Phytochemical Examination of the Lichen, *Lecanora gangaleoides* Nyl.

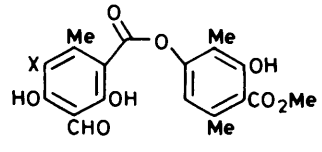
John P. Devlin, M. Mohan Mahandru, W. David Ollis,* and Christopher Smith
Department of Chemistry, The University, Sheffield S3 7HF

The natural products isolated from *Lecanora gangaleoides* include two depsides, atranorin (**1**) and chloroatranorin (**2**), two depsidones, gangaleoidin (**4**) and leoidin (**5**), and the bisanthraquinone, skyrin (**6**). The constitution (**5**) for leoidin has been established by its transformation into the diphenyl ether (**15**) which was also obtained from gangaleoidin (**4**).

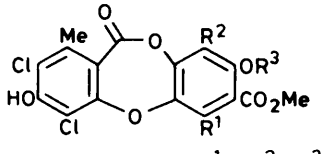
Six compounds, which were all believed to be natural products, were isolated when the lichen, *Lecanora gangaleoides*, was first investigated by Nolan during the period 1935—1943.[1-3] Three of these natural products were identified as the depsides, atranorin (**1**) and chloroatranorin (**2**) and the depsidone, gangaleoidin (**3**). In addition, three uncharacterised compounds were also isolated which included (i) a colourless compound, $C_{26}H_{21}Cl_3O_{10}$, m.p. 231—233 °C, (ii) a red pigment, rhodophyscin, and (iii) a yellow pigment, endococcin. The constitution (**3**) proposed by Nolan[3] for gangaleoidin was based upon an extensive investigation[1-3] by the Dublin group. However, much later it became clear that their structural proposal (**3**) for gangaleoidin required careful re-examination. The studies by Sargent, Vogel, and Elix[4] and our independent investigations[5,6] established that gangaleoidin had the constitution (**4**). Sargent, Vogel, and Elix[4] reported the isolation from their sample of *Lecanora gangaleoides* of atranorin (**1**), chloroatranorin (**2**), gangaleoidin (**4**), and an orange metabolite, which was not characterised but was probably identical with rhodophyscin.[2] We were also simultaneously examining this problem[5,6] and we now report upon our phytochemical examination of *Lecanora gangaleoides*.

The lichen, *Lecanora gangaleoides*, which was collected in North Wales, yielded six compounds which were obviously identical with the six substances previously described by Nolan.[1-3] Atranorin (**1**), chloroatranorin (**2**) and gangaleoidin (**4**) were easily identified. Leoidin, $C_{18}H_{14}Cl_2O_7$, m.p. 231—233 °C, is obviously identical with the unnamed compound, m.p. 231—233 °C, previously isolated by Nolan and Keane[2] and given the molecular formula, $C_{26}H_{21}Cl_3O_{10}$. Leoidin, which is isomeric with gangaleoidin, is now shown to be a new depsidone (**5**). The red pigment, previously described as rhodophyscin,[2] has now been identified as (+)-skyrin (**6**).[7] The yellow pigment, previously named endococcin,[2] has been shown to be an artefact rather than a genuine natural product. Endococcin has been identified as the known pseudoskyrin diethyl ether (**7**):[7] it is probably produced from skyrin (**6**) by reaction with the ethanol present in the chloroform used for the extraction. The identification of rhodophyscin as (+)-skyrin (**6**)[7] and of endococcin as pseudoskyrin diethyl ether (**7**)[7] provides an acceptable rationalisation for the observation made by Nolan and Keane[2] that treatment of endococcin with boiling acetic acid yields rhodophyscin. The elucidation of the constitution of leoidin (**5**) is now reported.

