67·9, 67·3; H, 5·6, 5·9; OMe, 36·5, 36·7%; *M*, 569, 596, 585. $C_{27}H_{11}O_2(OMe)_7,H_2O$ requires C, 67·7; H, 5·8; OMe, 36·1%; *M*, 602. Calc. for $C_{27}H_{11}O_2(OMe)_7$: C, 69·9; H, 5·5; OMe, 37·2%; *M*, 584]. The molecular-weight estimations were performed in benzene solution by the Menzies–Wright elevation of b. p. method.

The same tetramethyl ether (1·5—1·7 g.) was obtained by methylating santalin (2 g.) with methyl iodide (15 ml.) and potassium carbonate (10 g.) in boiling acetone (100 ml.) for 6 hr.

O-Tetramethylsantalylium chloride separated from aqueous-alcoholic hydrochloric acid as a *hemihydrate* in bright red prisms, with a magnificent green reflex, m. p. 210° (decomp.) [Found : C, 64·9, 64·3, 64·4; H, 6·1, 5·6, 5·9; Cl, 5·1; OMe, 33·1. $C_{27}H_{12}O_2Cl(OMe)_7,0{\cdot}5H_2O$ requires C, 64·9; H, 5·5; C, 5·5; OMe, 34·5%].

O-*Tetramethylsantalylium picrate* crystallised from 2% alcoholic picric acid in clusters of slender, red needles, m. p. 130—131°, or in rosettes of rectangular, red plates, m. p. 180—183° (decomp.) [Found : C, 58·8; H, 4·5; N, 4·9, 4·6; OMe, 26·8, 27·3. $C_{33}H_{14}O_9N_3(OMe)_7$ requires C, 59·0; H, 4·3; N, 5·0; OMe, 26·7%]. On being heated, the specimen of lower m. p. resolidified at *ca.* 140° and then melted at 180—183° (decomp.).

O-*Tetramethylsantalylium perchlorate* separated from aqueous acetic acid–perchloric acid (5 : 1) in deep red, flat parellelograms, m. p. 214—216° (decomp.), or in crimson, long slender needles, m. p. 180—185° (decomp.) [Found : C, 59·0, 59·2, 59·3; H, 5·4, 5·2, 5·5; Cl, 5·3; OMe, 30·8, 30·5. $C_{27}H_{12}O_6Cl(OMe)_7$ requires C, 59·6; H, 4·8; Cl, 5·2; OMe, 31·7%]. This salt was very sparingly soluble in methanol and ethanol.

O-*Pentamethylsantalanol*.—On being heated under reflux for 6 hr. a solution of *O*-tetramethylsantalin (1 g.) in benzene (50 ml.), containing methyl sulphate (2 ml.) and potassium carbonate (10 g.), became almost colourless and on isolation the product was dissolved in methanol (15 ml.). From the solution (stirred), *O*-pentamethylsantalanol was precipitated by an excess of 2N-aqueous sodium hydroxide as a colourless solid (1 g.) which did not crystallise. The *picrate*, which was moderately soluble in methanol, separated from 2% methanolic picric acid in crimson needles, m. p. 184—185° (decomp.) with previous darkening from *ca.* 150° [Found : C, 60·3; H, 4·5; N, 5·0, 4·9; OMe, 30·0. $C_{33}H_{13}O_8N_3(OMe)_8$ requires C, 59·5; H, 4·5; N, 5·1; OMe, 30·0%]. The *perchlorate* separated from a large volume of methanol containing 2% of perchloric acid in deep red, diamond shaped plates with a magnificent green sheen, m. p. 245—246° (decomp.), sparingly soluble in methanol and moderately soluble in acetic acid [Found : C, 60·0; H, 5·1; Cl, 5·8; OMe, 35·0, 35·1. $C_{27}H_{11}O_5Cl(OMe)_8$ requires C, 60·1; H, 5·0; Cl, 5·0; OMe, 35·5%].

