Naturally Occurring Compounds related to Phenalenone. Part VI.[1] Synthesis of Atrovenetin (8,9-Dihydro-3,4,5,6-tetrahydroxy-1,8,8,9-tetramethylphenaleno[1,2-*b*]furan-7-one) and Related Compounds †

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A synthesis of (±)-atrovenetin (19b) in ten steps from 3,4,5-trimethoxybenzaldehyde (5c) is described. A number of related phenalenone derivatives, including norxanthoherquein (2,3,4,7,8,9-hexahydroxy-6-methylphenalen-1-one) (27), one of the principal degradation products of norherqueinone (2), have also been synthesised.

ATROVENETIN (1) [2] is a metabolite of *P. atrovenetum*; its isolation from the mycelium of *P. herquei* has also been reported.[3] It has recently been the subject of structural [4] and biosynthetic [5] investigations, and by chemical correlation with (−)-(S)-ethyl lactate it has been shown that atrovenetin obtained from *P. atrovenetum* possesses the *R*-configuration as depicted in formula (1).[6] Some preliminary work directed towards a synthesis of atrovenetin has been described.[7] We now report a synthesis of (±)-atrovenetin and of norxanthoherquein (27) which is one of the principal degradation products of the closely-related mould metabolite norherqueinone (2).[2b,8] Since atrovenetin has already been converted

† Preliminary account, D. A. Frost and G. A. Morrison, *J.C.S. Chem. Comm.*, 1972, 93.

[1] Part V, D. A. Frost and G. A. Morrison, *J.C.S. Perkin I*, 1973, 2159.

[2] (*a*) K. G. Neill and H. Raistrick, *Biochem. J.*, 1957, **65**, 166; (*b*) D. H. R. Barton, P. de Mayo, G. A. Morrison, and H. Raistrick, *Tetrahedron*, 1959, **6**, 48; (*c*) I. C. Paul, G. A. Sim, and G. A. Morrison, *Proc. Chem. Soc.*, 1963, 352; (*d*) I. C. Paul and G. A. Sim, *J. Chem. Soc.*, 1965, 1097.

[3] N. Narasimhachari, K. S. Gopalkrishnan, R. H. Haskins, and L. C. Vining, *Canad. J. Microbiol.*, 1963, **9**, 134; D. A. Frost and G. A. Morrison, *Tetrahedron Letters*, 1972, 4729.

[4] (*a*) J. S. Brooks and G. A. Morrison, *Tetrahedron Letters*, 1970, 963; (*b*) *J.C.S. Perkin I*, 1972, 421.

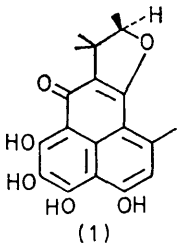
[5] A. B. Kriegler and R. Thomas, *Chem. Comm.*, 1971, 738.

[6] J. S. Brooks and G. A. Morrison, *Chem. Comm.*, 1971, 1359.

[7] B. W. Bycroft and A. J. Eglington, *Chem. Comm.*, 1968, 72.

[8] J. A. Galarraga, K. G. Neill, and H. Raistrick, *Biochem. J.*, 1955, **61**, 456.

into the anhydride (3),[2b] itself a metabolite of *P. atro-venetum*[9] (and also of *Roesleria pallida*[10]), the present work also constitutes a total synthesis of the racemic



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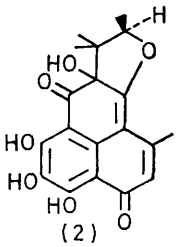

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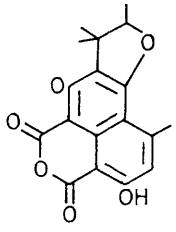

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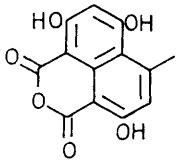
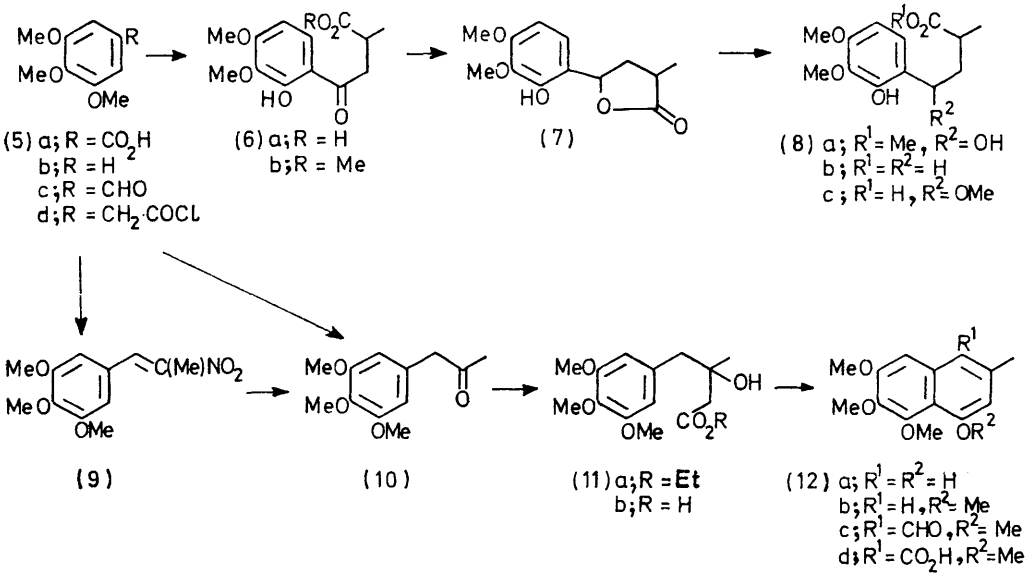


(4)

form of that compound. A synthesis of the anhydride (3) utilising lamellicolic anhydride (4) as an intermediate has recently been reported[11] but no details have yet been published.

The substituted naphthalene (12b) which we required as an intermediate has been prepared previously[12] but the published method involved nine stages from 3,4,5-trimethoxybenzoic acid (5a) and the overall yield is only 1%. Our first objective was therefore to devise an improved route to the naphthalene (12b). The keto-acid (6a) contains the required carbon and oxygen skeleton; accordingly, this material was prepared by Friedel-Crafts reaction between pyrogallol trimethyl ether (5b) and methylsuccinic anhydride as previously described.[13] Reduction of the derived methyl ester (6b) with sodium borohydride at room temperature gave none of the desired hydroxy-ester (8a) but instead proceeded with hydrogenolysis to give the acid (8b),[13] possibly through an intermediate quinone methide.[14] When reduction of the ester (6b) with sodium borohydride was carried out at 0° a small amount of the hydroxy-ester (8a) was obtained, but the major product (81%) was the γ-lactone (7), which was smoothly converted into the methoxy-acid (8c) by treatment with methanolic sodium methoxide, a reaction which might involve cleavage of the lactone by the rarely observed $B_{AL}2$ mechanism,[15] or may once again involve a quinone methide intermediate.* Methylation of the phenol (8c), followed by cycliacylation and dehydrogenation would complete a very direct synthesis of the naphthalene (12b). Unfortunately we were unable to methylate the phenol (8c) with methyl sulphate and sodium hydroxide or with methyl iodide and silver oxide; treatment with diazomethane resulted only in esterification of the carboxy-group. Attempts to bring about cyclisation of the acid chloride derived from (8c) using tin(IV) chloride as catalyst gave only intractable mixtures.



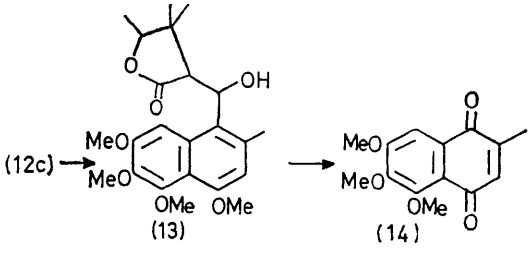
Preparation of the required naphthalene (12b) was finally achieved in an overall yield of 37% from 3,4,5-trimethoxybenzaldehyde (5c). Condensation of the

* We thank a referee for helpful comments on this reaction.