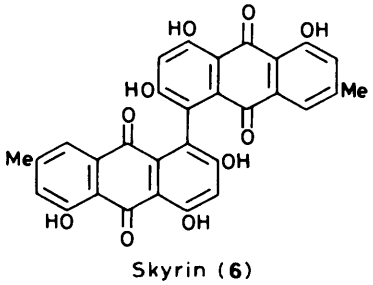
Leoidin, which was previously formulated as the compound, $C_{26}H_{21}Cl_3O_{10}$,[2] was found by analysis and mass spectrometry to have the molecular formula, $C_{18}H_{14}Cl_2O_7$. Its i.r. spectrum shows two carbonyl bands (1 730 and 1 665 cm^{-1}) which could be assigned to the lactone carbonyl group of a depsidone (*ca.* 1 730 cm^{-1}) and the carbonyl group (*ca.* 1 665 cm^{-1}) of an aromatic ester chelated with an *O*-hydroxy group. The ^1H n.m.r. spectrum (C_5D_5N) of leoidin shows singlets assignable to one methoxy group (δ 3.80; CO_2Me) and three aromatic methyl groups, (δ 2.75, 2.57, and 2.36; three Me). Leoidin was characterised as a di-*O*-methyl derivative, a di-*O*-benzyl derivative, and a di-*O*-acetate. These results indicated that leoidin was a depsidone associated with the partial formula (**8**).



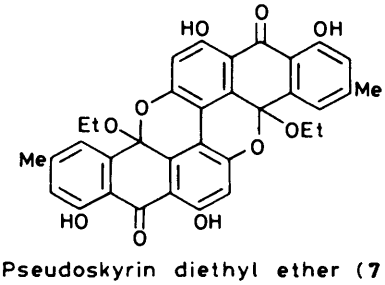
Atranorin (**1**) X = H
Chloroatranorin (**2**) X = Cl



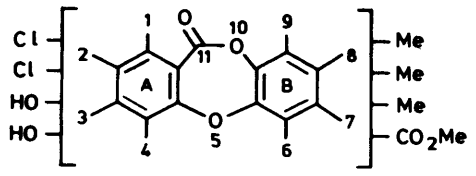
	R¹	R²	R³
(**3**)	H	Me	Me
Gangaleoidin (**4**)	Me	H	Me
Leoidin (**5**)	Me	Me	H



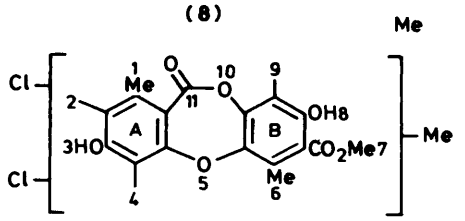
Skyrin (**6**)



Pseudoskyrin diethyl ether (**7**)

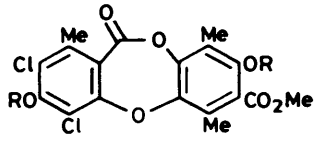


(8)



(9)

The natural co-occurrence of gangaleoidin (**4**) with leoidin (**8**) suggested that there could well be a correspondence in the location of similar functional groups in these two metabolites. This led to the partial formula (**9**) for leoidin: this suggestion was clearly supported by biogenetic structural correlations which are generally recognised for the many depsidones which are phytochemically characteristic of lichens.[8–10] Development of the partial formula (**9**) can, in principle, lead to three possible structural formulae for leoidin in which the unplaced aromatic methyl group is located on either C-2, C-4, or C-9. Of these three possibilities, the location of a methyl group at C-9 is clearly biogenetically favoured because this places the two chlorine atoms at positions C-2 and C-4 of ring A. Furthermore, the ring-B substitution pattern then corresponds with that of β-orcinol carboxylic acid which is characteristic of many known natural depsidones.[8–10] These considerations led to the constitution (**5**) as the biogenetically favoured structure for leoidin. This constitution (**5**) was firmly established by the conversion of leoidin (**5**) and gangaleoidin (**4**) into their common transformation product (**15**).

