Naturally Occurring Compounds related to Phenalenone. Part III.[1] The Structure of Herqueinone and Norherqueinone and their Relationships with Isoherqueinone and Isonorherqueinone †

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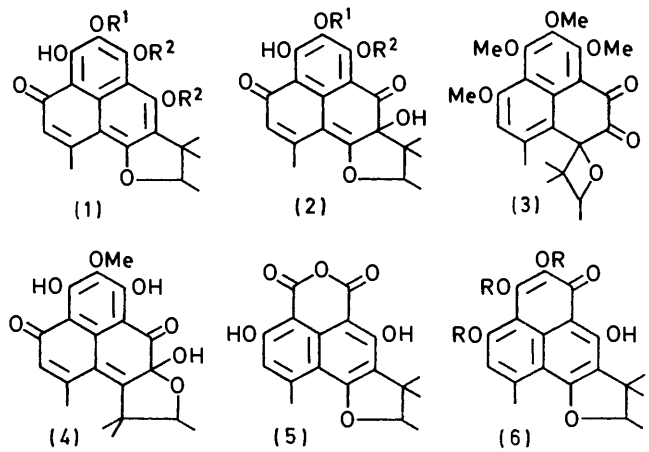
Herqueinone extracted from the mycelium of *P. herquei* has been found to be invariably contaminated with isoherqueinone, from which it has so far not been possible to separate it. By means of chemical degradation and spectral interpretation herqueinone has been shown to possess structure (2; R^1 = Me, R^2 = H) and to differ from isoherqueinone only in the configuration of the carbon atom carrying the secondary methyl group in the ether ring. Mild base treatment results in epimerisation of the tertiary asymmetric centre of herqueinone to produce *enantio*-isoherqueinone, and in those cases where the starting material contains a significant amount of isoherqueinone of natural configuration, the crystalline product obtained is (±)-isoherqueinone. Norherqueinone and isonorherqueinone have been shown to be the de-*O*-methyl analogues of herqueinone and isoherqueinone respectively.

NORHERQUEINONE, $C_{19}H_{18}O_7$, and herqueinone, $C_{19}H_{17}O_6$(OMe), are red pigments present in the mycelium of *P. herquei*.[2-5] The yellow pigment, atrovenetin, first isolated from *P. atrovenetum*,[6] and subsequently also from the mycelium of *P. herquei* grown in submerged culture,[7] has been shown to possess structure (1; R^1 = R^2 = H).[5,8] Norherqueinone is readily reduced to atrovenetin,[5] and may be converted into one of the trimethyl ethers of herqueinone under appropriate conditions.[3] On these and other bases norherqueinone was tentatively formulated as (2; R^1 = R^2 = H) and herqueinone as its monomethyl ether (2; R^1 = H, R^2 = Me) or (2; R^1 = Me, R^2 = H).[8a]

At about the same time, Cason and his co-workers showed that herqueinone trimethyl ether B could be represented by structure (3);[9] this led them to propose the hemiacetal structure (4) for herqueinone in which the position of the methoxy-group was assigned on the rather tenuous argument that since the compound exhibits no i.r. absorption above 3300 $cm.^{-1}$ all its hydroxy-groups must be chelated. Such a structure does not account for the relationships established between norherqueinone and deoxyherqueinone (obtained from herqueinone by reduction with zinc and acetic acid) on the one hand and atrovenetin on the other (see below). After the publication of structures (2) and (4) Professor Cason, in personal correspondence with Professor Barton, ascribed these relationships to the use of impure starting materials; at that time also he was convinced that herqueinone was not a monomethyl ether of norherqueinone and that the relationships between them were, once again, due to the use of impure starting materials.