[9] N. Narasimhachari and L. C. Vining, *Canad. J. Chem.*, 1963, **41**, 641.
[10] G. W. van Eijk, *Phytochemistry*, 1971, **10**, 3263.
[11] N. J. McCorkindale, A. McRitchie, and S. A. Hutchinson, *J.C.S. Chem. Comm.*, 1973, 108.
[12] J. Cason and D. M. Lynch, *J. Org. Chem.*, 1966, **31**, 1883.
[13] P. C. Mitter and L. K. De, *J. Indian Chem. Soc.*, 1939, **16**, 199.
[14] *Cf.* B. J. McLoughlin, *Chem. Comm.*, 1969, 540.
[15] C. K. Ingold, 'Structure and Mechanism in Organic Chemistry,' pp. 752—754, Cornell University Press, Ithaca, New York, 1953.

aldehyde (5c) with nitroethane gave 1,2,3-trimethoxy-5-(2-nitropropenyl)benzene (9),* from which the methyl ketone (10) * was obtained by reduction with iron and hydrochloric acid. The methyl ketone (10) was also obtained, in lower yield (see Experimental section) by the action of dimethylcadmium on the acid chloride (5d) derived from 3,4,5-trimethoxyphenylacetic acid, and by reduction with hydrogen iodide of the diazo-ketone derived from the acid chloride (5d) by treatment with diazomethane. Reformatsky reaction of the methyl ketone (10) with ethyl bromoacetate gave the hydroxy-ester (11a). The acid (11b), obtained by hydrolysis, was cyclised with polyphosphoric acid to afford the phenol (12a), which was methylated with methyl sulphate to give the required tetramethyl ether (12b) in an overall yield of 37% from 3,4,5-trimethoxybenzaldehyde.

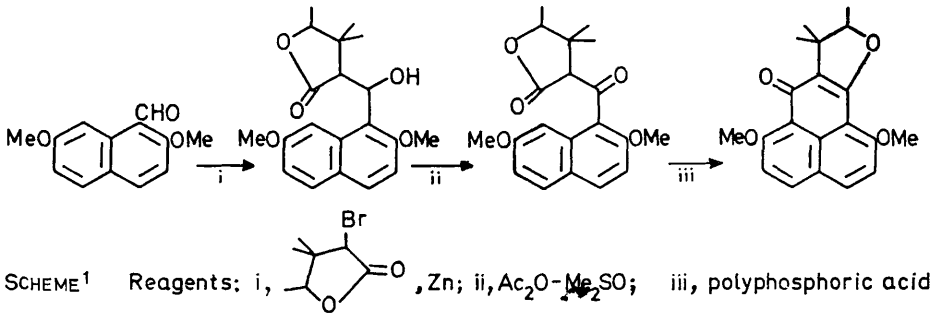
Earlier work [1] had shown that the basic ring system present in atrovenetin could be constructed as indicated in the Scheme. Accordingly, the naphthalene (12b) was formylated by a Vilsmeier reaction to give the aldehyde (12c). The orientation of substitution was evident from the n.m.r. spectrum of the product (see Experimental section). The corresponding carboxylic acid (12d) was obtained by oxidation of the aldehyde with potassium permanganate in aqueous pyridine. When the aldehyde (12c) was treated with zinc and α-bromo-ββ-dimethyl-γ-valerolactone, following the model sequence (Scheme), the alcohol (13) was obtained in good yield. However,



we were unable to oxidise the alcohol (13) to the corresponding ketone, and so this approach to the synthesis of atrovenetin was abandoned. Treatment of the alcohol (13) with Jones reagent [17] or with sodium dichromate gave the quinone (14); the action of silver carbonate–Celite [18] was to bring about a reverse aldol reaction in which the aldehyde (12c) was re-formed.

Atrovenetin was finally synthesised by a route involving application of the Claisen rearrangement (*cf.* ref. 1). Brief treatment of the naphthalene (12b) with malonic acid and polyphosphoric acid at 100° gave 3-hydroxy-6,7,8,9-tetramethoxy-4-methylphenalenone (15a) (73%), but attempted *O*-alkylation with 3,3-dimethylallyl bromide and potassium carbonate in acetone gave only the products (16) (38%) and (17a) (49%) of *C*-alkylation. Similar treatment of the phenalenone (15b) [obtained by selective hydrolysis of the 9-methoxy-group [4,19] of the tetramethyl ether (15a) with dilute hydrochloric acid], however, gave a suitable dimethylallyl ether (18) (42%), together with the bis-*C*-alkylated product (17b) (51%). When the substituted allyl ether (18) was heated at 100° in dimethylformamide (±)-atrovenetin yellow trimethyl ether (19a) [2] was obtained as the only isolated product, in a yield of 76%. Cyclisation of the initial product (22) of Claisen rearrangement in the required sense was no doubt favoured, since the alternative mode of cyclisation, to give the isomeric phenalenone (23), requires the conversion of the phenalenone (22) into the tautomer (24) in which the chelate hydrogen-bond has been broken. At higher temperatures, the phenalenones (20) and (21), which arise by cyclisation of the product of abnormal Claisen rearrangement,[20] were also isolated (see Experimental section). Structural assignments for compounds (19a), (20), and (21) were made unambiguously on the basis of their n.m.r. spectra. In each case the positioning of the methyl groups in the furan ring was evident from the chemical shift of the methine proton (*cf.* ref. 1); compound (21) differed from the other two in that it did not exhibit a low-field n.m.r. signal attributable to a chelated hydroxy-group.

Demethylation of (±)-atrovenetin yellow trimethyl ether with pyridine hydrochloride gave (±)-atrovenetin (19b) (for which spectra identical with those of the



* Compounds (9) and (10) have previously been reported as uncharacterised intermediates.[16]

[16] B.P. 940,596/1963 (*Chem. Abs.*, 1964, **60**, 4063a).

[17] R. G. Curtis, Sir I. Heilbron, E. R. H. Jones, and G. F. Woods, *J. Chem. Soc.*, 1963, 5313.

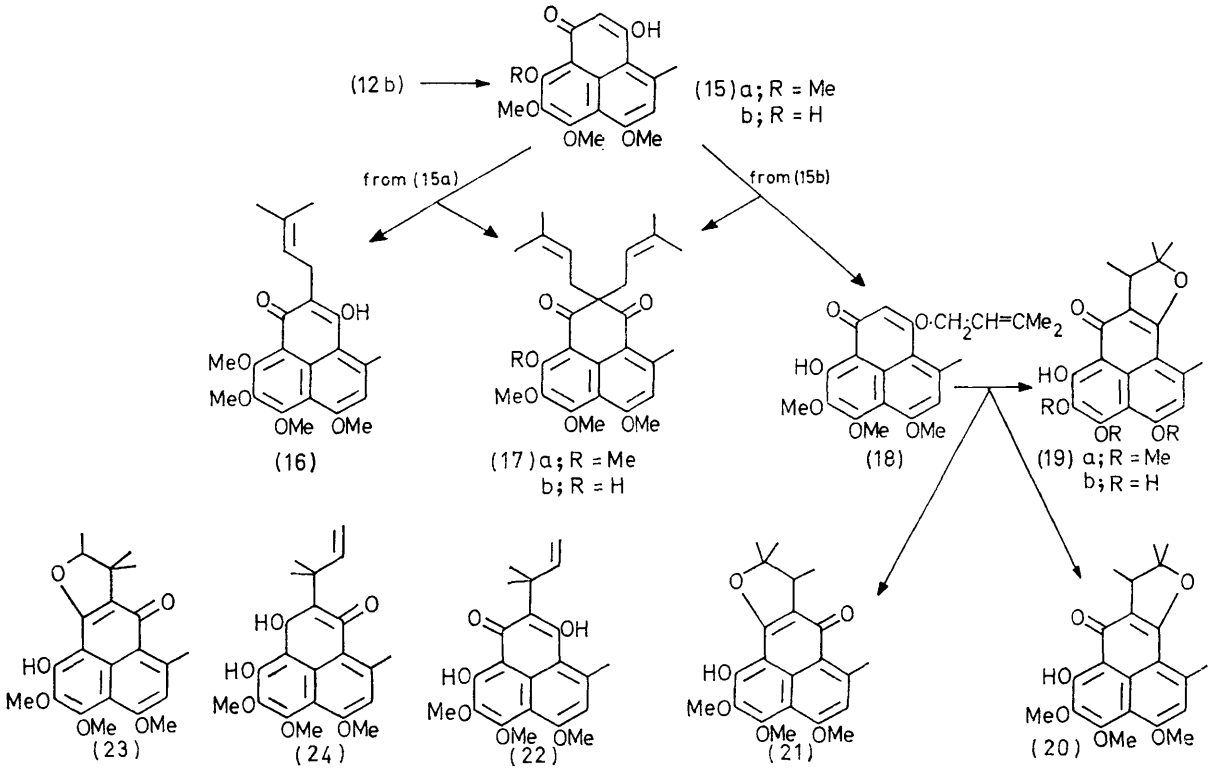
[18] *Cf.* M. Fétizon and M. Golfier, *Compt. rend.*, 1968, **267**, 900.