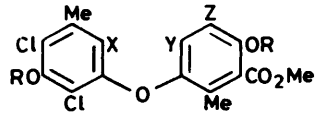


R

(**10**) Me

(**11**) CH_2Ph

(**12**) Ac



	R	X	Y	Z
(**13**)	Me	CO_2H	OH	Me
(**14**)	Me	CO_2Me	OH	Me
(**15**)	H	CO_2Me	OH	Me
(**16**)	Me	CO_2Me	OMe	Me
(**17**)	Me	CO_2Me	OMe	H
(**18**)	H	CO_2Me	OH	H
(**19**)	Ac	CO_2Me	OAc	H
(**20**)	H	H	OH	H
(**21**)	H	CO_2Me	OH	CHO

Leoidin di-*O*-methyl ether (**10**) and aqueous potassium hydroxide in acetone yielded the hydroxy acid (**13**) which reformed di-*O*-methyl-leoidin (**10**) by cyclodehydration with boiling acetic anhydride–sodium acetate. Base-catalysed methanolysis of leoidin di-*O*-methyl ether (**10**) with methanolic potassium hydroxide cleaved the lactone ring yielding the diaryl ether (**14**). Similarly, methanolysis of leoidin (**5**) gave the diaryl ether (**15**) which was characterised as the tri-*O*-methyl derivative (**16**). These three transformations, (**10**)→(**13**)→(**10**), (**10**)→(**14**), and (**5**)→(**15**), established that leoidin was a depsidone.

The diaryl ether (**15**) was also synthesized from natural gangaleoidin (**4**) by the following sequence. Base-catalysed methanolysis of gangaleoidin (**4**) followed by methylation with diazomethane gave the known trimethoxy diester (**17**).[2] Demethylation of the trimethoxy diester (**17**) with aluminium chloride in boiling benzene gave the corresponding trihydroxy diester (**18**) and the demethoxycarbonyl derivative (**20**). Direct *C*-methylation of the trihydroxy diester (**18**) with methyl iodide and silver tetrafluoroborate in methylene chloride at room temperature gave the diaryl ether (**15**) in low yield (11%). The diaryl ether (**15**) was also obtained (overall yield, 27%) by *C*-formylation of the trihydroxy diester (**18**), using dichloromethyl methyl ether and titanium tetrachloride, followed by catalytic reduction of the intermediate aldehyde (**21**). The partial synthesis of the diaryl ether (**15**) from gangaleoidin (**4**) establishes the constitution (**5**) for leoidin.

Experimental

Separations by column chromatography, preparative t.l.c., and thin-layer t.l.c. were carried out using Merck silica gel (Kieselgel G). During isolation processes, the appropriate combinations of fractions were determined by examination of their i.r. spectra and t.l.c. behaviour. Light petroleum refers to the fraction boiling in the range 60—80 °C. Evaporation refers to evaporation under diminished pressure.

Unless otherwise stated, i.r. spectra were measured (Perkin-Elmer 157G spectrophotometer) in chloroform, u.v. spectra were measured (Cary-14 spectrometer) in ethanol, and ^1H n.m.r. spectra were measured (Varian HA-100 spectrometer) in deuteriochloroform. Only significant bands from i.r. spectra are quoted.

All ^1H n.m.r. chemical shifts (δ) are related to tetramethylsilane as internal standard and spectral details are reported as follows: δ (solvent); δ values in p.p.m., multiplicity, coupling constant Hz, and assignments. The multiplicity of signals is expressed by the following symbols: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, dd = double doublet, dt = double triplet, dm = double multiplet, and br s = broad singlet.

High resolution mass spectra were determined with an AEI MS-9 spectrometer and low resolution mass spectra with an AEI MS-12 spectrometer.

M.p.s were determined using a Kofler hot-stage apparatus and are uncorrected.

When substances are stated to be identical, this refers to their m.p.s, mixed m.p.s, i.r. spectra, n.m.r. spectra, mass spectra, and chromatographic behaviour.