The present paper describes experiments which clearly establish that herqueinone is to be represented by (2; R^1 = Me, R^2 = H), and that it is a monomethyl ether of norherqueinone; we have also elucidated the relationship between these compounds and isoherqueinone and isonorherqueinone. After our preliminary account of this work was submitted for publication, an account[10] of the mass spectra of herqueinone and norherqueinone and certain derivatives appeared which purported to establish that herqueinone did indeed



possess structure (2; R^1 = Me, R^2 = H) and that herqueinone was in fact a methyl ether of norherqueinone. No additional chemical evidence was presented for these structures, and, while accepting that herqueinone possessed the structure originally proposed by Paul, Sim, and Morrison,[8a] Cason *et al.* still denied

† For a preliminary account of this work see J. S. Brooks and G. A. Morrison, *Tetrahedron Letters*, 1970, 963.

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

[2] F. H. Stodola, K. B. Raper, and D. I. Fennell, *Nature*, 1951, **167**, 773.

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

[4] R. E. Harman, J. Cason, F. H. Stodola, and A. L. Adkins, *J. Org. Chem.*, 1955, **20**, 1260.

[5] (*a*) D. H. R. Barton, P. de Mayo, G. A. Morrison, W. H. Schaeppi, and H. Raistrick, *Chem. and Ind.*, 1956, 551; (*b*) D. H. R. Barton, P. de Mayo, G. A. Morrison, and H. Raistrick, *Tetrahedron*, 1959, **6**, 48.

[6] K. G. Neill and H. Raistrick, *Biochem. J.*, 1957, **65**, 166.

[7] N. Narasimhachari, K. S. Gopalkrishnan, R. H. Haskins, and L. C. Vining, *Canad. J. Microbiology*, 1963, **9**, 134.

[8] (*a*) I. C. Paul, G. A. Sim, and G. A. Morrison, *Proc. Chem. Soc.*, 1962, 352; (*b*) I. C. Paul and G. A. Sim, *J. Chem. Soc.*, 1965, 1097.

[9] J. Cason, J. S. Correia, R. B. Hutchison, and F. Porter, *Tetrahedron*, 1962, **18**, 839.

[10] J. Cason, C. W. Koch, and J. S. Correia, *J. Org. Chem.*, 1970, **35**, 179.

the validity of the crucial experiments relating atrovenetin with herqueinone and norherqueinone.

Relationship of Atrovenetin, Herqueinone, and Norherqueinone.—The reduction of norherqueinone to atrovenetin [5] and the chromic acid oxidation of deoxyherqueinone to afford the naphthalic anhydride (5) (also obtainable by oxidation of atrovenetin with alkaline hydrogen peroxide) [5b] have been questioned by Cason *et al.*[10] who state that they have been unable to duplicate our results. We are unable to account for their failure to reduce norherqueinone, a reaction we have carried out on a considerable number of occasions; however, their inability to obtain the naphthalic anhydride (5) from deoxyherqueinone follows simply from the fact that their published conditions [9] for the oxidation are quite different from those recorded in the original literature.[5b] By omitting sulphuric acid from the reaction mixture they attempted the oxidation at a much higher pH than that used in the earlier work. During the present investigation it has been established that the amount of sulphuric acid present in the oxidising mixture is critical (see Experimental section).

Other correlating experiments to which no reference was made by the American workers may be summarised as follows: (*a*) photolytic oxidation of both atrovenetin and deoxyherqueinone to the anhydride (5);[11] (*b*) obtainment of atrovenetin by demethylation of deoxyherqueinone and by reductive demethylation of herqueinone;[12] and (*c*) methylation of deoxyherqueinone with diazomethane to afford atrovenetin orange trimethyl ether (1; $R^1 = R^2 = Me$).[5b] During the present work this last reaction has been shown to give both the orange (1; $R^1 = R^2 = Me$) and yellow (6; R = Me) trimethyl ethers of atrovenetin in overall yields from herqueinone of 15 and 25% respectively. It follows that deoxyherqueinone is to be represented as (1; $R^1 = Me$, $R^2 = H$) and that the methoxy-group of herqueinone is located as shown in our tentative structure (2; $R^1 = Me$, $R^2 = H$).

