Naturally Occurring Compounds Related to Phenalenone. Part 8.[1] Structure and Synthesis of Demethylherqueichrysin [2]

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The isolation of herqueichrysin from *Penicillium herquei* and its conversion into atrovenetin (1b) are described. The structure of demethylherqueichrysin (3a) (8,9-dihydro-2,3,4,7-tetrahydroxy-6,8,8,9-tetramethylphenaleno[1,2-*b*]furan-1-one) is established by synthesis from 9-hydroxy-6,7,8-trimethoxy-4-methyl-3-(3-methylbut-2-enyloxy)-phenalen-1-one (6). The isolation of partially racemised atrovenetin (1b) and deoxyherqueinone (1a) from *P. herquei* is also described.

As reported in our preliminary communication,[2a] we have isolated, during an investigation of the metabolic products of *Penicillium herquei* grown in submerged culture, a hitherto undescribed metabolite, isomeric with deoxyherqueinone (1a). The new metabolite exhibited i.r., u.v., and n.m.r. spectra characteristic of a methoxytrihydroxyphenalenone fused to a 2,3,3-trimethyldihydrofuran ring, and gave a triacetate (with acetic anhydride–pyridine at room temperature), a dimethyl ether (upon treatment with ethereal diazomethane at 0 °C) and a trimethyl ether (when treated at room temperature with ethereal diazomethane). Further, the material obtained by demethylation with pyridine hydrochloride or hydriodic acid was not identical with atrovenetin (1b); it followed that in the new metabolite the orientation of the ether ring must differ from that in the other phenalenone-derived pigments of *P. herquei*.

After completion of our preliminary studies, Narasimhachari and Vining reported the isolation of a new metabolite of herqueinone which they named herqueichrysin.[3] The identity of their material and ours was subsequently established by direct comparison.

If herqueichrysin, like atrovenetin (1b) and norherqueinone (13a),[4] is biosynthesised by oxidation and prenylation of an intermediate acetate–polymalonate derived chain [*e.g.* (2)], followed by closure to a cyclic ether, three possible structures, (3a), (4), and (5), may be written for its demethyl derivative. Other structures which would arise by oxidation or alkylation at C-12 of the polyketide chain (2) are excluded since the aromatic

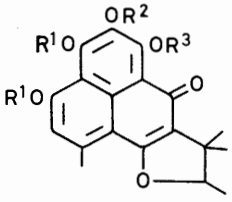
[1] Part 7, J. S. Brooks and G. A. Morrison, *J.C.S. Perkin I*, 1974, 2114.

[2] Preliminary accounts, (*a*) D. A. Frost and G. A. Morrison, *Tetrahedron Letters*, 1972, 4729; (*b*) D. D. Halton and G. A. Morrison, *ibid.*, 1975, 1443.

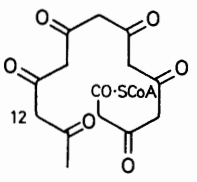
[3] N. Narasimhachari and L. C. Vining, *J. Antibiotics*, 1972, **25**, 155 (*Chem. Abs.*, 1972, **76**, 153,460).

[4] R. Thomas, *Biochem. J.*, 1961, **78**, 807; *Pure Appl. Chem.*, 1973, **34**, 515.

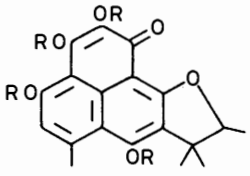
proton and the aromatic methyl group of herqueichrysin are on adjacent positions in the aromatic nucleus, as indicated by coupling between them in the n.m.r. spectrum.[3]



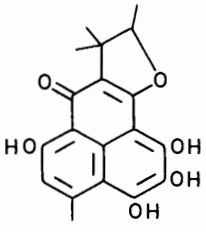
(1) a; $R^1 = R^3 = H, R^2 = Me$
b; $R^1 = R^2 = R^3 = H$
c; $R^1 = R^2 = Me, R^3 = H$
d; $R^1 = R^2 = R^3 = Me$



(2)



(3) a; R = H
b; R = Me



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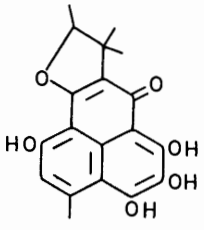
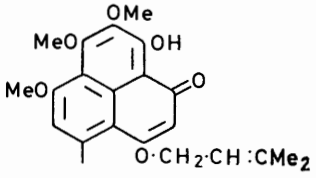


(5)



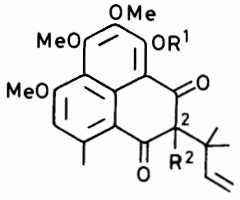
(6)

This paper describes a synthesis of compound (3a), now shown to be identical with demethylherqueichrysin; syntheses of compounds (4) and (5) will be the subject of a later paper.