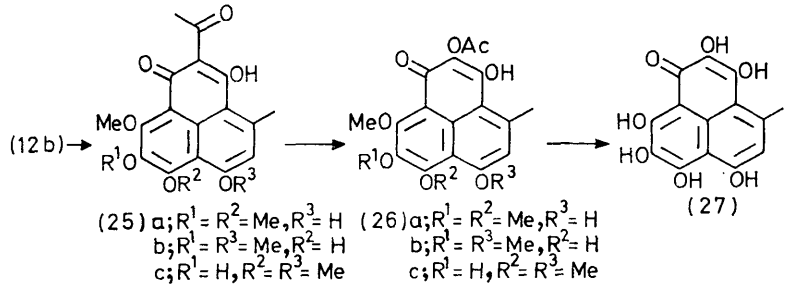
[19] B. Laundon and G. A. Morrison, *J. Chem. Soc.* (*C*), 1971, 1694.

[20] H. J. Shine, ' Aromatic Rearrangements,' Elsevier, London, 1967, pp. 89—123.

natural product were recorded), which was further characterised by preparation of its tri- and tetra-acetates.[2,4b]

Using the naphthalene (12b) as an intermediate we have also achieved a synthesis of norxanthoherquein (27),[2b] one of the principal degradation products of norherqueinone (2). Treatment of the naphthalene (12b) with an excess of malonic acid and polyphosphoric acid at 100° for 16 h converted it into a 2-acetylphenalenone which is assigned one of the three structures (25a—c). That acetylation (which presumably occurs by decarboxylation of an intermediate malonyl compound) had occurred at the 2-position was apparent from the absence of any signal at about τ 3·85 which could be assigned to a 2-proton [*cf.* n.m.r. spectra of 4,9-dimethoxy-3-hydroxyphenalenone [1] and the phenalenone (15a)]. Surprisingly, under the strong acid conditions employed in the preparation of the phenalenone (25) it appears that it is the 6-, 7-, or 8-methoxy-group and not that at the 9-position which is hydrolysed. This conclusion is based on two observations. First, the chemical shifts (τ −8·27 and −0·07) of the two hydroxy-groups of compound (25) indicate that only one of them is chelated with a carbonyl group, and secondly, at reaction times intermediate between the 15 min employed in the preparation of the phenalenone (15a) and the 16 h employed to prepare the phenalenone (25), a third product of the polyphosphoric acid-catalysed reaction between malonic acid and the naphthalene (12b) could be isolated in small yield. This compound was not fully characterised, but its n.m.r. spectrum revealed it to be an isomer of the 9-hydroxyphenalenone (15b), from which it differed considerably in R_F value on t.l.c. It appears likely that this material, which is clearly not a





9-hydroxyphenalenone,* is the immediate precursor of the acetylphenalenone (25).

The phenalenone (25) was subjected to a Baeyer–Villiger oxidation with *m*-chloroperbenzoic acid; the resulting acetate (26a, b, or c) exhibited n.m.r. signals at τ −0·20 and 0·12 for its two hydroxy-groups, thus indicating that neither was chelated with a carbonyl group, and therefore supporting other evidence for a 9-methoxy-group in compounds (25) and (26). When the phenalenone (26) was treated with pyridine hydrochloride at 220° it afforded norxanthoherquein (27), identical with material obtained by degradation of norherqueinone (2).

EXPERIMENTAL

M.p.s were measured on a Kofler hot-stage apparatus. I.r. spectra were recorded on a Unicam SP 200 or 1000 G spectrophotometer or on a Perkin-Elmer 125 instrument and refer to KCl discs unless stated otherwise. U.v. spectra were recorded on a Unicam SP 800 spectrophotometer (95% ethanol as solvent). N.m.r. spectra were recorded on a Varian A 60A instrument with deuteriochloroform as solvent, unless specified otherwise. Mass spectra were recorded on an A.E.I. MS 902 spectrometer. T.l.c. was carried out using plates coated with Merck Kieselgel G or GF_{254}. Light petroleum refers to the fraction of boiling range 60—80°. Solutions in organic solvents were dried with anhydrous sodium sulphate or magnesium sulphate.

4-(2-*Hydroxy*-3,4-*dimethoxyphenyl*)-2-*methyl*-4-*oxobutyric Acid* (6a).—This compound was prepared as previously described,[13] except that the product was isolated by chromatography on Kieselgel G with chloroform–methanol–formic acid (85 : 10 : 5) as eluant. Recrystallisation from aqueous ethanol gave white crystals, m.p. 153—155° (lit.,[13] 155°), $\lambda_{max.}$ 218, 232infl, and 284 nm (log ε 4·18, 4·00, and 4·19); $\nu_{max.}$ (Nujol) 1626, 1732, and 3260 cm^{-1}; τ (Na_2CO_3–D_2O) 2·30 (1H, d, *J* 9 Hz, phenyl 6-H), 3·36 (1H, d, *J* 9 Hz, phenyl 5-H), 6·05 and 6·18 (each 3H, s, OMe), 7·17 (1H, q, *J* 7·5 Hz, 2-H), and 8·80 (3H, d, *J* 7·5 Hz, 2-Me); *m/e* 268 (34%, M^+) and 181 (100%, $ArC\overset{+}{O}$).

Treatment with diazomethane resulted in quantitative formation of the *methyl ester* (6b), m.p. 65—66° (from aqueous methanol) (Found: C, 59·6; H, 6·35. $C_{14}H_{18}O_6$ requires C, 59·55; H, 6·45%), $\lambda_{max.}$ 219, 232infl, and 284 nm (log ε 4·15, 4·01, and 4·26); $\nu_{max.}$ (Nujol) 1640 and 1740 cm^{-1}; τ −2·40 (1H, s, OH), 2·44 (1H, d, *J* 9 Hz, phenyl 6-H), 3·50 (1H, d, *J* 9 Hz, phenyl 5-H), 6·06 and 6·10 (each 3H, s, ArOMe), 6·27 (3H, s, CO_2Me), 6·4—7·2 (3H, m, 2- and 3-H), and 8·73 (3H, d, *J* 7 Hz, 2-Me).

Reduction of the Keto-ester (6b) *with Sodium Borohydride.*—(a) *In aqueous ethanol at room temperature.* To a solution of the keto-ester (6b) (100 mg) in 60% aqueous ethanol (5 ml) was added a solution of sodium borohydride (50 mg) in the same solvent mixture (5 ml). The solution was left at room temp. for 16 h, then acidified with dil. hydrochloric acid, and extracted with chloroform. The extract was washed with water, dried, and evaporated *in vacuo*. Recrystallisation of the residue from chloroform–light petroleum gave 4-(2-hydroxy-3,4-dimethoxyphenyl)-2-methylbutyric acid (8b) (80 mg, 89%) as white crystals, m.p. 85—86° (lit.,[13] 83—85°) (Found: C, 61·3; H, 6·85. Calc. for $C_{13}H_{18}O_5$: C 61·4; H, 7·15%); $\nu_{max.}$ 1700 and 3480 cm^{-1}; τ 3·22 (1H, d, *J* 8·5 Hz, phenyl 5- or 6-H), 3·62 (1H, d, *J* 8·5 Hz, phenyl 5- or 6-H), 6·11 and 6·16 (each 3H, s, OMe), 7·1—8·4 (5H, m, 2-, 3-, and 4-H), and 8·77 (3H, d, *J* 7 Hz, 2-Me); *m/e* 254 (18%, M^+) and 167 (100%, $Ar\overset{+}{C}H_2$).