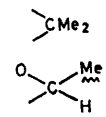
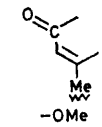
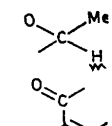
Purity of Herqueinone and Norherqueinone.—It was not possible by chromatography or by crystallisation to obtain herqueinone free from accompanying isoherqueinone. The identity of the impurity, as well as the proportion of it present (usually between 30 and 50%, depending on the particular batch of mycelium extracted) was established by comparing the n.m.r. spectrum of the herqueinone–isoherqueinone mixture with that of the homogeneous isoherqueinone into which it could be converted by mild base treatment.[3] The great similarity of the spectra of herqueinone and isoherqueinone, together with the fact that they give analogous hydrogenation products and can both be reduced to deoxy-compounds of the same gross structure (1; $R^1 = Me$, $R^2 = H$) (see below) indicate that they are stereoisomers. However, as will be shown in the sequel, it is an oversimplification to assume (as it has been [10]) that the isoherqueinone co-extracted with herqueinone from the mycelium is identical with that formed by base isomerisation of the latter compound.

The n.m.r. spectrum of our herqueinone contained no signals which could be ascribed to deoxyherqueinone, although by experiment we found that it was easily possible to detect less than 5% of the latter. The presence of added deoxyherqueinone was also clearly shown by t.l.c. (*cf.* ref. 13) and its removal by chromatography presented no difficulties. These observations are at variance with the report [10] that herqueinone is contaminated by substantial amounts of deoxyherqueinone and that the two compounds form a charge-transfer complex.

Purification of our norherqueinone by crystallisation from acetic acid gave material which, from its n.m.r. spectrum was clearly contaminated with herqueinone and with either or both of isoherqueinone and isonorherqueinone. No signals which could be assigned to atrovenetin were visible in the n.m.r. spectrum, however, and there was no evidence that atrovenetin represented a major impurity, as has been reported.[10]

TABLE 1

N.m.r. spectra of herqueinone and of isoherqueinone (for solutions in pyridine)

	Herqueinone (2; $R^1 = Me$, $R^2 = H$)	Isoherqueinone present as impurity in herqueinone	(±)-Isoherqueinone prepared by base-catalysed isomerisation of the herqueinone–isoherqueinone mixture extracted from the mycelium
	8·38 8·88	9·08 8·41	9·08 8·41
	8·30 (d, *J* 6·5 Hz)	8·64 (d, *J* 6·5 Hz)	8·64 (d, *J* 6·5 Hz)
	7·54 (d, *J* 1 Hz)	7·57 (d, *J* 1 Hz)	7·57 (d, *J* 1 Hz)
–OMe	6·04		6·04
	5·26 (q, *J* 6·5 Hz)	4·80 (q, *J* 6·5 Hz)	4·80 (q, *J* 6·5 Hz)
	3·64 (q, *J* 1 Hz)		3·64 (q, *J* 1 Hz)

[11] N. Narasimhachari, V. B. Joshi, and S. Krishnan, *Experientia*, 1969, **24**, 538.

[12] N. Narasimhachari and B. S. Ramaswami, *Current Science*, 1966, 66.

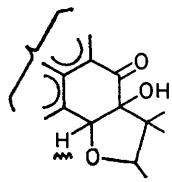
[13] S. Krishnan, N. Narasimhachari, and B. S. Ramaswami, *Hindustan Antibiotics Bull.*, 1966, **8**, 205.