Extraction of the Total Lichen, Lecanora gangaleoides *Nyl.*— The lichen was collected from the dry stone walls near Dyffryn Ardudwy, Merionethshire.* Additional quantities of the lichen were collected in Devonshire and Hampshire.†

* We thank Mr. N. Woodhead of the Department of Botany, University College of North Wales, Bangor, for his advice regarding the location of this lichen near Dyffryn Ardudwy, Merionethshire.

† We thank Dr. D. H. S. Richardson, Department of Botany, University of Exeter, for his help in the location and identification of this lichen material in Devonshire and Hampshire.

The air-dried, powdered lichen (960 g) was continuously extracted (Soxhlet) with hot ether until the extracts were colourless. Evaporation gave a residue (38.5 g) which was then extracted with hot benzene. This gave a rather insoluble, red pigment (150 mg) and concentration of the benzene solution gave gangaleoidin (12.3 g). Evaporation of the benzene mother liquors gave a residue (26.0 g) which yielded the following compounds after extensive column chromatography, preparative t.l.c., and recrystallisation.

Atranorin (**1**) (1.71 g) as colourless rods, m.p. 196 °C (lit.,[8] m.p. 196 °C) from chloroform. It was identical with an authentic sample.*

Chloroatranorin (**2**) (1.5 g) as pale yellow plates, m.p. 207 °C (lit.,[8] m.p. 208—208.5 °C), from chloroform. It was identical with an authentic sample.*

Gangaleoidin (**4**) (total yield, 17.7 g) as fine, colourless needles, m.p. 213 °C (lit.,[1] m.p. 213—214 °C) from xylene (Found: $M^{+\bullet}$, 412. Calc. for $C_{18}H_{14}Cl_2O_7$: *M*, 412); $\nu_{max.}$ 3 470 and 1 730 cm^{-1}; δ 6.64 (1 H, s, ArH), 6.50 (1 H, br s, ArOH), 3.88 and 3.76 (s, OMe and s, CO_2Me), 2.49 (s, ArMe), and 2.47 (s, ArMe).

Leoidin (**5**) (2.4 g), characteristic coral-like clusters, m.p. 232—233 °C (lit.,[1] m.p. 231—233 °C) from benzene (Found: C, 52.2; H, 3.3; Cl, 16.9; $M^{+\bullet}$, 412. $C_{18}H_{14}Cl_2O_7$ requires C, 52.3; H, 3.4; Cl, 17.15%; *M*, 412); $\nu_{max.}$(KBr) 3 370, 1 730, and 1 665 cm^{-1}; δ(C_5D_5N) 3.80 (s, CO_2Me), 2.75 (s, ArMe), 2.57 (s, ArMe), and 2.36 (s, ArMe).

(+)-Skyrin (**6**) (150 mg), red crystals, m.p. >360 °C (lit.,[7] m.p. >360 °C) from acetone–methanol (Found: $M^{+\bullet}$, 538. Calc. for $C_{38}H_{18}O_{10}$, *M*, 538); c.d. (*c*, 0.81, dioxane) 487 nm (positive maximum). This c.d. spectrum was superimposable upon the c.d. spectrum of authentic (+)-skyrin.[7],†

Pseudoskyrin diethyl ether (**7**) (85 mg), yellow microcrystals, m.p. >360 °C (lit.,[7] m.p. >360 °C) from dioxane (Found: C, 68.1; H, 4.6%; $M^{+\bullet}$, 594. Calc. for $C_{34}H_{26}O_{10}$: C, 68.7; H, 4.4%; *M*, 594); $\nu_{max.}$ 3 450, 1 655, and 1 648 cm^{-1}.