Claisen rearrangement of the allyl ether (6) in dimethylformamide at 100 °C to give (±)-atrovenetin yellow trimethyl ether (1c) has previously been described.[5] In the present work the allyl ether (6) was rearranged under the same conditions, but in the presence of potassium carbonate to inhibit cyclic ether formation; the product (yield 87%) was the 1,3-diketone (7a). The assignment of structure (7a) rather than the tautomeric phenalenone structure (8a) rests on the i.r. carbonyl absorption at 1 674 cm^{-1} and an n.m.r. singlet at τ 6.53, attributable to H-2. The preferred adoption of the diketone tautomeric form is possibly a consequence of the considerable steric compression associated with the phenalenone structure (8a).

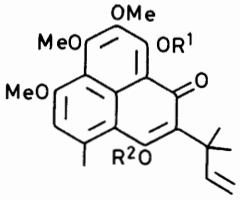
* This compound was originally wrongly assigned structure (8b)[2a] (*cf.* ref. 2*b*).

Treatment of the diketone (7a) with diazomethane gave two isomeric methyl ethers, which were separated by chromatography. The structure of the major product (7b) * (68% yield) follows from its i.r. ($\nu_{max.}$ 1 650 and 1 684 cm^{-1}) and n.m.r. (singlet at τ 6.55, H-2) spectra, and from the compounds obtained from it by prolonged treatment with silver oxide and boiling methyl iodide; these were the *C*-methylated derivative (7c), which exhibited spectra closely similar to those reported for the analogous compound (7d),[5] and the iodo-ethers (9) and (10). The structures assigned to the iodo-ethers, the production of which presumably arises from the presence in the methyl iodide of some elemental iodine, are fully supported by the analytical, mass spectral, and n.m.r. data recorded in the Experimental section.



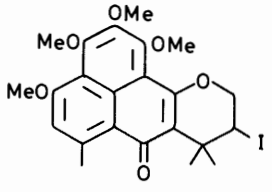
(7)

a; $R^1 = R^2 = H$
b; $R^1 = Me, R^2 = H$
c; $R^1 = R^2 = Me$
d; $R^1 = Me, R^2 = CMe_2 \cdot CH{:}CH_2$



(8)

a; $R^1 = R^2 = H$
b; $R^1 = H, R^2 = Me$



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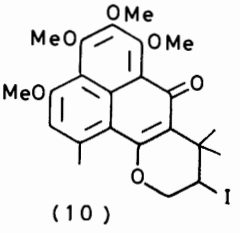

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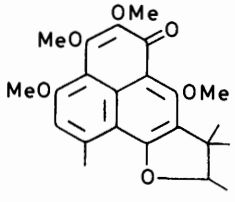


(11)

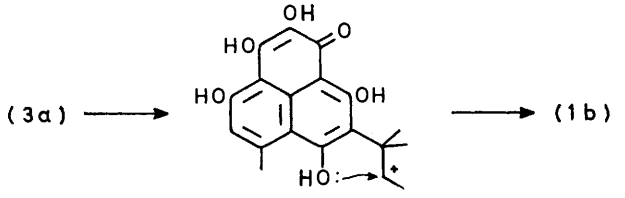
Treatment of the tetramethyl ether (7b) with toluene-*p*-sulphonic acid gave the dihydrofuran derivative (1d), a hitherto unknown tetramethyl ether of atrovenetin, which was smoothly demethylated with hydriodic acid to yield (±)-atrovenetin (1b). Since the tetramethyl ether (1d) is not identical with atrovenetin tetramethyl ether B [previously formulated [6] as either (1d) or (11)] it

[5] D. A. Frost and G. A. Morrison, *J.C.S. Perkin I*, 1973, 2388.
[6] D. H. R. Barton, P. de Mayo, G. A. Morrison, and H. Raistrick, *Tetrahedron*, 1959, **6**, 48; I. C. Paul, G. A. Sim, and G. A. Morrison, *Proc. Chem. Soc.*, 1963, 352; I. C. Paul and G. A. Sim, *J. Chem. Soc.*, 1965, 1097.

follows that the latter is correctly represented by structure (11).

With the structure of the major product arising by treatment of the diketone (7a) with diazomethane thus established as (7b), the minor product (which also contains four methoxy-groups) may be assigned structure (8b). This formulation is supported by an n.m.r. signal at very low field (τ — 8.7), characteristic of a 9-hydroxyphenalenone. Upon treatment with toluene-*p*-sulphonic acid compound (8b) was converted into the tetracyclic compound (3b), demethylation of which with hydrogen iodide then gave (±)demethylherqueichrysin (3a), which exhibited i.r., u.v., and n.m.r. spectra and t.l.c. behaviour identical with those recorded for the same material derived from a natural source.