We were able to show that less than 5% of atrovenetin would be quite evident from the n.m.r. spectrum.*

Methyl Ethers of Dihydroherqueinone and Dihydroisoherqueinone.—Hydrogenation of herqueinone gives a product originally named herqueinic acid.[4] No structure was assigned to this compound, but on the basis of our tentative structure for herqueinone (2; $R^1 = Me$, $R^2 = H$) it may be formulated as the naphthalene (7; $R^1 = R^2 = R^3 = R^4 = H$), and is more appropriately referred to as dihydroherqueinone. Treatment of dihydroherqueinone with diazomethane at 0° converts it into the known[4] monomethyl ether which we now formulate as (7; $R^1 = R^3 = R^4 = H$, $R^2 = Me$). It has now been found that at room temperature the product obtained is the dimethyl ether (7; $R^1 = R^2 = Me$, $R^3 = R^4 = H$), which can be further methylated with potassium carbonate and methyl sulphate to give the trimethyl ether (7; $R^1 = R^2 = R^3 = Me$, $R^4 = H$). The methyl ethers were all obtained in a chromatographically pure state and gave analytical figures and

TABLE 2

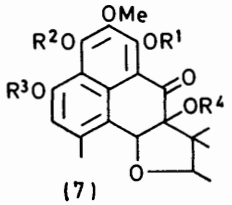
N.m.r. spectra of dihydroherqueinone and dihydroisoherqueinone methyl ethers and their derived acetates

	CMe_2	O·CH·*Me*	Aliphatic $CH_3CO·O$	Aromatic $CH_3CO·O$	Ar-CH_3	O·*CH*·Me	Ar-OMe		Ar-H	OH
Dihydroherqueinone monomethyl ether (7; $R^1 = R^3 = R^4 = H$, $R^2 = Me$)	9·19s 8·81s	8·65d *J* 6·5 Hz			7·43s	6·30q *J* 6·5 Hz	6·00s 5·70s	4·53s	3·25s	6·46s 0·65s −4·03s
Dihydroherqueinone dimethyl ether (7; $R^1 = R^2 = Me$, $R^3 = R^4 = H$)	9·07s 8·89s	8·73d *J* 6·5 Hz			7·43s	6·32q *J* 6·5 Hz	6·02s 5·90s 5·76s	4·50s	3·18s	5·81s 0·73s
Dihydroherqueinone trimethyl ether (7; $R^1 = R^2 = R^3$ Me, $R^4 = H$)	9·08s 8·90s	8·76d *J* 6·5 Hz			7·41s	6·33q *J* 6·5 Hz	6·04s (6H) 6·02s 5·91s	4·50s	3·28s	5·28s
Dihydroisoherqueinone monomethyl ether (7; $R^1 = R^3 = R^4 = H$, $R^2 = Me$)	9·43s 8·91s	8·95d *J* 6·5 Hz			7·46s	6·06q *J* 6·5 Hz	6·04s 5·73s	4·79s	3·28s	6·50s 0·70s −4·00s
Dihydroisoherqueinone dimethyl ether (7; $R^1 = R^2 = Me$, $R^3 = R^4 = H$)	9·36s 9·00s	8·99d *J* 6·5 Hz			7·46s	5·92q *J* 6·5 Hz	6·06s 5·92s 5·79s	4·75s	3·21s	5·88s 0·58s
Dihydroisoherqueinone trimethyl ether (7; $R^1 = R^2 = R^3 = Me$, $R^4 = H$)	9·34s 8·98s	8·95d *J* 6·5 Hz			7·39s	6·02q *J* 6·5 Hz	6·02s (6H) 6·01s 5·90s	4·70s	3·25s	5·82s
Dihydroherqueinone monomethyl ether diacetate (7; $R^1 = R^3 = Ac$, $R^2 = Me$, $R^4 = H$)	9·17s 8·91	8·73d *J* 6·5 Hz		7·60s 7·56s	7·37s	6·34q *J* 6·5 Hz	6·09s 5·99s	4·48s	2·94s	
Dihydroherqueinone monomethyl ether triacetate (7; $R^1 = R^3 = R^4 = Ac$, $R^2 = Me$)	9·07s 8·75s	8·73d *J* 6·5 Hz	7·83s	7·60s 7·56s	7·40s	6·32q *J* 6·5 Hz	6·08s 5·98s	4·48s	2·96s	
Dihydroherqueinone dimethyl ether monoacetate (7; $R^1 = R^2 = Me$, $R^3 = OAc$, $R^4 = H$)	9·10s 8·90s	8·77d *J* 6·5 Hz		7·62s	7·41s	6·35q *J* 6·5 Hz	6·06s 5·99s 5·92s	4·50s	3·02s	
Dihydroherqueinone dimethyl ether diacetate (7; $R^1 = R^2 = Me$, $R^3 = R^4 = Ac$)	9·00s 8·76s	8·80d *J* 6·5 Hz	7·86s	7·64	7·47s	6·34s *J* 6·5 Hz	6·08s 6·01s 5·94s	4·50	3·04s	
Dihydroherqueinone trimethyl ether monoacetate (7; $R^1 = R^2 = R^3 = Me$, $R^4 = Ac$)	8·96s 8·73s	8·75d *J* 6·5 Hz	7·85s		7·44s	6·30q *J* 6·5 Hz	6·04s (6H) 6·02s 5·91s	4·49s	3·27s	
Dihydroisoherqueinone monomethyl ether diacetate (7; $R^1 = R^3 = Ac$, $R^2 = Me$, $R^4 = H$)	9·41s 9·03s	8·98d *J* 6·5 Hz		7·64s 7·58s	7·39s	6·01q *J* 6·5 Hz	6·11s 6·02s	4·71s	2·99s	
Dihydroisoherqueinone dimethyl ether monoacetate (7; $R^1 = R^2 = Me$, $R^3 = Ac$, $R^4 = H$)	9·35s 8·97s	8·97d *J* 6·5 Hz		7·62s	7·39s	6·00q *J* 6·5 Hz	6·04s 5·98s 5·90s	4·69s	3·00s	5·83s