Hexa-acetylskyrin.—Skyrin (**6**) (40 mg), acetic anhydride (1 ml), and pyridine (1 ml) after 16 h (room temperature) yielded hexa-acetylskyrin (45 mg, 77%) as yellow needles, m.p. 295—296 °C (lit.,[7] m.p. 295—296 °C) (Found: *m/z*, 748. $C_{42}H_{30}O_{16}$ – C_2H_2O requires *m/z* 748); $\nu_{max.}$ 1 770 and 1 670 cm^{-1}; δ 8.14 (s, two $ArCH_3$), 7.68 and 7.13 (2 AB systems, J_{AB} 2 Hz, two *m*-ArH_2), 7.36 (s, two ArH), 2.44 (s, two $OCOCH_3$), 2.42 (s, two $OCOCH_3$), 2.35 (s, two $OCOCH_3$), and 1.88 (6 H, s, two ArMe).

Skyrin Hexa-O-ethyl Ether.—Skyrin (100 mg), anhydrous potassium carbonate (500 mg), and ethyl iodide (1 ml) in acetone (20 ml) were heated under reflux (16 h). This yielded *skyrin hexa-O-ethyl ether* (121 mg, 92%) as red crystals, m.p. 280 °C (decomp.) (Found: C, 71.4; H, 6.1%; $M^{+\bullet}$, 706. $C_{42}H_{42}O_{10}$ requires C, 71.4; H, 6.0%; *M*, 706); $\nu_{max.}$ 1 670 cm^{-1}; δ 7.24, 6.96, and 6.76 (br m, six ArH); δ_A 4.32, δ_B 4.21, δ_A 4.25, δ_B 4.14, δ_A 3.99, δ_B 3.85 (six AB systems of three pairs of ABX_3 systems, three pairs of OCH_2CH_3), δ_X 1.57, δ_X 1.50, δ_X 1.00 (six X_3 systems of three pairs of ABX_3 systems, three pairs of OCH_2CH_3).

Formation of Pseudoskyrin Diethyl Ether (**7**).—Skyrin (30 mg) in ethanol (5 ml) and concentrated sulphuric acid (0.2 ml) was heated under reflux (2 h) to yield pseudoskyrin diethyl ether (22 mg, 67%) as yellow microcrystals, m.p. >350 °C from chloroform, identical with material isolated from the lichen extract (see above).

Methylation with methyl iodide and potassium carbonate in boiling acetone gave *pseudoskyrin di-O-ethyl tetra-O-methyl ether* (63%) as yellow needles, m.p. 225—230 °C from chloroform (Found: $M^{+\bullet}$, 650.2156. $C_{33}H_{34}O_{10}$ requires *M*, 650.2151); δ 7.55 (s, two ArH), 6.89 (m, four ArH), 4.03 (s, two OMe), 3.95 (s, two OMe), 3.43 (m, two OCH_2CH_3), and 0.9 (t, two OCH_2CH_3).

Leoidin Di-O-methyl Ether (*Methyl* 2,4-*Dichloro*-3,8-*dimethoxy*-1,6,9-*trimethyl*-11-*oxo*-11H-*dibenzo*[b,e][1,4]-*dioxepin*-7-*carboxylate*) (**10**).—(a) Leoidin (0.2 g) in dry acetone (20 ml) was treated (24 h, room temperature) with an excess of an ethereal solution of diazomethane. Addition of glacial acetic acid and evaporation yielded a residue which gave *leoidin di-O-methyl ether* (0.19 g, 89%) as colourless crystals, m.p. 142—144 °C (lit.,[2] m.p. 143—144 °C) from benzene–light petroleum (Found: C, 54.45; H, 4.2; Cl, 15.9%; $M^{+\bullet}$, 440. $C_{20}H_{18}Cl_2O_7$ requires C, 54.4; H, 4.1; Cl, 16.1%; *M*, 440); $\nu_{max.}$ 1 730 cm^{-1}; δ 3.92, 3.91, and 3.74 (three s, three OMe), 2.50 (s, two ArMe), and 2.27 (s, ArMe).

(b) The hydroxy acid (**13**) (0.1 g), acetic anhydride (5 ml), and freshly fused sodium acetate (0.1 g) were heated under reflux (2 h), cooled, and poured into aqueous sodium hydrogen carbonate. The precipitate was collected and crystallisation from benzene–light petroleum gave (**10**) (78 mg), m.p. and mixed m.p. 142—144 °C.