When demethylation of the ether (3b) was carried out by prolonged treatment with pyridine hydrochloride at 220° there was obtained a mixture of (±)-demethylherqueichrysin (3a) and (±)-atrovenetin (1b), which were separated as their tetra-acetates. Similar treatment of (+)-demethylherqueichrysin, followed by acetylation, gave a mixture of (+)-demethylherqueichrysin tetra-acetate (33% yield; 83% optical purity) and (±)-atrovenetin tetra-acetate (30% yield). It thus appears that when demethylherqueichrysin is subjected to stringent acidic conditions, it is partly converted into atrovenetin by cleavage of its dihydrofuran ring and recyclisation (Scheme). The fact that the unrearranged

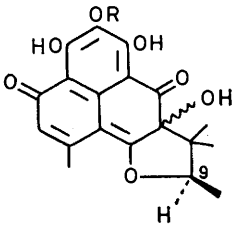


(12)

SCHEME

demethylherqueichrysin which is recovered is of high optical purity indicates that ring closure of the intermediate cation (12) occurs mainly to afford atrovenetin.

During the present investigation, in addition to herqueichrysin, atrovenetin (1b) and deoxyherqueinone (1a) were isolated from the mycelium of *P. herquei* grown in submerged culture.[7] The possibility that under these culture conditions *P. herquei* gives rise to both (+)-(*R*)- and (—)-(*S*)-atrovenetin which serve as biosynthetic precursors for herqueinone (13b) and its C-9 epimer, isoherqueinone, respectively (through the appropriate enantiomer of deoxyherqueinone[8]), has already been mooted.[9] In accord with this view the atrovenetin isolated in the present work and its tri- and tetra-acetates have specific rotations of +54.6°,* +39.4°, and +18.3°, respectively. Since the corresponding $[\alpha]_D$ values for (+)-(*R*)-atrovenetin and its acetates derived from *P. atrovenetum* are +100.6°,* +74.9°, and +34°, the atrovenetin obtained from *P. herquei* has an optical purity of only 54%. Similarly the deoxyherqueinone isolated



(13) a; R = H
b; R = Me

in the present work gave a diacetate, $[\alpha]_D$ +43.6°, which corresponds to an optical purity of 53%, assuming a value of +82° for the specific rotation of the pure enantiomer.[9] Atrovenetin is stable to the conditions employed in extracting the mycelial products; while the occurrence of racemisation during the growth of *P. herquei* is not excluded, the possibility remains that both (+)- and (—)-atrovenetin are metabolites of *P. herquei*.

It may be that demethylherqueichrysin is also a metabolite and that it undergoes isomerisation to (±)-atrovenetin (*cf.* Scheme), thereby giving rise to the *S*-enantiomer of atrovenetin.

EXPERIMENTAL

M.p.s were measured with a Kofler hot-stage apparatus. I.r. spectra were recorded with a Unicam SP 1000 G or Perkin-Elmer 125 instrument, for Nujol mulls unless stated otherwise. U.v. spectra were recorded with a Unicam SP 800 spectrophotometer, using 95% ethanol as solvent. N.m.r. spectra were recorded with a Perkin-Elmer R12B or R32 spectrophotometer or a Varian A60A instrument, using deuteriochloroform as solvent, unless specified otherwise. Mass spectra were recorded with an A.E.I. MS 902 spectrometer. Optical rotations were measured with a Perkin-Elmer 141 polarimeter using chloroform solutions in a 1 dm cell, unless otherwise stated. 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 °C. Solutions in organic solvents were dried with anhydrous sodium sulphate or magnesium sulphate.

Isolation of Herqueichrysin and Related Metabolites from Penicillium herquei.—The culture of *P. herquei* used in these studies was of strain number I.M.I. 89376. The growth conditions were the same as those already described.[7] The mycelium was separated from the culture fluid by filtration, pressed on a Buchner funnel under suction to remove as much moisture as possible, then continuously extracted with ether (Soxhlet) for 48 h. Evaporation of the extract gave a yellow-brown powder (6.0 g from 2.8 l of culture fluid).

A portion (2.8 g) of this material was treated with acetic anhydride (10 ml) and pyridine (20 ml) for 4 days. Chromatography of the crude product on kieselgel G (300 g) using ether–benzene (3 : 7) as eluant afforded three major products: deoxyherqueinone diacetate (158 mg), which crystallised from chloroform–light petroleum as yellow

* Dioxan solution: all other specific rotations refer to chloroform solutions.