(b) *In aqueous methanol at* 0°. A solution of sodium borohydride (95 mg) in water (3 ml) was added to a solution of the keto-ester (6b) (1·40 g) in methanol (20 ml) at 0°. The temperature was maintained at 0° and further additions of sodium borohydride (25 mg) in water (1 ml) were made after 2 and 4 h. After a total of 6 h the solution was poured into ice-cold brine and extracted with ether. The extract was washed with water, dried, and evaporated under reduced pressure to leave a brown oil from which, by chromatography on a column of Kieselgel G (80 g) [chloroform–methanol (99 : 1) as eluant], two products were isolated. The material of higher R_F value, 4-(2-*hydroxy*-3,4-*dimethoxyphenyl*)-2-*methylbutan*-4-*olide* (7) (1·015 g, 81%), gave white crystals, m.p. 88—89° (from benzene–light petroleum) (Found: C, 61·9; H, 6·45. $C_{13}H_{16}O_5$ requires C, 61·9; H, 6·4%), $\lambda_{max.}$ 274 nm (log ε 3·20); $\nu_{max.}$ 1755 and 3420 cm^{-1}; τ 2·98 (1H, d, *J* 9 Hz, phenyl 5- or 6-H), 3·53 (1H, d, *J* 9 Hz, phenyl 5- or 6-H), 3·83 (1H, s, exchangeable with D_2O, OH), 4·43 (1H, dd, *J* 10·5 Hz and 5 Hz, 4-H), 6·09 and 6·15 (each 3H, s, OMe), 6·9—8·3 (3H, m, 2- and 3-H), and 8·70 (3H, d, *J* 6·5 Hz, 2-Me); *m/e* 252 (100%, M^+). In the n.m.r. spectrum the appearance of two additional aromatic doublets [at τ 3·08 (*J* 9 Hz) and 3·52 (*J* 9 Hz)] suggested the presence of a minor amount (*ca.* 25%) of another diastereoisomer.

The product of lower R_F value was recrystallised from benzene–pentane to give *methyl* 4-*hydroxy*-4-(2-*hydroxy*-3,4-*dimethoxyphenyl*)-2-*methylbutyrate* (8a) (90 mg, 6%) as white crystals, m.p. 67—68° (Found: C, 59·5; H, 7·15. $C_{14}H_{20}O_6$ requires C, 59·15; H, 7·1%), $\lambda_{max.}$ 226infl and 275 nm (log ε 3·91 and 3·11); $\nu_{max.}$ 1720, 3437, and 3503 cm^{-1}; τ 3·10 (1H, d, *J* 9 Hz, phenyl 5- or 6-H), 3·57 (1H, d, *J* 9 Hz, phenyl 5- or 6-H), 5·3br (1H; addition of D_2O gives dd, *J* 6 and 10·5 Hz, 4-H), 6·11 and 6·15 (each 3H, s, OMe), 6·33 (3H, s, CO_2Me), 7·13 (1H, s, exchangeable with D_2O, OH), 7·2—8·6 (3H, m, 2- and 3-H), and 8·75 (3H, d, *J* 7 Hz, 2-Me); *m/e* 284 (2%, M^+), 266 (60%, $M^+ - H_2O$), and 207 (100%, $ArCH{=}CH{-}\overset{+}{C}HMe$).

4-(2-*Hydroxy*-3,4-*dimethoxyphenyl*)-4-*methoxy*-2-*methylbutyric Acid* (8c).—Methanolic sodium methoxide (2N; 2 ml) was added to a solution of the lactone (7) (200 mg) in methanol (2 ml). The mixture was warmed to dissolve precipitated solids, left at room temperature overnight, then poured into ice–water and acidified with concentrated hydrochloric acid. The aqueous solution was extracted with chloroform, and the extract was then itself extracted with sodium hydrogen carbonate. The latter extract was acidified, then re-extracted with chloroform, and the chloroform extract was washed with water, dried, and evaporated *in vacuo* to give a colourless gum from which, by preparative t.l.c. [20 × 20 cm plate, coated with 16 g Kieselgel G_{F254}; chloroform–methanol (19 : 1) as eluant],

* In agreement with this, the chemical shift of its 2-proton is τ 3·87. Generally, it appears that 3,9-dihydroxyphenalenones [*e.g.* 3,9-dihydroxy-4-methoxyphenalenone [1] and compound (15b)] exhibit a signal for this proton at about τ 3·0; the corresponding absorption in 3-hydroxy-9-methoxyphenalenones [*e.g.* 3-hydroxy-4,9-dimethoxyphenalenone and compound (15a)] appears at about τ 3·85.

the *methoxy-derivative* (8c) (140 mg, 62%) was obtained, m.p. 112—114° (from methylcyclohexane) (Found: C, 59·4; H, 7·1. $C_{14}H_{20}O_6$ requires C, 59·15; H, 7·1%), $\lambda_{max.}$ 226infl and 275 nm (log ε 3·92 and 3·45); $\nu_{max.}$ 1700, 2500—2700, and 3400 cm^{-1}; τ 3·14 and 3·56 (each 1H, d, *J* 8·5 Hz, ArH), 5·5 (1H, m, 4-H), 6·13 and 6·17 (each 3H, s, ArOMe), 6·74 (3H, s, 4-OMe), 7·1—8·4 (3H, m, 2- and 3-H), and 8·80 (3H, d, *J* 7 Hz, 2-Me); *m/e* 252 (100%, M^+ — MeOH).

1,2,3-*Trimethoxy*-5-(2-*nitropropenyl*)*benzene* (9) (*cf.* ref. (16).—A solution of 3,4,5-trimethoxybenzaldehyde (19·6 g), nitroethane (13·2 g), n-butylamine (0·8 ml), and glacial acetic acid (1 ml) in toluene (25 ml) was heated under reflux for 7 h with continuous azeotropic removal of water. The solvent and the excess of reactants were removed under reduced pressure, and the residue was recrystallised from benzene–light petroleum to give the *nitro-compound* (9) (22 g, 87%) as yellow crystals, m.p. 95—96° (Found: C, 56·8; H, 5·95; N, 5·4. $C_{12}H_{15}NO_5$ requires C, 56·9; H, 5·95; N, 5·55%), $\lambda_{max.}$ 215 and 343 nm (log ε 4·30 and 4·04); $\nu_{max.}$ 1575 and 1640 cm^{-1}; τ 2·01br (1H, s, olefinic H), 3·34 (2H, s, ArH), 6·12 (9H, s, OMe), and 7·54 (3H, d, *J* 1 Hz, MeC·NO_2); *m/e* 253 (100%, M^+) and 207 (25%, M^+ — NO_2).

1-(3,4,5-*Trimethoxyphenyl*)*propan*-2-*one* (10) (*cf.* ref. 16). —(*a*) To a solution of the nitro-compound (9) (22 g) in toluene (30 ml) were added iron powder (36·2 g), hydrated iron(III) chloride (0·73 g), and water (45 ml). The mixture was heated to its b.p. and concentrated hydrochloric acid (71 ml) was added slowly, so as to maintain vigorous reflux. Heating under reflux was continued for a further 4 h, and the mixture was then cooled and filtered through a short column of alumina. The column was washed with benzene and the combined organic solution was washed with water, dried, and evaporated *in vacuo* to afford a brown crystalline solid from which, by trituration and washing with cold ether, the *ketone* (10) (9 g) was obtained as pale brown prisms, m.p. 63—65°. Chromatography of the remaining material on Kieselgel G (400 g) [ether–benzene (1 : 4) as eluant] gave more of the same ketone (5 g; total 14 g, 72%). Recrystallisation from benzene–light petroleum gave white crystals, m.p. 64—65° (Found: C, 64·2; H, 7·15%; *m/e* 224·1046. $C_{12}H_{16}O_4$ requires C, 64·25; H, 7·2%; *M*, 224·1049), $\lambda_{max.}$ 273 nm (log ε 2·93); $\nu_{max.}$ 1712 cm^{-1}; τ 3·60 (2H, s, ArH), 6·17 (9H, s, OMe), 6·41 (2H, s, CH_2), and 7·86 (3H, s, COMe); *m/e* 224 (35%, M^+) and 181 (100%, $Ar\overset{+}{C}H_2$).