Leoidin Di-O-benzyl Ether (*Methyl* 3,8-*Dibenzyloxy*-2,4-*dichloro*-1,6,9-*trimethyl*-11-*oxo*-11H-*dibenzo*[b,e,][1,4]-*dioxepin*-7-*carboxylate* (**11**).—Leoidin (0.35 g), benzyl bromide (1 ml), and anhydrous potassium carbonate (1 g) in boiling acetone (25 ml) (2 h) yielded *leoidin di-O-benzyl ether* (**11**) as needles (0.39 g, 78%), m.p. 134—135 °C from benzene–light petroleum (Found: C, 65.1; H, 4.6; Cl, 12.0%; $M^{+\bullet}$, 592. $C_{32}H_{26}Cl_2O_7$ requires C, 64.8; H, 4.4; Cl, 12.0%; *M*, 592); $\nu_{max.}$ 1 740 cm^{-1}; δ 7.60—7.22 (10 H, m, ArH), 5.06 and 4.86 (two s, two CH_2Ph), 3.80 (s, OMe), 2.51, 2.48, and 2.28 (three s, three ArMe).

Leoidin Di-O-acetate (*Methyl* 3,8-*Diacetoxy*-2,4-*dichloro*-1,6,9-*trimethyl*-11-*oxo*-11H-*dibenzo*[b,e][1,4]*dioxepin*-7-*carboxylate*) (**12**).—Leoidin (20 mg), acetic anhydride (2 ml), and concentrated sulphuric acid (1 drop) were kept (24 h) at room temperature. Addition to ice–water gave *leoidin di-O-acetate* as rods (22 mg, 92%), m.p. 170—171 °C from benzene–light petroleum (Found: $M^{+\bullet}$, 496.0321. $C_{22}H_{18}Cl_2O_9$ requires *M*, 496.0328); $\nu_{max.}$ 1 780 and 1 730 cm^{-1}; δ 3.86 (s, OMe), 2.55, 2.52, 2.40, 2.26, and 2.16 (five s, three ArMe and two COMe).

Methyl 3-(2-*Carboxy*-4,6-*dichloro*-5-*methoxy*-3-*methylphenoxy*)-4-*hydroxy*-6-*methoxy*-2,5-*dimethylbenzoate* (**13**).—An aqueous solution of potassium hydroxide (0.2 g) in water (1 ml) was added to leoidin di-*O*-methyl ether (**10**) (0.1 g) in acetone (5 ml). The solution was boiled (5 min), evaporated, and acidified. Crystallisation of the precipitate from methanol gave the *hydroxy-acid* (**13**) (90 mg, 87%) as colourless needles, m.p. 204—206 °C (Found: C, 52.2; H, 4.35; Cl, 15.3%; $M^{+\bullet}$, 458. $C_{20}H_{20}Cl_2O_8$ requires C, 52.3; H, 4.4; Cl, 15.5%; *M*, 458); $\nu_{max.}$(KBr) 3 460, 3 160, and 1 705 cm^{-1}; δ($CDCl_3$ + C_5D_5N) 11.54 and 11.46 (two br s, two OH), 3.84, 3.78, and 3.67 (three s, three OMe), 2.46, 2.24, and 2.07 (three s, three ArMe).

Methyl 3-(4,6-*Dichloro*-5-*methoxy*-2-*methoxycarbonyl*-3-*methylphenoxy*)-4-*hydroxy*-6-*methoxy*-2,5-*dimethylbenzoate* (**14**).—A solution of leoidin di-*O*-methyl ether (**10**) (70 mg) in methanol (5 ml) containing potassium hydroxide (0.1 g) was

* We thank Dr. C. A. Wachtmeister, Institutionen för organisk Kemi, Kungl. Universitet J, Stockholm, for his kind assistance in providing authentic samples of lichen metabolites.