* Despite the fact that herqueinone and norherqueinone contain at most only very small amounts of deoxyherqueinone and atrovenetin respectively, both these compounds exhibit peaks at $M - 16$ in their mass spectra, as reported also by Cason *et al.*[10] In this connection it must be stressed that it is not possible to deduce the composition of a mixture from the relative abundances of molecular ions derived from the various components. For a detailed discussion of the mass spectra of atrovenetin and certain related compounds, see ref. 14.

[14] E. S. Waight, in ' Some Newer Physical Methods in Structural Chemistry, eds. R. Bonnett and J. G. Davis, United Trades Press, London, 1967, p. 67; D. R. Buckle and E. S. Waight, *Org. Mass Spectrometry*, 1969, 367.

spectra (see Experimental section and Table 2) fully in accord with the structures assigned to them. (Evidence for the placement of the methoxy-groups is presented later.) However, in each case the material obtained exhibited signals in its n.m.r. spectrum corresponding to an impurity.



(7)

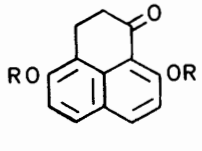
That the impurity arose from isoherqueinone present in the original herqueinone was indicated when isoherqueinone, obtained by base-catalysed isomerisation of the herqueinone–isoherqueinone mixture was hydrogenated and converted into the corresponding mono-, di-, and tri-methyl ethers. The dihydroisoherqueinone methyl ethers prepared in this way were homogeneous compounds giving n.m.r. spectra (Table 2) which corresponded exactly with the signals assigned to the impurities in the dihydroherqueinone methyl ethers.

The dihydroisoherqueinone methyl ethers prepared as described were racemic. In contrast, a small quantity of dihydroisoherqueinone monomethyl ether, obtained in a pure state by careful chromatography of the product arising by successive hydrogenation and methylation, on a relatively large scale, of the herqueinone–isoherqueinone mixture produced by *P. herquei*, proved to be dextrorotatory and to give a laevorotatory diacetate. The optically active monomethyl ether gave spectra identical with those recorded for its racemic isomer. The significance of these observations will become clear in the sequel.