(*b*) A solution of 3,4,5-trimethoxyphenylacetic acid (1·13 g) and oxalyl chloride (10 ml) in benzene (10 ml) was heated under reflux for 1 h. The solvent was removed under reduced pressure and a solution of the residual 3,4,5-trimethoxyphenylacetyl chloride in benzene (10 ml) was added dropwise to an ice-cold, stirred solution of diazomethane (0·012 mole) in ether (120 ml). The mixture was stirred at room temperature for 2 h, then evaporated *in vacuo*, and the residue was dissolved in chloroform (3 ml) and shaken with aqueous hydriodic acid (55%; 2 ml) for 5 min. More chloroform was added, and the solution was washed successively with dilute aqueous sodium thiosulphate, saturated aqueous sodium hydrogen carbonate, and water, then dried and chromatographed on a column of Kieselgel G (25 g) (chloroform as eluant) to give 1-(3,4,5-trimethoxyphenyl)propan-2-one (650 mg, 58%), identical with material obtained by method (*a*).

(*c*) Cadmium chloride (2 g) was stirred for 2 h with a solution of methylmagnesium bromide [prepared from magnesium turnings (0·5 g) and an excess of methyl iodide] in ether (30 ml), 3,4,5-trimethoxyphenylacetyl chloride (5d) [prepared by heating 3,4,5-trimethoxyphenylacetic acid (1·13 g) with oxalyl chloride (10 ml) under reflux in ether (10 ml) for 1 h, then removing the excess of oxalyl chloride and ether under reduced pressure] was added slowly, and the mixture was heated under reflux for 3 h. The cooled mixture was acidified with dilute sulphuric acid and extracted with ether. The extract was washed with water, dried, and evaporated to leave an oil (800 mg) which was shown by t.l.c. to contain two compounds. Chromatography (Kieselgel H_{F254}) of a small sample (100 mg) gave ethyl 3,4,5-trimethoxyphenylacetate (35 mg), $\nu_{max.}$ 1725 cm^{-1}, and a ketone fraction (49 mg), $\nu_{max.}$ 1700 cm^{-1}. The product mixture was recombined and dissolved in ethanol (10 ml), aqueous sodium hydroxide (2N; 1 ml) was added, and the mixture was left overnight. The ethanol was removed under reduced pressure, water (20 ml) was added, and an ether extract was made. The extract was washed successively with aqueous 2N-sodium hydroxide and water, then dried and evaporated under reduced pressure to give a non-acidic fraction (360 mg), chromatography of which on a column of Kieselgel G gave 1-(3,4,5-trimethoxyphenyl)-propan-2-one (250 mg, 23%) identical with material obtained as in (*a*) and (*b*). Acidification of the alkaline washings gave 3,4,5-trimethoxyphenylacetic acid (300 mg).

When benzene was substituted for ether in the reaction between 3,4,5-trimethoxyphenylacetyl chloride and dimethylcadmium the yield of the ketone (10) was 32%.

Ethyl 3-*Hydroxy*-3-*methyl*-4-(3,4,5-*trimethoxyphenyl*)-*butyrate* (11a).—Granulated zinc (3 g) was added to a stirred solution of the ketone (10) (8·3 g) in benzene–toluene (1 : 1; 25 ml). The mixture was heated under reflux, and a solution of ethyl bromoacetate (4·8 ml) in benzene–toluene (1 : 1; 75 ml) was added in portions during 1 h. The mixture was heated under reflux for a further 3 h, then cooled to room temperature. Dilute sulphuric acid was added, and the organic phase was separated, washed with water, dried, and evaporated *in vacuo* to yield the *ester* (11a) (10 g, 87%) as a clear liquid which appeared to be pure by t.l.c. and from its n.m.r. spectrum. The product was distilled from an oil-bath at 210° and 0·05 mmHg (Found: C, 61·2; H, 7·7%; *m/e* 312·1568. $C_{16}H_{24}O_6$ requires C, 61·5; H, 7·75%; *M*, 312·1573), $\lambda_{max.}$ 213, 217infl, and 273 nm (log ε 3·84, 3·49, and 2·60); $\nu_{max.}$ (film) 1725 and 3580 cm^{-1}; τ 3·56 (2H, s, ArH), 5·86 (2H, q, *J* 7 Hz, $CO_2{\cdot}C\mathit{H}_2{\cdot}CH_3$), 6·17 (9H, s, OMe), 6·53 (1H, s, exchangeable with D_2O, OH), 7·24 (2H, s, 2- or 4-H_2), 7·56 (2H, s, 2- or 4-H_2), and 8·74 (6H, m, 2-Me and $CO_2{\cdot}CH_2\mathit{Me}$); *m/e* 312 (16%, M^+), 294 (5%, M^+ — H_2O), 182 (100%), and 181 (90%, $Ar\overset{+}{C}H_2$).

3-*Hydroxy*-3-*methyl*-4-(3,4,5-*trimethoxyphenyl*)*butyric Acid* (11b).—A solution of the ester (11a) (10 g) in ethanol (50 ml) and aqueous sodium hydroxide (2N; 30 ml) was heated at 100° for 1 h, then diluted with water, washed with chloroform, and acidified (2N-HCl). The acidic solution was extracted with chloroform and the extract was washed with water, dried, and evaporated under reduced pressure to give the *acid* (11b) (9·1 g, 100%) as a pale brown oil which, although pure (t.l.c. and n.m.r. spectrum), could not be crystallised (Found: *m/e*, 284·1266. $C_{14}H_{20}O_6$ requires *M*, 284·1260); τ 3·54 (2H, s, ArH), 4·33 (1H, s, exchangeable with D_2O, OH), 6·17 (9H, s, OMe), 7·21 (2H, s, 2- or 4-H_2),

7·50 (2H, s, 2- or 4-H_2), and 8·71 (3H, s, 3-Me); *m/e* 284 (48%, M^+), 269 (4%, M^+ — Me), 266 (5%, M^+ — H_2O), 225 (14%, M^+ — $CH_2{\cdot}CO_2H$), 224 (16%), 182 (100%), and 181 (100%, $ArCH_2^+$).

6,7,8-*Trimethoxy*-3-*methyl*-1-*naphthol* (12a).—The hydroxy-acid (11b) (1·1 g) was stirred with polyphosphoric acid (6 g) at 60° for 10 min. More polyphosphoric acid (4 g) was added, and stirring was continued a further 10 min, then the cooled mixture was hydrolysed with ice–water and extracted with chloroform. The extract was washed successively with dilute aqueous sodium hydrogen carbonate and water, dried, and evaporated under reduced pressure to afford the naphthol (12a) (700 mg, 73%) as straw-coloured crystals, pure by t.l.c. and from its n.m.r. spectrum. Recrystallisation from aqueous ethanol gave white crystals, m.p. 80—81° (lit.,[12] 81—83°) (Found: C, 67·5; H, 6·6%; *m/e*, 248·1037. Calc. for $C_{14}H_{16}O_4$: C, 67·75; H, 6·5%; *M*, 248·1049), $\lambda_{max.}$ 226 and 245 nm (log ε 4·35 and 4·46); $\nu_{max.}$ 3360 cm^{-1}; τ 0·70 (1H, exchangeable with D_2O, OH), 3·06 (1H, d, *J* 1·5 Hz, 4-H), 3·20 (1H, s, 5-H), 3·41 (1H, d, *J* 1·5 Hz, 2-H), 5·89 (3H, s, OMe), 6·08 (6H, s, OMe), and 7·64 (3H, s, CMe), *m/e* 248 (100%, M^+) and 233 (78%, M^+ — Me).

1,2,3,8-*Tetramethoxy*-6-*methylnaphthalene* (12b).—Dimethyl sulphate (4 ml) was added to a solution of the naphthol (12a) (960 mg) in ethanol (20 ml) and aqueous sodium hydroxide (2N; 20 ml), the mixture was heated at 100°, and further portions of dimethyl sulphate (1 ml) and aqueous sodium hydroxide (2N; 5 ml) were added at intervals of 30 min. After three such additions, the mixture was cooled and extracted with ether. The extract was washed with water, dried, and evaporated *in vacuo* to afford 1,2,3,8-tetramethoxy-6-methylnaphthalene (930 mg, 92%), pure as judged by t.l.c. and n.m.r. spectroscopy. Recrystallisation from aqueous methanol gave white crystals, m.p. 86—87° (lit.,[12] 87—89°) (Found: C, 68·75: H, 6·95. Calc. for $C_{15}H_{18}O_4$: C, 68·7; H, 6·9%), $\lambda_{max.}$ 226, 241, and 284 nm (log ε 4·45, 4·54, and 3·71); τ 2·97br (1H, s, 5-H), 3·17 (1H, s, 4-H), 3·46br (1H, s, 7-H), 6·05, 6·08, 6·11, and 6·13 (each 3H, s, OMe), and 7·60 (3H, s, 6-Me); *m/e* 262 (100%, M^+), and 247 (36%, M^+ — Me).