Degradation of O-*Tetramethylsantalin with Alkali*.—A solution of *O*-tetramethylsantalin (1 g.) and potassium hydroxide (15 g.) in water (10 ml.) and methanol (25 ml.) was refluxed for 3½ hr. in an atmosphere of nitrogen. The cooled combined hydrolysates from 6 experiments were diluted with water, and the brown precipitate (4 g.) collected. Extraction of the alkaline liquors with ether furnished only a trace of product. After acidification with 2N-sulphuric acid the aqueous liquors were exhaustively extracted with ether, and the brown resin thus obtained was purified by repeated sublimation at 120°/0·001 mm., giving 2 : 4-dihydroxy-5-methoxybenzaldehyde (10 mg.) in pale yellow needles, m. p. 149°, which had an intense green ferric reaction in alcohol and were identical with an authentic specimen (Found : C, 57·5; H, 5·1; OMe, 16·6%; *M*, 166. Calc. for $C_7H_5O_3{\cdot}OMe$: C, 57·1; H, 4·8; OMe, 18·4%; *M*, 168) (Head and Robertson, *J.*, 1931, 1241).

Chromatography of the brown alkali-insoluble product (3 g.) from benzene solution on aluminium oxide and elution with the same solvent furnished (*a*) an almost colourless, non-crystalline solid (0·4 g.) with an intense green-brown ferric reaction in alcohol, and (*b*) a pale yellow, non-crystalline solid (0·5 g.) with a deep brown ferric reaction in alcohol. A quantity (0·5 g.) of unchanged *O*-trimethylsantalin was obtained subsequently by washing the column with methanol.

Fraction (*a*) gave a *semicarbazone* forming prisms, m. p. 202° (decomp.), from benzene [Found : C, 63·1; H, 5·8; N, 7·1; OMe, 35·0. $C_{28}H_{16}O_3N_3(OMe)_7$ requires C, 63·7; H, 5·6; N, 6·4; OMe, 33·0%], and a 2 : 4-*dinitrophenylhydrazone* which separated from much alcohol in red needles or from ethyl acetate in short, stout, squat, deep crimson prisms, m. p. 233° (decomp.) with darkening at *ca.* 200° [Found : C, 61·2, 61·0; H, 5·3, 5·2; N, 6·9, 6·8; OMe, 29·9. $C_{33}H_{17}O_6N_4(OMe)_7$ requires C, 61·4; H, 4·9; N, 7·2; OMe, 27·8%]. By the standard method the semicarbazone was converted into the 2 : 4-dinitrophenylhydrazone, m. p. 233° (decomp.).

Fraction (*b*) gave a *semicarbazone* which separated from alcohol in orange-yellow prisms, m. p. 203° (decomp.) (Found : C, 62·3; H, 5·6; N, 7·1, 7·1; OMe, 36·0, 36·1%). This could not be converted into the 2 : 4-*dinitrophenylhydrazone* which, however, was prepared directly from the crude fraction (*b*) and formed crimson plates, m. p. 202° (decomp.), from ethyl acetate (Found: C, 59·8; H, 4·8; N, 7·6, 7·7; OMe, 30·2, 30·3%). A mixture of the 2 : 4-dinitrophenylhydrazones from fractions (*a*) and (*b*) had m. p. *ca.* 180°.