[7] N. Narasimhachari, K. S. Gopalkrishnan, R. H. Haskins, and L. C. Vining, *Canad. J. Microbiol.*, 1963, **9**, 134.
[8] A. B. Kriegler and R. Thomas, *Chem. Comm.*, 1971, 738.
[9] J. S. Brooks and G. A. Morrison, *J.C.S. Perkin I*, 1972, 421.

needles, m.p. 174—176°, $[\alpha]_D$ +43.6° (*c* 0.7), atrovenetin triacetate (176 mg), which crystallised from methanol as yellow needles, m.p. 185—187°, $[\alpha]_D$ +39.4° (*c* 0.8), and herqueichrysin triacetate (570 mg), which crystallised from benzene–light petroleum as yellow rosettes, m.p. 187—188° (lit.,[3] 185°), $[\alpha]_D$ +129.1° (*c* 1.3) (Found: C, 65.0; H, 5.45. Calc. for $C_{26}H_{26}O_9$: C, 64.7; H, 5.45%), $\lambda_{max.}$ 219, 243, 264infl, 353 nm (log ε 4.49, 4.58, 4.28, and 4.23); $\nu_{max.}$ 1 622, 1 641, 1 771, and 1 788 cm^{-1}; τ 2.84 (1 H, s, ArH), 5.47 (1 H, q, *J* 7 Hz, OC*H*Me), 6.10 (3 H, s, ArOMe), 7.04 (3 H, s, ArMe), 7.60 (9 H, s, OAc), 8.50 and 8.73 (each 3 H, s, CMe_2), and 8.58 (3 H, d, *J* 7 Hz, OCH*Me*).

A second portion (1.8 g) of the material obtained by extraction of the mycelium with ether was washed with acetone, and recrystallised from acetone to yield atrovenetin (290 mg), $[\alpha]_D$ +55° (*c* 0.92, in dioxan), which gave i.r. and u.v. spectra identical with those of an authentic specimen extracted from *P. atrovenetum*. Acetylation of a sample (220 mg) of this material with acetic anhydride (0.7 ml) and pyridine (1.4 ml) for 16 h gave a mixture of atrovenetin triacetate (161 mg), m.p. 186—187° (from MeOH), $[\alpha]_D$ +39° (*c* 0.5) and atrovenetin tetra-acetate (98 mg), m.p. 183—185° (from benzene–light petroleum), $[\alpha]_D$ +18° (*c* 0.7), which were separated by preparative t.l.c. The material obtained by evaporation of the acetone washings was chromatographed on kieselgel G (150 g) using ether–benzene (1 : 9) as eluant. From the orange band of higher R_F value was obtained a mixture of herqueinone and isoherqueinone (484 mg) (75 : 25, according to the n.m.r. spectrum), identified by comparison of t.l.c. and spectral data with those of an authentic mixture. The yellow band of lower R_F value yielded herqueichrysin (520 mg). This material, which was also obtained by saponification of its triacetate (see above), crystallised from chloroform–light petroleum as fine yellow needles, m.p. 166—167° (lit.,[3] 174°), $[\alpha]_D$ +144° (*c* 0.5) (Found: *m/e*, 356.1271. Calc. for $C_{20}H_{20}O_6$: *M*, 356.1260), $\lambda_{max.}$ (CH_2Cl_2) 248, 283, and 376 nm (log ε 4.28, 3.94, and 4.17); $\nu_{max.}$ ($CHCl_3$) 1 600, 1 640, 3 430, and 3 610 cm^{-1}; τ 3.31br (1 H, s, ArH), 5.22 (1 H, q, *J* 6.8 Hz, OC*H*Me), 6.02 (3 H, s, ArOMe), 7.13br (3 H, s, ArMe), 8.45 (3 H, d, *J* 6.8 Hz, OCH*Me*), and 8.37 and 8.67 (each 3 H, s, CMe_2).

Herqueichrysin Dimethyl Ether.—Treatment of herqueichrysin (40 mg) with ethereal diazomethane at 0 °C for 3 h gave the *dimethyl ether* (42 mg), which crystallised from benzene–light petroleum as yellow prisms, m.p. 168—169°, $[\alpha]_D$ +126° (*c* 0.6) (Found: C, 68.5; H, 6.15. $C_{22}H_{24}O_6$ requires C, 68.75; H, 6.3%), $\lambda_{max.}$ 222, 268, 349, 394, and 410 nm (log ε 4.40, 4.46, 3.92, 4.11, and 4.10); $\nu_{max.}$ ($CHCl_3$) 1 600, 1 614, 1 634, and 3 320 cm^{-1}; τ − 0.16 (1 H, s, exchangeable with D_2O, OH), 3.15 (1 H, s, ArH), 5.45 (1 H, q, *J* 6.5 Hz, OC*H*Me), 5.74, 5.97, and 6.00 (each 3 H, s, ArOMe), 7.05 (3 H, s, ArMe), 8.53 (3 H, d, *J* 6.5 Hz, OCH*Me*), and 8.47 and 8.69 (each 3 H, s, CMe_2).