4,5,6,7-*Tetramethoxy*-2-*methyl*-1-*naphthaldehyde* (12c).—1,2,3,8-Tetramethoxy-6-methylnaphthalene (1·47 g) was stirred and heated at 100° for 2 h with a mixture of toluene (10 ml), dimethylformamide (550 mg), and phosphoryl chloride (980 mg). A solution of sodium acetate was added to the cooled solution, and the mixture was heated at 100° for 15 min. It was then extracted with benzene, and the extract was washed with water, dried, and evaporated *in vacuo*. Chromatography of the residue on a column of Kieselgel G (60 g) (chloroform as eluant) afforded the *aldehyde* (12c) (1·54 g, 95%), which gave pale-yellow crystals, m.p. 103—104° (from light petroleum) (Found: C, 66·5; H, 6·45. $C_{16}H_{18}O_5$ requires C, 66·2; H, 6·25%), $\lambda_{max.}$ 229, 245, 269, and 348 nm (log ε 4·21, 4·13, 4·22, and 3·80); $\nu_{max.}$ 1663 cm^{-1}; τ −0·76 (1H, s, CHO), 1·19 (1H, s, 8-H), 3·44 (1H, s, 3-H), 5·95, 6·00, 6·05, and 6·11 (each 3H, s, OMe), and 7·24 (3H, s, 2-Me); *m/e* 290 (100%, M^+), 275 (20%, M^+ — Me), and 262 (58%, M^+ — CO).

4,5,6,7-*Tetramethoxy*-2-*methyl*-1-*naphthoic Acid* (12d).—A solution of potassium hydroxide (100 mg) in water (7 ml) was added to an ice-cold stirred solution of the aldehyde (12c) (210 mg) in pyridine (20 ml). The ice-bath was removed, and a solution of potassium permanganate (400 mg) in water (10 ml) was added dropwise during 30 min. The mixture was stirred at room temperature for 1 h, then acidified with conc. hydrochloric acid. The excess of permanganate was destroyed by adding sodium hydrogen sulphite, the solution was extracted with chloroform, and the extract was then extracted with dilute aqueous sodium hydrogen carbonate. The latter extract was washed with chloroform, acidified, and extracted with chloroform, and the chloroform extract was washed with water, dried, and evaporated under reduced pressure to give the *acid* (12d) (198 mg, 89%), m.p. 162—168°. Recrystallisation from chloroform–light petroleum gave white crystals, m.p. 172—173° (Found: C, 62·6; H, 5·95. $C_{16}H_{18}O_6$ requires C, 62·75; H, 5·9%), $\lambda_{max.}$ 248 and 275 nm (log ε 4·59 and 4·11); $\nu_{max.}$ 1742 and 3200 cm^{-1}; τ 2·66 (1H, s, 8-H), 3·44 (1H, s, 3-H), 6·00, 6·06, and 6·10 (total 12H, 3s, OMe), and 7·43 (3H, s, 2-Me); *m/e* 306 (100%, M^+) and 291 (30%, M^+ — Me).

2-[*Hydroxy*-(2-*methyl*-4,5,6,7-*tetramethoxy*-1-*naphthyl*)-*methyl*]-3,3-*dimethylpentan*-4-*olide* (13).—Zinc wool (325 mg) was added to a solution of the naphthaldehyde (12c) (960 mg) and 2-bromo-3,3-dimethylpentan-4-olide [1] (900 mg) in a mixture of benzene (5 ml) and toluene (5 ml). The mixture was stirred and heated under reflux for 3 h, then cooled, acidified with dilute sulphuric acid, and extracted with benzene. The extract was washed with water, dried, and evaporated under reduced pressure. Chromatography of the residue on a column of Kieselgel G (70 g) [ether–benzene (1 : 1) as eluant] gave the *lactone* (13) (1·32 g, 98%), which afforded white crystals, m.p. 147—148° (from benzene–light petroleum) (Found: C, 65·65; H, 7·05. $C_{23}H_{30}O_7$ requires C, 66·0; H, 7·25%), $\lambda_{max.}$ 248, 294infl and 305 nm (log ε 4·70, 3·84, and 3·86); $\nu_{max.}$ (Nujol) 1740 and 3520 cm^{-1}; τ 2·16 (1H, s, naphthyl 8-H), 3·50 (1H, s, naphthyl 3-H), 4·48 (1H, dd, *J* 2 and 10 Hz, collapses to d, *J* 10 Hz, upon treatment with D_2O, C*H*·OH), 5·25 (1H, d, *J* 2 Hz, exchangeable with D_2O, OH), 6·04, 6·06, and 6·14 (total 12H, 3s, OMe), 6·42 (1H, d, *J* 10 Hz, 2-H), 7·45 (3H, s, ArMe), 8·84 (3H, d, *J* 7 Hz, 4-Me), and 9·30 and 9·95 (each 3H, s, CMe_2); *m/e* 418 (15%, M^+), 400 (6%, M^+ — H_2O), and 291 (100%, $ArCHOH^+$).

Oxidation of the Hydroxy-lactone (13).—(*a*) A solution of the hydroxy-lactone in benzene was heated under reflux for several days with a large excess of silver carbonate on Celite.[18] A slow reaction occurred, yielding the aldehyde (12c) as the only product.

(*b*) A solution of the hydroxy-lactone (13) (105 mg) in ether (2 ml) was stirred at room temperature for 2 h with a solution of sodium dichromate dihydrate (63 mg) and concentrated sulphuric acid (0·05 ml) in water (0·3 ml). The ether layer was separated, washed successively with aqueous sodium hydrogen carbonate and water, dried, and evaporated under reduced pressure. The residue was separated by preparative t.l.c. (20 × 20 cm plate, coated with 16 g Kieselgel G; chloroform as eluant) into starting material (72 mg) and 2-*methyl*-5,6,7-*trimethoxy*-1,4-*naphthoquinone* (14) (25 mg, 97% based on starting material consumed), which crystallised from benzene–light petroleum as pale-yellow needles, m.p. 142—143° (Found: C, 63·95; H, 5·3. $C_{14}H_{14}O_5$ requires C, 64·1; H, 5·4%), $\lambda_{max.}$ 213, 268, and 370 nm (log ε 4·32, 4·36, and 3·51); $\nu_{max.}$ 1631, 1654, and 1660 cm^{-1}; τ 2·52 (1H, s, 8-H), 3·34 (1H, q *J* 1·6 Hz, 3-H), 6·00, 6·04, and 6·08 (each 3H, s, OMe), and 7·90 (3H, d, *J* 1·6 Hz, CMe).

(*c*) In three separate experiments, the hydroxy-lactone (13) was dissolved in acetone and treated with Jones reagent [17] at 20, −5, and −78°. In each case, the only product was the quinone (14).

3-*Hydroxy*-6,7,8,9-*tetramethoxy*-4-*methylphenalen*-1-*one* (15a).—A mixture of the naphthalene (12b) (1 g), malonic acid (420 mg), and polyphosphoric acid (15 ml) was stirred at 100° for 15 min, then cooled, hydrolysed with water, and extracted with chloroform. The aqueous solution was made alkaline with dilute aqueous sodium hydroxide, re-acidified with glacial acetic acid, and again extracted with chloroform. The combined chloroform extracts were washed with water, dried, and evaporated *in vacuo* to give, after chromatography on Grade III alumina (chloroform as eluant), the *phenalenone* (15a) (915 mg, 73%), which afforded yellow crystals, m.p. 166—167° (from benzene–light petroleum) (Found: C, 65·5; H, 5·5. $C_{18}H_{18}O_6$ requires C, 65·45; H, 5·5%), $\lambda_{max.}$ 216, 271, 353, 388, 407, and 430infl nm (log ε 4·42, 4·45, 3·98, 4·04, 4·06, and 3·92); $\nu_{max.}$ (Nujol) 1608, 1620, and 2500—2800 cm^{-1}; τ 3·17 (1H, s, 5-H), 3·87 (1H, s, 2-H), 5·76 and 5·91 (each 3H, s, OMe), 6·00 (6H, s, OMe), and 7·04 (3H, s, CMe); *m/e* 330 (100%, M^+), 315 (43%, M^+ — Me), and 287 [56%, M^+ — (Me, CO)].