† We thank Professor S. Shibata, Meiji College of Pharmacy, Tokyo, for a sample of (+)-skyrin.

boiled (1 min). Evaporation, addition of water, acidification, extraction (ethyl acetate), evaporation of the ethyl acetate, and crystallisation from light petroleum gave the *diaryl ether* (**14**) (64 mg, 85%), m.p. 115—116 °C (Found: C, 53.0; H, 4.8; Cl, 14.9%; $M^{+\cdot}$, 472. $C_{21}H_{22}Cl_2O_8$ requires C, 53.3; H, 4.65; Cl, 15.0%; *M*, 472); $\nu_{max.}$ 3 542, 3 260, and 1 730 cm^{-1}; δ 3.85 (s, two OMe), 3.72 and 3.68 (two s, two OMe), 2.27, 2.13, and 2.02 (three s, three ArMe).

Methyl 3-(4,6-*Dichloro*-5-*hydroxy*-2-*methoxycarbonyl*-3-*methylphenoxy*)-4,6-*dihydroxy*-2,5-*dimethylbenzoate* (**15**).—(*a*) Leoidin (**5**) (0.15 g) was added to a solution of sodium (0.25 g) in methanol (5 ml), and the mixture was stirred (2 h) at room temperature. Acidification, extraction (ethyl acetate), and evaporation gave a residue which was fractionated on silica gel plates using ethyl acetate–light petroleum (25:75) as the eluant. The major product crystallised from chloroform–light petroleum to give the *diaryl ether* (**15**) as crystals (98 mg, 60%), m.p. 188—189 °C (Found: C, 51.25; H, 4.2; Cl, 15.9%; $M^{+\cdot}$, 444. $C_{19}H_{18}Cl_2O_8$ requires C, 51.2; H, 4.0; Cl, 16.0%; *M*, 444); $\nu_{max.}$(KBr) 3 500, 3 260, 1 695, and 1 655 cm^{-1}; δ[$(CD_3)_2CO$] 10.33 (s, OH), 3.89, 3.42 (two s, two OMe), 2.18 (s, two ArMe), and 2.09 (s, ArMe).

(*b*) To a solution of the trihydroxy diester (**18**) (0.3 g) in dichloromethane (5 ml) were added silver tetrafluoroborate (0.5 g) and methyl iodide (2 ml). The solution was stirred (8 h) at room temperature and then filtered. Evaporation of the filtrate gave a residue which was fractionated on silica gel plates using benzene–dioxane–acetic acid (95:25:4) as the eluant to give the starting material (0.1 g) and the diphenyl ether (**15**) (23 mg, 11%), m.p. 188—189 °C.

(*c*) The aldehyde (**21**) (0.1 g) in methanol (20 ml) was hydrogenated with 10% palladium on carbon (0.2 g) at room temperature and atmospheric pressure for 16 h. Filtration, evaporation, and chromatography yielded the diphenyl ether (**15**) (52 mg, 54%), m.p. 188—189 °C.

Methyl 3-(4,6-*Dichloro*-5-*methoxy*-2-*methoxycarbonyl*-3-*methylphenoxy*)-4,6-*dimethoxy*-2,5-*dimethylbenzoate* (**16**).—The diphenyl ether (**15**) (70 mg) in acetone (5 ml) was treated (10 min) with an excess of an ethereal solution of diazomethane at room temperature. Evaporation and crystallisation from methanol yielded the *diphenyl ether* (**16**) as plates (67 mg, 87%), m.p. 110—111 °C (Found: C, 54.2; H, 5.0; Cl, 14.5%; $M^{+\cdot}$, 486. $C_{22}H_{24}Cl_2O_8$ requires C, 54.2; H, 4.9; Cl, 14.6%; *M*, 486); $\nu_{max.}$($CHCl_3$) 1 730 cm^{-1}; δ 3.93 (s, two OMe), 3.76, 3.57, and 3.42 (three s, three OMe), 2.22, 2.19, and 2.16 (three s, three ArMe).