Evidence for the presence of an aliphatic tertiary hydroxy-group in the dihydro-derivatives of herqueinone and of isoherqueinone was obtained by acetylating their methyl ethers. Under mild conditions, the mono- and di-methyl ethers of dihydroherqueinone gave, respectively, a diacetate (7; R^2 = Me, R^1 = R^3 = Ac, R^4 = H) and a monoacetate (7; R^1 = R^2 = Me, R^3 = Ac, R^4 = H) which exhibited carbonyl bands in their i.r. spectra at 1767 and 1760 cm.$^{-1}$ respectively, indicating that only phenolic hydroxy-groups had been acetylated; the trimethyl ether (7; R^1 = R^2 = R^3 = Me, R^4 = H) was not acetylated under these mild conditions. However, when forcing conditions were employed in the acetylation, the mono-, di-, and trimethyl ethers gave respectively a triacetate (7; R^2 = Me, R^1 = R^3 = R^4 = Ac), a diacetate (7; R^1 = R^2 = Me, R^3 = R^4 = Ac), and a monoacetate (7; R^1 = R^2 = R^3 = Me, R^4 = Ac) the first two of which gave i.r. bands at 1768 and 1760 cm.$^{-1}$ respectively (phenolic acetate) and also at 1735 cm.$^{-1}$ (aliphatic acetate), while the last-named exhibited only a band at 1730 cm.$^{-1}$ The forcing conditions required for its acetylation are, in themselves, good evidence for the tertiary nature of the aliphatic hydroxy-group. Further confirmation came by comparing the n.m.r. spectra of the acetates (Table 2) with those of the parent alcohols. In no case was there observed a downfield shift of any proton as would be expected if the hydroxy-group were primary or secondary.

Of the acetates mentioned above only dihydroherqueinone monomethyl ether triacetate was obtained absolutely pure. Even after careful chromatography the others still exhibited signals in their n.m.r. spectra arising from small amounts of the corresponding compounds in the iso-series. In the case of the monomethyl ether diacetate and the dimethyl ether monoacetate the assignment of these impurity peaks was confirmed by direct comparison with the n.m.r. spectra of the isomers derived from isoherqueinone obtained by base-catalysed isomerisation of the herqueinone–isoherqueinone mixture extracted from the mycelium of the mould.

The placement of the methoxy-groups in dihydroherqueinone dimethyl ether (7; R^1 = R^2 = Me, R^3 = R^4 = H) followed from the acid-catalysed dehydration of its hydride reduction product (9; R = H), $[\alpha]_D$ +64°, (see below) to afford the phenalenone (10), in which the position of the carbonyl group was revealed by the coupling evident in its n.m.r. spectrum between the 3-methyl group and the 2-hydrogen atom. The methylation pattern in the monomethyl ether follows from a comparison of its n.m.r. spectrum [Table 2; only the monomethyl ether (7; R^1 = R^3 = R^4 = H, R^2 = Me) exhibits a signal due to a strongly hydrogen-bonded phenolic hydroxy-group] and its i.r. carbonyl stretching frequency with those of the dimethyl ether. The monomethyl ether absorbs at 1620 cm.$^{-1}$ (H-bonded aryl C=O), and the dimethyl ether (7; R^1 = R^2 = Me, R^3 = R^4 = H) at 1670 cm.$^{-1}$ (normal aryl C=O). In agreement with our interpretation of the i.r. data, 2,3-dihydro-4,9-dimethoxyphenalen-1-one (8; R = Me) [1] absorbs at 1670 cm.$^{-1}$, while the corresponding dihydric phenol (8; R = H), obtained by demethylation with pyridine hydrochloride, absorbs at 1620 cm.$^{-1}$. The derived diacetate (8; R = Ac) exhibits a ketonic carbonyl band at 1685 cm.$^{-1}$.