3,9-*Dihydroxy*-6,7,8-*trimethoxy*-4-*methylphenalen*-1-*one* (15b).—A solution of the phenalenone (15a) (1·21 g) in ethanol (20 ml) and hydrochloric acid (6N; 20 ml) was heated at 100° for 30 min, then diluted with water and extracted with chloroform. The extract was washed with water, dried, and evaporated under reduced pressure to afford a yellow crystalline solid which was triturated with chloroform to give the *dihydroxyphenalenone* (15b) (1·1 g, 95%), m.p. 268—270° (Found: C, 64·5; H, 5·1. $C_{17}H_{16}O_6$ requires C, 64·55; H, 5·1%), $\lambda_{max.}$ 217, 239infl, 270infl, 374, 398, and 414infl nm (log ε 4·47, 4·28, 4·11, 4·28, 4·31, and 4·26); $\nu_{max.}$ (Nujol) 1586, 1633, and 3360 cm^{-1}; τ ([$^2H_5$]-pyridine) 2·98 (1H, s, 2-H), 3·22 (1H, s, 5-H), 5·83, 5·90, and 5·95 (each 3H, s, OMe), and 6·91 (3H, s, CMe).

Alkylation of 3-*Hydroxy*-6,7,8,9-*tetramethoxy*-4-*methylphenalen*-1-*one* (15a) *with* 3-*Methylbut*-2-*enyl Bromide*.—Potassium carbonate (1·05 g) and 3-methylbut-2-enyl bromide (700 mg) were added to a solution of the phenalenone (15a) (924 mg) in acetone (140 ml), and the mixture was stirred and heated under reflux for 1·5 h. The acetone was removed under reduced pressure, water was added, and the aqueous mixture was acidified with dilute hydrochloric acid and extracted with chloroform. The extract was washed with water, dried, and evaporated *in vacuo* to leave a residue from which two products were isolated by chromatography on a column of Kieselgel G (150 g) (benzene as eluant).

The band of highest R_F value gave 6,7,8,9-*tetramethoxy*-4-*methyl*-2,2-*bis*-(3-*methylbut*-2-*enyl*)*phenalene*-1,3(2H)-*dione* (17a) (640 mg, 49%) as an oil (Found: *m/e* 466·2325. $C_{28}H_{34}O_6$ requires *M*, 466·2355), $\lambda_{max.}$ 221, 255, and 350 nm (log ε 4·35, 4·50, and 3·95); $\nu_{max.}$ (film) 1655, 1660, and 1699 cm^{-1}; τ 3·23 (1H, s, ArH), 4·98 (2H, t, *J* 7 Hz, with further allylic splitting, olefinic H), 5·92 and 6·00 (each 6H, s, OMe), 7·20 (3H, s, ArMe), 7·37br (4H, d, *J* 7 Hz, CH_2), and 8·43br (12H, s, CMe_2).

The yellow band of second-highest R_F value afforded 3-*hydroxy*-6,7,8,9-*tetramethoxy*-4-*methyl*-2-(3-*methylbut*-2-*enyl*)*phenalen*-1-*one* (16) (423 mg, 38%), which crystallised from benzene–light petroleum as yellow needles, m.p. 139—140° (Found: C, 69·05; H, 6·45. $C_{23}H_{26}O_6$ requires C, 69·35; H, 6·6%), $\lambda_{max.}$ 218, 267, 353, 390, and 410infl nm (log ε 4·59, 4·59, 4·11, 4·19, and 4·17); $\nu_{max.}$ (Nujol) 1606, 1652, and 3275 cm^{-1}; τ −0·32 (1H, s, exchangeable with D_2O, OH), 3·17 (1H, s, ArH), 4·71 (1H, t, *J* 7 Hz, with further allylic splitting, olefinic H), 5·78 and 5·91 (each 3H, s, OMe), 6·02 (6H, s, OMe), 6·60br (2H, d, *J* 7 Hz, CH_2), 7·03 (3H, s, ArMe), and 8·16 and 8·33 (each 3H, broad s, CMe_2).

Alkylation of 3,9-*Dihydroxy*-6,7,8-*trimethoxy*-4-*methylphenalen*-1-*one* (15b) *with* 3-*Methylbut*-2-*enyl Bromide*.—Potassium carbonate (1·7 g) and 3-methylbut-2-enyl bromide (1·11 g) were added to a solution of the phenalenone (15b) (1·4 g) in acetone (220 ml), and the mixture was stirred and heated under reflux for 15 h, then worked up as described in the previous experiment. Chromatography on a column of Kieselgel G (100 g), with chloroform as eluant, afforded two major products.

The colourless band of highest R_F value yielded 9-*hydroxy*-6,7,8-*trimethoxy*-4-*methyl*-2,2-*bis*-(3-*methylbut*-2-*enyl*)*phenalene*-1,3(2H)-*dione* (17b) (1·02 g, 51%), which crystallised from light petroleum as white needles, m.p. 95—96° (Found: C, 71·9; H, 7·05. $C_{27}H_{32}O_6$ requires C, 71·65; H, 7·15%), $\lambda_{max.}$ 229, 262, 350, and 386infl nm (log ε 4·44, 4·52, 4·04, and 3·91); $\nu_{max.}$ (Nujol) 1585—1605 and 1655 cm^{-1}; τ −4·92 (1H, s, exchangeable with D_2O, OH), 3·26 (1H, s, ArH), 5·10 (2H, t, *J* 7·5 Hz, with further allylic splitting, olefinic H), 5·92, 5·96, and 5·97 (each 3H, s, OMe), 7·19 (3H, s, ArMe), 7·30br (4H, d, *J* 7·5 Hz, CH_2), and 8·42—8·47 (12H, m, allylic Me).

From the yellow band of second highest R_F value was obtained 9-*hydroxy*-6,7,8-*trimethoxy*-4-*methyl*-3-(3-*methylbut*-2-*enyloxy*)*phenalen*-1-*one* (18) (706 mg, 42%), which crystallised from benzene–light petroleum as yellow crystals, m.p. 132—133: (Found: C, 68·6; H, 6·35. $C_{22}H_{24}O_6$ requires C, 68·75; H, 6·3%), $\lambda_{max.}$ 214, 240, 270infl, 376infl, 395, and 411infl nm (log ε 4·62, 4·30, 4·04, 4·25, 4·28, and 4·24); $\nu_{max.}$ (Nujol) 1624 cm^{-1}; τ 3·16 (1H, s, 5-H), 3·66 (1H, s, 2-H), 4·43 (1H, t, *J* 7 Hz, with further allylic splitting, olefinic H), 5·31br (2H, d, *J* 7 Hz, CH_2), 5·93 and 5·98 (3H and 6H, s, OMe), 7·19 (3H, s, ArMe), and 8·22br (6H, s, CMe_2); *m/e* 384 (100%, M^+), 369 (83%), 316 (98%), and 301 (100%).

Claisen Rearrangement of the Allyl Ether (18).—The allyl ether (18) (50 mg) was heated in dimethylformamide (2 ml) at the temperatures and for the times specified in the Table, which also summarises the yields of the various products obtained.