Methyl 3-(4,6-*Dichloro*-5-*hydroxy*-2-*methoxycarbonyl*-3-*methylphenoxy*)-4,6-*dihydroxy*-2-*methylbenzoate* (**18**) *and Methyl* 3-(4,6-*Dichloro*-5-*hydroxy*-3-*methylphenoxy*-4,6-*dihydroxy*-2-*methylbenzoate* (**20**).—A mixture of the trimethoxy diester (**17**)[2] (0.5 g), anhydrous aluminium chloride (1.5 g), and dry benzene (100 ml) was heated (15 h) under reflux, poured into ice–water and acidified. Extraction with ether, evaporation, and fractionation on silica gel plates using benzene–dioxane–acetic acid (95:25:4) gave two bands. The product from the top band crystallised from aqueous acetone to give the *trihydroxy diester* (**18**) as needles (0.245 g, 54%), m.p. 231—232 °C (Found: C, 49.9; H, 3.9; Cl, 16.7%; $M^{+\cdot}$, 430. $C_{18}H_{16}Cl_2O_8$ requires C, 50.1; H, 3.7; Cl, 16.5%; *M*, 430); $\nu_{max.}$(KBr) 3 530, 3 280, 1 690, and 1 660 cm^{-1}; δ[$(CD_3)_2CO$] 6.28 (1 H, s, ArH), 3.91 and 3.43 (6 H, two s, two OMe), 2.33 and 2.17 (6 H, two s, two ArMe). Treatment of the trihydroxy diester (**18**) with acetic anhydride and concentrated sulphuric acid gave the *triacetate* (**19**) (83%) which crystallised from aqueous ethanol as plates, m.p. 147—148 °C (Found: $M^{+\cdot}$, 556.0539. $C_{24}H_{22}Cl_2O_{11}$ requires *M*, 556.0539); $\nu_{max.}$ 1 780 and 1 730 cm^{-1}; δ 7.10 (s, ArH), 4.08 and 3.74 (two s, two OMe), 2.57, 2.52, 2.47, 2.40, and 2.08 (five s, two ArMe and three COMe). Crystallisation of the product from the lower band from aqueous methanol gave the *diphenyl ether* (**20**) as needles (60 mg, 15%), m.p. 206—208 °C (Found: $M^{+\cdot}$ 372.0161. $C_{16}H_{14}Cl_2O_6$ requires *M*, 372.0161); $\nu_{max.}$ 3 500, 2 900, and 1 660 cm^{-1}; δ[$(CD_3)_2CO$] 6.51 and 6.08 (two s, two ArH), 3.81 (s, OMe), 2.31 and 2.16 (two s, two ArMe).

Methyl 3-(4,6-*Dichloro*-5-*hydroxy*-2-*methoxycarbonyl*-3-*methylphenoxy*)-5-*formyl*-4,6-*dihydroxy*-2-*methylbenzoate* (**21**).—A solution of the trihydroxy diester (**18**) (0.5 g) in dichloromethane (8 ml) and dichloromethyl methyl ether (0.2 ml) was cooled to 0 °C and titanium tetrachloride (0.5 ml) was added. The solution was slowly warmed to room temperature and then stirred for a further 2 h. The red reaction mixture was decomposed with dilute hydrochloric acid and extracted with chloroform. Evaporation of the extract and fractionation of the residue on silica gel plates using benzene–dioxane–acetic acid (95:25:4) gave the starting material (**18**) (0.12 g) and the *aldehyde* (**21**) as yellow crystals (0.11 g, 27%), m.p. 182—184 °C from methanol (Found: $M^{+\cdot}$, 458.0169. $C_{19}H_{16}Cl_2O_9$ requires *M*, 458.0171); $\nu_{max.}$(KBr) 3 360, 1 713, and 1 645 cm^{-1}; δ(C_5D_5N) 11.48 (s, C*H*O), 3.82 and 3.57 (two s, two OMe), 2.45 and 2.23 (two s, two ArMe).

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