Herqueichrysin Trimethyl Ether.—Treatment of herqueichrysin (20 mg) with ethereal diazomethane at room temperature for 1 h gave the *trimethyl ether*, which crystallised from light petroleum as yellow rosettes, m.p. 125—126°, $[\alpha]_D$ +161° (*c* 0.3) (Found: *m/e*, 398.1730. $C_{23}H_{26}O_6$ requires *M*, 398.1729), $\lambda_{max.}$ 223, 249, 269, 353infl, 391, and 412infl nm (log ε 4.31, 4.28, 4.36, 3.95, 4.03, and 3.98); $\nu_{max.}$ ($CHCl_3$) 1 605 and 1 628 cm^{-1}; τ 3.20 (1 H, s, ArH), 5.46 (1 H, q, *J* 6.5 Hz, OC*H*Me), 5.93 and 5.97 (each 3 H, s, ArOMe), 6.00 (6 H, s, ArOMe), 7.00 (3 H, s, ArMe), 8.54 (3 H, d, *J* 6.5 Hz, OCH*Me*), and 8.48 and 8.69 (each 3 H, s, CMe_2).

Demethylherqueichrysin (3a).—A mixture of herqueichrysin (60 mg) and pyridine hydrochloride (1.5 g) was heated at 220 °C for 10 min. The mixture was poured into dilute hydrochloric acid and extracted with chloroform. Removal of solvent afforded a yellow powder which was purified by trituration with chloroform to give demethylherqueichrysin (50 mg), m.p. (vacuum-sealed capillary) 250° (initial melting and discolouration), 298—302° (final liquefaction) [lit.,[3] 250° (decomp.)], $[\alpha]_D$ +347° (*c* 0.3) (Found: *m/e* 342.1106. $C_{19}H_{18}O_6$ requires *M*, 342.1103), $\lambda_{max.}$ 220, 254, 285infl, 378, and 434 nm (log ε 4.44, 4.33, 3.97, 4.04, and 4.02); $\nu_{max.}$ ($CHCl_3$) 1 597, 1 605, 3 430, 3 600, and 3 680 cm^{-1}; τ (C_5D_5N) 2.94 (1 H, s, ArH), 5.38 (1 H, q, *J* 7 Hz, OC*H*Me), 6.91 (3 H, s, ArMe), 8.60 (3 H, d, *J* 7 Hz, OCH*Me*), and 8.36 and 8.62 (each 3 H, s, CMe_2).

Acetylation with acetic anhydride–pyridine at room temperature for 16 h gave the *tetra-acetate* as a yellow gum, $[\alpha]_D$ +109° (*c* 0.2) (Found: *m/e* 510.1530. $C_{27}H_{26}O_{10}$ requires *M*, 510.1526), $\lambda_{max.}$ 218, 243, 265infl, 350, and 400infl nm (log ε 4.38, 4.45, 4.15, 4.10, and 3.82); $\nu_{max.}$ ($CHCl_3$) 1 622 and 1 786 cm^{-1}; τ 2.83 (1 H, s, ArH), 5.52 (1 H, q, *J* 7 Hz, OC*H*Me), 7.06 (3 H, s, ArMe), 7.65 and 7.68 (each 6 H, s, OAc), 8.63 (3 H, d, *J* 7 Hz, OCH*Me*), and 8.54 and 8.76 (each 3 H, s, CMe_2).

2,(1,1-*Dimethylprop*-2-*enyl*)-9-*hydroxy*-4-*methyl*-6,7,8-*trimethoxyphenalene*-1,3(2H)-*dione* (7a).—A solution of 9-hydroxy-6,7,8-trimethoxy-4-methyl-3-(3-methylbut-2-enyloxy)phenalen-1-one (6)[5] (600 mg) in dimethylformamide (10 ml) was stirred with anhydrous potassium carbonate (600 mg) at 100 °C for 16 h. The mixture was then diluted with water, neutralised with dilute hydrochloric acid, 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 (50 g) [ether–benzene (1 : 5) as eluant] afforded 2-(1,1-*dimethylprop*-2-*enyl*)-9-*hydroxy*-4-*methyl*-6,7,8-*trimethoxyphenalene*-1,3(2H)-*dione* (7a) (525 mg, 87%) as a yellow gum (Found: *m/e*, 384.1553. $C_{22}H_{24}O_6$ requires *M*, 384.1573), $\lambda_{max.}$ 228, 261, and 350 nm (log ε 4.54, 4.50, and 4.20); $\nu_{max.}$ (film) 1 603, 1 674, and 3 355 cm^{-1}; τ − 5.81 (1 H, s, OH), 3.33 (1 H, s, ArH), 4.30 (1 H, dd, J_{trans} 17.5, J_{cis} 10 Hz, C*H*=CH_2), 5.13—5.46 (2 H, m, CH=CH_2), 5.94 (3 H, s, OMe), 5.96 (3 H, s, OMe), 6.00 (3 H, s, OMe), 6.53 (1 H, s, 2-H), 7.31 (3 H, s, ArMe), and 8.88 (6 H, s, CMe_2).