Temp. (°C)	Reaction time (h)	Yields of products (%) (19a)	(20)	(21)
100	16	76		
153	3	60	22	6
190	2·5	28	44	20

The cooled mixture was diluted with chloroform, washed with water, dried, and evaporated under reduced pressure. Preparative t.l.c. [20 × 20 cm plate coated with 16 g Kieselgel G; ether–benzene (1 : 9) as eluant] afforded, from the yellow band of highest R_F value, 8,9-dihydro-6-hydroxy-3,4,5-trimethoxy-1,8,8,9-tetramethylphenaleno[1,2-*b*]-furan-7-one [(±)-atrovenetin yellow trimethyl ether] (19a), which crystallised from benzene–light petroleum as yellow plates, m.p. 166—167°, identical [with respect to t.l.c., i.r. (KCl), u.v., n.m.r., and mass spectra] with an authentic sample of (+)-atrovenetin yellow trimethyl ether derived from a natural source [2] (Found: C, 69·0; H, 6·25. Calc. for $C_{22}H_{24}O_6$: C, 68·75; H, 6·3%); τ −8·13 (1H, s, exchangeable with D_2O, OH), 3·15 (1H, s, ArH), 5·34 (1H, q,

J 7 Hz, MeC*H*), 5·91 and 5·97 (3H and 6H, s, OMe), 7·12 (3H, s, ArMe), 8·43 and 8·65 (each 3H, s, CMe_2), and 8·53 (3H, d, *J* 7 Hz, *Me*CH); *m/e* 384 (40%, M^+) and 369 (100%, $M^+ - 15$).

The yellow band of second highest R_F value afforded 8,9-*dihydro*-6-*hydroxy*-3,4,5-*trimethoxy*-1,8,9,9-*tetramethylphenaleno*[1,2-b]*furan*-7-*one* (20), which crystallised from benzene–light petroleum as yellow plates, m.p. 147—148° (Found: C, 68·7; H, 6·25. $C_{22}H_{24}O_6$ requires C, 68·75; H, 6·3%), $\lambda_{max.}$ 217, 267—273infl, 377, 403, and 423infl nm (log ε 4·60, 4·15, 4·29, 4·30, and 4·22); $\nu_{max.}$ (Nujol) 1610 cm^{-1}; τ −8·13 (1H, s, exchangeable with D_2O, OH), 3·14 (1H, s, ArH), 5·90 and 5·96 (3H and 6H, s, OMe), 6·64 (1H, q, *J* 7 Hz, MeC*H*), 7·12 (3H, s, ArMe), 8·47 (6H, s, CMe_2), and 8·63 (3H, d, *J* 7 Hz, *Me*CH); *m/e* 384 (50%, M^+) and 369 (100%, M^+ — Me).

From the yellow band of lowest R_F value there was obtained 8,9-*dihydro*-1-*hydroxy*-2,3,4-*trimethoxy*-6,8,9,9-*tetramethylphenaleno*[1,2-b]*furan*-7-*one* (21) as a yellow gum which, although it was chromatographically homogeneous, could not be crystallised (Found: C, 68·7; H, 6·6. $C_{22}H_{24}O_6$ requires C, 68·75; H, 6·3%), $\lambda_{max.}$ 217, 242infl, 270, 367, 384, 410, and 434infl nm (log ε 4·43, 4·25, 4·32, 4·13, 4·09, 4·05, and 3·86); $\nu_{max.}$ ($CHCl_3$) 1641 and 3380 cm^{-1}; τ 0·87 (1H, s, exchangeable with D_2O, OH), 3·16 (1H, s, ArH), 5·90 and 5·96 (3H and 6H, s, OMe), 6·72 (1H, q, *J* 7 Hz, MeC*H*), 6·97 (3H, s, ArMe), 8·42 (6H, s, CMe_2), and 8·64 (3H, d, *J* 7 Hz, *Me*CH); *m/e* 384 (60%, M^+) and 369 (100%, M^+ — Me).

(±)-*Atrovenetin* (19b).—A mixture of (±)-atrovenetin yellow trimethyl ether (19a) (81 mg) and pyridine hydrochloride (1·6 g) was heated under reflux for 5 min. Dilute sulphuric acid was added, and the precipitated solid was filtered off, washed with water, and dried under reduced pressure to give (±)-atrovenetin (59 mg, 82%) as a yellow powder, identical [with respect to i.r. (KCl), u.v., and mass spectra] with an authentic sample of (+)-atrovenetin.

A portion (37 mg) of the product was acetylated with acetic anhydride (0·25 ml) and pyridine (0·5 ml) at room temperature for 16 h to give, after chromatography of the product on Kieselgel G, (±)-atrovenetin triacetate (30 mg), which crystallised from methanol as yellow needles, m.p. 181—183°, and (±)-atrovenetin tetra-acetate (23 mg), which crystallised from benzene–light petroleum as yellow crystals, m.p. 181—183°. The identities of the acetates were confirmed by comparison of their i.r., u.v., and n.m.r. spectra with those of authentic samples [4] of the (+)-isomers.

2-*Acetyl*-3,6(*or* 3,7 *or* 3,8)-*dihydroxy*-7,8,9(*or* 6,8,9 *or* 6,7,9)-*trimethoxy*-4-*methylphenalen*-1-*one* (25a, b, or c).—A mixture of the naphthalene (12b) (2 g), malonic acid (5 g), and polyphosphoric acid (25 ml) was stirred at 100° for 30 min, and then maintained at 100° for a further 16 h. After cooling, the mixture was hydrolysed with water, and extracted with chloroform. The extract was washed with water, dried, and evaporated under reduced pressure. Chromatography of the residue on a column of Kieselgel G (200 g) (chloroform as eluant) afforded 2-acetyl-3,6(or 3,7 or 3,8)-dihydroxy-7,8,9(or 6,8,9 or 6,7,9)-trimethoxy-4-methylphenalen-1-one (25a, b, or c) (870 mg, 32%), which gave yellow crystals, m.p. 193—194° from chloroform–light petroleum (Found: C, 64·1; H, 5·2. Calc. for $C_{19}H_{18}O_7$: C, 63·7; H, 5·05%), $\lambda_{max.}$ 275, 347, 408, and 428 nm (log ε 4·53, 3·79, 4·13, and 4·14); $\nu_{max.}$ 1604, 1610, 1630, and 3270 cm^{-1}; τ −8·27 (1H, s, exchangeable with D_2O, 3-OH), −0·07 (1H, s, exchangeable with D_2O, remaining OH), 3·18 (1H, s, ArH), 5·81, 5·89, and 6·02 (each 3H, s, OMe), 7·07 (3H, s, COMe or ArMe), and 7·20 (3H, s, COMe or ArMe); *m/e* 358 (50%, M^+) and 343 (100%, M^+ — Me).

2-*Acetoxy*-3,6(*or* 3,7 *or* 3,8)-*dihydroxy*-7,8,9(*or* 6,8,9 *or* 6,7,9)-*trimethoxy*-4-*methylphenalenone* (26a, b, or c).—A solution of the 2-acetylphenalenone (25) (630 mg), prepared as described in the preceding experiment, and *m*-chloroperbenzoic acid (345 mg) in chloroform (20 ml) was left at room temperature for 1 h, then concentrated by distillation of some of the solvent under reduced pressure, and applied to a column of Kieselgel G (60 g). Elution with chloroform gave starting material (340 mg) and 2-acetoxy-3,6(or 3,7 or 3,8)-dihydroxy-7,8,9(or 6,8,9 or 6,7,9)-trimethoxy-4-methylphenalen-1-one (26a, b, or c) (255 mg, 84%, based on starting material consumed), which afforded yellow crystals, m.p. 180—182°, from chloroform–light petroleum (Found: C, 61·15; H, 5·05. $C_{19}H_{18}O_8$ requires C, 60·95; H, 4·85%), $\lambda_{max.}$ 219, 248infl, 256, 274, 280, 353, and 424 nm (log ε 4·30, 4·14, 4·17, 4·31, 4·30, 3·89, and 3·98); $\nu_{max.}$ (Nujol) 1608, 1617, 1668, 1763, and 3240 cm^{-1}; τ −0·20 and 0·12 (each 1H, s, exchangeable with D_2O, OH), 3·20 (1H, s, ArH), 5·74, 5·84, and 6·05 (each 3H, s, OMe), 7·05 (3H, s, ArMe), and 7·62 (3H, s, OAc); *m/e* 374 (12%, M^+) and 332 (100%, $M^+ - CH_2CO$).

Norxanthoherquein (27).—The 2-acetoxyphenalenone derivative (26) (100 mg), prepared as described in the preceding experiment, was heated under reflux for 5 min with pyridine hydrochloride (2 g). The mixture was quenched with water, and the precipitate was filtered off and dried under reduced pressure to give a yellow powder (56 mg) which was sublimed at 250° and 0·1 mmHg to yield norxanthoherquein (27) (39 mg, 50%), identical (i.r., u.v., and mass spectra) with an authentic specimen.

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