Oxidation of O-*Tetramethylsantalin*.—A solution of potassium permanganate (3 g.) in water (80 ml.) was added gradually during 5 hr. to *O*-tetramethylsantalin (1 g.), dissolved in acetone

(80 ml.). Next day the reaction mixtures from 3 experiments were combined, clarified with sulphur dioxide, and acidified with 2N-sulphuric acid (10 ml.). After the evaporation of the greater part of the acetone in a vacuum the residual mixture was saturated with ammonium sulphate and exhaustively extracted with ether. The combined ethereal extracts (*A*) were washed with 2N-aqueous sodium hydrogen carbonate (50 ml. × 3), and the acidified washings saturated with ammonium sulphate and exhaustively extracted with ether to give extract (*B*). Distillation of extract (*A*) furnished veratraldehyde as a colourless oil (*ca.* 100 mg.) which rapidly solidified and then had m. p. 45—46°, identified by comparison with an authentic specimen [Found: C, 65·5; H, 6·2; OMe, 38·0. Calc. for $C_7H_4O(OMe)_2$: C, 65·1; H, 6·0; OMe, 37·4%]. The 2 : 4-dinitrophenylhydrazone of this aldehyde had m. p. 262—263° (decomp.) and was identical (crystal form and solubilities) with an authentic specimen (Found: N, 16·2. Calc. for $C_{15}H_{14}O_6N_4$: N, 16·2%).

By a combination of distillation at 0·001 mm. and fractional crystallisation from benzene, the colourless solid (450 mg.) left on evaporation of extract (*B*) was separated into 2 : 4-dimethoxybenzoic acid, m. p. and mixed m. p. 105° [Found: C, 59·8; H, 5·7; OMe, 33·0. Calc. for $C_7H_4O_2(OMe)_2$: C, 59·4; H, 5·5; OMe, 34·1%], and veratric acid, m. p. and mixed m. p. 177° (Found: C, 60·0; H, 5·7; OMe, 33·6%).

Isolation of Santarubin.—The amorphous red solid (1·5 g.), which separated from the concentrated carbon tetrachloride extracts of camwood (or barwood) (300 g.) (Part I, *loc. cit.*), was repeatedly crystallised from alcohol, giving santarubin (0·2 g.) in chocolate-coloured prisms with an intense green reflex, m. p. *ca.* 325° (decomp.), $\lambda_{max.}$ 506, 353, 316 mμ ($E^{1\%}_{1\,cm.}$ 450, 144, 294) [Found, in specimen dried at 100°/0·01 mm. for 16 hr.: C, 68·7, 68·4; H, 5·0, 5·3; OMe, 24·5. $C_{27}H_{14}O_5(OMe)_4$ requires C, 68·6; H, 4·8; OMe, 22·9%]. This pigment, which is readily soluble in 2N-aqueous sodium hydroxide, forming a deep red-violet solution, is sparingly soluble in the usual organic solvents and has an intense red-violet ferric reaction in alcohol.

Santarubylium chloride separated from alcoholic hydrochloric acid as a *hydrate* in silky deep-red needles, which, on prolonged contact with the solvent changed to long, deep red, parallelograms, with a green-black reflex, m. p. 211—214° (decomp.) (for either crystalline form) [Found: C, 62·5, 62·5; H, 5·2, 5·2; Cl, 5·6, 5·1; OMe, 21·2. $C_{27}H_{15}O_5Cl(OMe)_4,H_2O$ requires C, 62·4; H, 4·9; Cl, 5·8; OMe, 20·9%]. The ferrichloride, picrate, and perchlorate could not be obtained crystalline.

O-*Trimethylsantarubin.*—Methylation of santarubin (2 g.) derived from camwood or barwood, by the methyl iodide–potassium carbonate method in boiling acetone during 8 hr. gave O-*trimethylsantarubin* which separated from methanol in orange needles (1·5 g.), m. p. 167—168° (decomp.) [Found, in specimen dried at 100°/0·01 mm. for 12 hr.: C, 69·2, 70·1; H, 5·4, 5·8; OMe, 36·2%; *M*, 618, 629. $C_{27}H_{11}O_2(OMe)_7$ requires C, 69·9; H, 5·5; OMe, 37·2%; *M*, 584]. This compound is insoluble in 2N-aqueous sodium hydroxide and has a negative ferric reaction in alcohol.