Methylation of the Phenalenedione (7a) *with Diazomethane.*—A solution of the dione (7a) (525 mg) in chloroform (15 ml) was treated with an excess of ethereal diazomethane at room temperature for 30 min. Removal of solvent under reduced pressure left a residue which was chromatographed on a column of kieselgel G (75 g), using ether–benzene (1 : 5) as eluant, to yield two major fractions. The material of higher R_F crystallised from light petroleum to yield 2-(1,1-*dimethylprop*-2-*enyl*)-9-*hydroxy*-4-*methyl*-3,6,7,8-*tetramethoxyphenalen*-1-*one* (8b) (130 mg, 24%) as yellow rods, m.p. 121—122° (Found: C, 69.85; H, 6.65%; *m/e*, 398.1721. $C_{23}H_{26}O_6$ requires C, 69.3; H, 6.6%; *M*, 398.1729), $\lambda_{max.}$ 219, 240infl, 265, and 410 nm (log ε 4.63, 4.37, 4.23, and 4.24); $\nu_{max.}$ 1 630 cm^{-1}; τ −8.71 (1 H, s, exchangeable with D_2O, OH), 3.05 (1 H, s, ArH), 3.40 (1 H, dd, J_{trans} 17.5, J_{cis} 10.5 Hz, C*H*=CH_2), 4.99 (1 H, dd, J_{trans} 17.5, J_{gem} 1.5 Hz, CH=CH_tH), 5.15 (1 H, dd, J_{cis} 10.5, J_{gem} 1.5 Hz, CH=CH_cH), 5.90, 5.94, 5.96, and 6.45 (each 3 H, s, OMe), 7.10 (3 H, s, ArMe), and 8.30 (6 H, s, CMe_2).

The material of lower R_F value crystallised from benzene–light petroleum to afford 2-(1,1-*dimethylprop*-2-*enyl*)-4-

methyl-6,7,8,9-*tetramethoxyphenalene*-1,3(2*H*)-*dione* (7b) (367 mg, 68%) (see footnote * on p. 2445) as pale yellow crystals, m.p. 119—120° (Found: C, 69.4; H, 6.6%; *m/e*, 398.1729. $C_{23}H_{26}O_6$ requires C, 69,35; H, 6.6%; *M*, 398.1729), $\lambda_{max.}$ 222, 255, and 350 nm (log ε, 4.44, 4.47, and 4.00); $\nu_{max.}$ 1 650 and 1 684 cm^{-1}; τ 3.28 (1 H, s, ArH), 4.38 (1 H, dd, J_{trans} 17.5, J_{cis} 10 Hz, C*H*=CH_2), 5.15—5.50 (2 H, m, CH=CH_2), 5.95 and 6.02 (each 6 H, s, OMe), 6.55 (1 H, s, 2-H), 7.23 (3 H, s, ArMe), and 8.92 (6 H, s, CMe_2).

Methylation of the Phenalenedione (7b) *with Methyl Iodide and Silver Oxide*.—A mixture of the dione (7b) (100 mg), methyl iodide (15 ml), and silver oxide (300 mg) was stirred and heated under reflux for 16 h, then cooled, filtered, and diluted with chloroform. The organic solution was washed successively with dilute aqueous sodium disulphite and water, dried, and evaporated *in vacuo*. The residue was separated into three compounds by preparative t.l.c. [20 × 20 cm plate, coated with 16 g of kieselgel GF_{254}; ether–benzene (1 : 5) as eluant].

The band of higher R_F value gave 2,4-*dimethyl*-2-(1,1-*dimethylprop*-2-*enyl*)-6,7,8,9-*tetramethoxyphenalene*-1,3(2*H*)-*dione* (7c) (50 mg, 48%) as white crystals, m.p. 75—76° (from benzene–light petroleum) (Found: C, 69.75; H, 6.65%; *m/e*, 412.1879. $C_{24}H_{28}O_6$ requires C, 69.9; H, 6.8%; *M*, 412.1886), $\lambda_{max.}$ 224, 256, and 356 nm (log ε 4.16, 4.56, and 3.93); $\nu_{max.}$ 1 655 and 1 690 cm^{-1}; τ 3.21 (1 H, s, ArH), 4.30 (1 H, dd, J_{trans} 17.5, J_{cis} 10.5 Hz, C*H*=CH_2), 5.26 (1 H, dd, J_{trans} 17.5, J_{gem} 1.5 Hz, CH=CH_tH), 5.33 (1 H, dd, J_{cis} 10.5, J_{gem} 1.5 Hz, CH=CH_cH), 5.90 and 6.00 (each 6 H, s, OMe), 7.19 (3 H, s, ArMe), 8.55 (3 H, s, 2-Me), and 9.03 (6 H, s, CMe_2).