O-*Trimethylsantarubylium picrate* separated from 2% alcoholic picric acid in clusters of bright red, flat prisms, or red slender needles, m. p. 219° (decomp.) with darkening from *ca.* 200° [Found: C, 59·6, 59·5, 59·5; H, 4·6, 4·7, 4·6; N, 4·8, 4·5; OMe, 27·2, 27·5. $C_{33}H_{14}O_9N_3(OMe)_7$ requires C, 59·1; H, 4·3; N, 5·2; OMe, 26·7%].

The chloride, perchlorate, and ferrichloride could not be satisfactorily purified.

O-*Tetramethylsantarubanol.*—Methylation of *O*-trimethylsantarubin (1 g.) with methyl sulphate (2 g.) and potassium carbonate (10 g.) in boiling benzene (50 ml.) during 6 hr. furnished a quantitative yield of *O*-tetramethylsantarubanol as a colourless, amorphous solid which could not be crystallised. The readily formed *perchlorate* separated from methanol, containing 2% perchloric acid, in long, slender, crimson prisms, m. p. 178—180° (decomp.), which on prolonged contact with the solvent changed to almost black tablets, m. p. 178—180° (decomp.) [Found: C, 60·4, 60·4; H, 4·9, 5·1; Cl, 4·9, 5·1, 5·1; OMe, 36·1, 33·6. $C_{27}H_{11}O_5Cl(OMe)_8$ requires C, 60·1; H, 5·0; Cl, 5·1; OMe, 35·5%]. The *picrate* separated from a large volume of alcohol in long slender, crimson needles, m. p. 215—217° (decomp.) [Found: C, 59·7, 59·5, 59·5, 59·6, 60·0; H, 4·2, 4·6, 4·7, 4·6, 4·5; N, 4·3, 4·3, 4·9, 4·6, 4·7; OMe, 30·2, 30·1, 30·3. $C_{33}H_{13}O_8N_3(OMe)_8$ requires C, 59·5; H, 4·5; N, 5·1; OMe, 30·0%].

The chloride and ferrichloride were amorphous.

Degradation of O-*Trimethylsantarubin with Alkali.*—Degradation of *O*-trimethylsantarubin (1 g.) from either camwood or barwood by the method used for *O*-tetramethylsantalin gave 2 : 4-dihydroxy-5-methoxybenzaldehyde in pale yellow needles, (5 mg.), m. p. and mixed m. p. 148°, together with a non-crystalline resin which furnished a 2 : 4-*dinitrophenylhydrazone* which separated from much alcohol or a small volume of ethyl acetate in slender, crimson needles,

m. p. 222° (decomp.) [Found : C, 60·9, 60·5; H, 5·1, 5·2; N, 7·3, 7·4; OMe, 29·5, 29·5. $C_{33}H_{17}O_6N_4(OMe)_7$ requires C, 61·4; H, 4·9; N, 7·2; OMe, 27·8%].

Oxidation of O-Tetramethylsantarubin.—Oxidation of *O*-trimethylsantarubin (1 g. × 3) was effected by the method used for *O*-tetramethylsantalin, and the product resolved into neutral and acidic fractions. From the neutral portion 2 : 4-dimethoxybenzaldehyde was obtained (15 mg.), m. p. and mixed m. p. 71—72°, giving a 2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 257—258° (decomp.) (Found : N, 15·4. Calc. for $C_{15}H_{14}O_6N_4$: N, 16·2%). By distillation (at 0·001 mm.) and fractional crystallisation from benzene 2 : 4-dimethoxybenzoic acid (10 mg.), m. p. 108°, was isolated from the acidic fraction and was identified by comparison with an authentic specimen. The residue (10 mg.) left on the removal of this acid was purified by sublimation followed by crystallisation from benzene and then had m. p. *ca.* 150° (yield, *ca.* 3 mg.); admixed with veratric acid, it had m. p. *ca.* 170°.

UNIVERSITY OF LIVERPOOL.

[*Received, March 27th,* 1954.]