The band of second highest R_F value yielded 9,10-dihydro-9-iodo-1,2,3,4-tetramethoxy-6,8,8-trimethylphenaleno[1,2-*b*]pyran-7-one (9) or 9,10-dihydro-9-iodo-3,4,5,6-tetramethoxy-1,8,8-trimethylphenaleno[1,2-*b*]pyran-7-one (10) (45 mg, 34%) as pale yellow crystals, m.p. 168—170° (from light petroleum) (Found: C, 52.4; H, 4.7; I, 24.6%; *m/e*, 524.0716. Calc. for $C_{23}H_{25}IO_6$: C, 52.7; H, 4.8; I, 24.2%; *M*, 524.0704), $\lambda_{max.}$ 220, 251infl, 268, 354, 390, and 408 nm (log ε 4.49, 4.44, 4.53, 4.02, 4.08, and 4.05; $\nu_{max.}$ 1 632 cm^{-1}; τ 3.10 (1 H, s, ArH), 5.24 (1 H, t, *J* 6.5 Hz, CHI), 5.80 and 5.85 (each 3 H, s, OMe), 5.95 (6 H, s, OMe), 6.45 (2 H, d, *J* 6.5 Hz, CH_2CHI), 6.97 (3 H, s, ArMe), and 8.34 and 8.59 (each 3 H, s, CMe_2).

From the band of lowest R_F value was obtained 9,10-dihydro-9-iodo-3,4,5,6-tetramethoxy-1,8,8-trimethylphenaleno[1,2-*b*]pyran-7-one (10) or 9,10-dihydro-9-iodo-1,2,3,4-tetramethoxy-6,8,8-trimethylphenaleno[1,2-*b*]pyran-7-one (9) (17 mg, 13%) as a yellow gum (Found: *m/e*, 524.0709. Calc. for $C_{23}H_{25}IO_6$: *M*, 524.0704), $\lambda_{max.}$ 222, 241, 255, 275, 285infl, 343, 359, 410, and 426 nm (log ε 4.50, 4.36, 4.34, 4.37, 4.30, 3.97, 3.92, 3.90, and 3.90); $\nu_{max.}$ (film) 1 630 cm^{-1}; τ 3.19 (1 H, s, ArH), 5.30 (1 H, dd, *J* 6 and 8 Hz, CHI), 5.85, 5.89, 5.96, and 6.00 (each 3 H, s, OMe), 6.50 (2 H, m, CH_2CHI), 7.06 (3 H, s, ArMe), and 8.37 and 8.59 (each 3 H, s, CMe_2).

8,9-*Dihydro*-3,4,5,6-*tetramethoxy*-1,8,8,9-*tetramethylphenaleno*[1,2-b]*furan*-7-*one* (1d).—A solution of the dione (7a) (100 mg) in chloroform (15 ml) was treated with toluene-*p*-sulphonic acid (200 mg) at room temperature for 1 h, then washed successively with aqueous sodium hydrogen carbonate and water, dried, and evaporated *in vacuo* to yield the *phenalenofuranone* (1d) (100 mg, 100%). This crystallised from light petroleum as yellow crystals, m.p. 118—119° (Found: C, 69.35; H, 6.45. $C_{23}H_{26}O_6$ requires C, 69.3; H, 6.6%), $\lambda_{max.}$ 222, 240infl, 255, 275, 283infl, 344, 372, 410, and 427 nm (log ε 4.51, 4.37, 4.34, 4.37, 4.29, 3.99, 4.01, 3.99, and 3.99); $\nu_{max.}$ 1 620 cm^{-1}; τ 3.20 (1 H, s, ArH), 5.45 (1 H, q, *J* 6.5 Hz, OC*H*Me), 5.83, 5.89, 5.94, and 5.95 (each 3 H, s, OMe), 7.11 (3 H, s, ArMe), 8.44 and 8.66 (each 3 H, s, CMe_2), and 8.54 (3 H, d, *J* 6.5 Hz, OCH*Me*).

Demethylation of the Phenalenofuranone (1d) *with Hydroiodic Acid*.—The tetramethyl ether (1d) (70 mg) was heated under reflux for 15 min with aqueous hydriodic acid (55%; 10 ml). The product was filtered off, washed with water, and dried under high vacuum to give (±)-atrovenetin (55 mg, 91%) as yellow-orange needles, identical with an authentic specimen [5] (i.r., u.v., and n.m.r. spectra, and t.l.c. behaviour).

8,9-*Dihydro*-2,3,4,7-*tetramethoxy*-6,8,8,9-*tetramethylphenaleno*[1,2-b]*furan*-1-*one* (3b).—A solution of the phenalenone (8b) (95 mg) in chloroform (10 ml) was treated with toluene-*p*-sulphuric acid (200 mg) at room temperature for 3 h. The mixture was then washed successively with aqueous sodium hydrogen carbonate and water, dried, and evaporated *in vacuo*. The residue was purified by preparative t.l.c. [20 × 20 cm plate, coated with 16 g kieselgel GF_{254}; methanol–chloroform (1 : 19) as eluant] to afford the *phenalenofuranone* (3b) (90 mg, 94%) as yellow crystals, m.p. 170—171° (from benzene–light petroleum) (Found: C, 69.7; H, 6.7%; *m/e*, 398.1717. $C_{23}H_{26}O_6$ requires C, 69.3; H, 6.6%; *M*, 398.1729), $\lambda_{max.}$ 218, 260, 274, 279infl, 393, and 414infl (log ε 4.59, 4.32, 4.37, 4.34, 4.23, and 4.10); $\nu_{max.}$ 1 622 cm^{-1}; τ 2.95 (1 H, s, ArH), 5.26 (1 H, q, *J* 6.5 Hz, OC*H*Me), 5.88, 5.91, 5.96, and 6.12 (each 3 H, s, OMe), 7.02 (3 H, s, ArMe), 8.40 and 8.62 (each 3 H, s, CMe_2), and 8.45 (3 H, d. *J* 6.5 Hz, OCH*Me*).

(±)-*Demethylherqueichrysin* (3a).—A solution of the phenalenofuranone (3b) (60 mg) in aqueous hydroiodic acid (55%; 5 ml) was heated under reflux for 15 min, then cooled, diluted with water, and extracted with chloroform. The extract was washed with water, dried, and evaporated *in vacuo* to yield (±)-demethylherqueichrysin (3a) (50 mg, 97%) as a yellow powder, identical [i.r. (KCl), u.v., n.m.r., and t.l.c.] with authentic (+)-demethylherqueichrysin.

Demethylation of the Tetramethyl Ether (3b) *with Pyridine Hydrochloride*.—A mixture of the tetramethyl ether (3b) (85 mg) and pyridine hydrochloride (1.8 g) was heated under reflux for 30 min, then cooled, acidified with dilute hydrochloric acid, and extracted with chloroform. The extract was washed with water, dried, and evaporated under reduced pressure to give a yellow powder (41 mg), which from its n.m.r. spectrum and behaviour in t.l.c. was shown to be a two-component mixture. The mixture was acetylated with acetic anhydride (4 ml) and pyridine (4 ml) at room temperature for 16 h to give two tetra-acetates, which were separated by preparative t.l.c. [20 × 20 cm plate, coated with 16 g kieselgel GF_{254}; ether–benzene (1 : 5) as eluant]. From the band of higher R_F value (±)-demethylherqueichrysin tetra-acetate (17 mg, 28%) was obtained as a yellow glass, identical (i.r., n.m.r., u.v., and t.l.c.) with authentic (+)-demethylherqueichrysin tetra-acetate.

The band of lower R_F value yielded (±)-atrovenetin tetra-acetate (36 mg, 59%), which gave yellow crystals, m.p. 178—180° (from benzene–light petroleum), identical (i.r., n.m.r., u.v., and t.l.c.) with authentic (+)-atrovenetin tetra-acetate.[9]

Prolonged Treatment of Demethylherqueichrysin (3a) *with Pyridine Hydrochloride*.—A mixture of demethylherqueichrysin (3a) (40 mg) and pyridine hydrochloride (1 g) was

heated at 220 °C for 1 h. The mixture was worked up and the product acetylated to give, after preparative t.l.c. (details as in preceding experiment), (+)-demethylherqueichrysin tetra-acetate (20 mg, 33%), $[\alpha]_D$ +91° (*c* 0.2) (identified by direct comparison of n.m.r. and u.v. spectra, and t.l.c. behaviour with an authentic sample, $[\alpha]_D$ +109°), and (±)-atrovenetin tetra-acetate (18 mg, 30%), identical (n.m.r., u.v., and t.l.c.) with an authentic specimen.[9]

We thank the S.R.C. for research studentships (to D. A. F. and D. D. H.), and Dr. L. C. Vining for a sample of authentic herqueichrysin.

[7/719 *Received*, 29*th April*, 1977]