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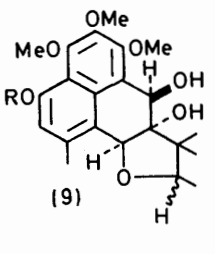


(9)

Lithium Aluminium Hydride Reduction of Methyl Ethers of Dihydroherqueinone and Dihydroisoherqueinone.—Lithium aluminium hydride reduction of the dimethyl ethers of dihydroherqueinone and dihydroisoherqueinone (the two being present in a mixture) gave respectively glycol A and glycol B. These stereo-

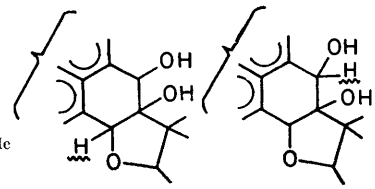
isomeric compounds were separated chromatographically and are to be represented by the gross structure (9; R = H). Similarly, the trimethyl ethers of dihydroherqueinone and dihydroisoherqueinone gave respectively glycols C and D, of gross structure (9; R = Me).*

Glycols B and D are dextrorotatory, from which it follows that the isoherqueinone co-extracted with herqueinone from the mycelium is itself optically active; this is supported by the isolation of a small amount of (+)-dihydroisoherqueinone monomethyl ether (see above). In contrast the crystalline isoherqueinone obtained by base treatment of the herqueinone–isoherqueinone mixture isolated from the gave spectra identical with those recorded for the (±)-isomer already described. By similar oxidation of glycol C a specimen of dihydroherqueinone trimethyl ether free from the corresponding iso-compound was obtained.

Acid Treatment of Glycols A, B, and C.—Brief treatment of glycol A (9; R = H) on the steam-bath with toluene-*p*-sulphonic acid and benzene or with concentrated hydrochloric acid and dioxan at room temperature gave a mixture of two compounds, separable by chromatography, which from their spectroscopic properties (see Table 4 and Experimental section) were clearly phenalenones, and were designated as phenalenones

TABLE 3

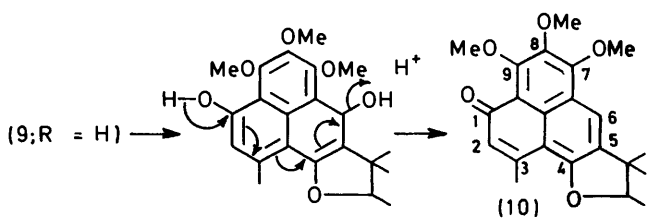
N.m.r. spectra of glycols A, B, C, and D



	CMe_2	O·CH·*Me*	$Ar\text{-}CH_3$	Ar-OMe	O·C*H*·Me		Ar-H	Benzylic OH group	Other OH groups
Glycol A (9; R = H)	8·84s 8·60s	8·73d *J* 6·5 Hz	7·50s	6·03s 5·98s 5·86s	5·69q *J* 6·5 Hz	5·06d *J* 2 Hz	4·77dd J_1 2 Hz J_2 10·5 Hz	3·25s	7·33d *J* 10·5 Hz	8·70s 0·44s
Glycol B (9; R = H)	8·80s 8·60s	8·74d *J* 6·5 Hz	7·51s	6·02s 5·98s 5·86s	Obscured by OMe signals	5·24d *J* 2 Hz	4·89dd J_1 2 Hz J_2 11 Hz	3·21s	6·44d *J* 11 Hz	0·44s (Aliphatic OH signal obscured by signals due to aliphatic methyl groups)
Glycol C (9; R = Me)	8·81s 8·57s	8·69d *J* 6·5 Hz	7·43s	6·04s 5·98s 5·97s 5·95s	5·64q *J* 6·5 Hz	5·02d *J* 2 Hz	4·70dd J_1 2 Hz J_2 10 Hz	3·29s	7·40d *J* 10 Hz	Obscured by signals due to aliphatic methyl groups
Glycol D (9; R = Me)	8·80s 8·61s	8·64d *J* 6 5 Hz	7·48s	6·08s 6·01s 6·00s 5·98s	5·90q *J* 6·5 Hz	5·20d *J* 2 Hz	4·80dd J_1 2 Hz J_2 11 Hz	3·28s	6·50d *J* 11 Hz	Obscured by signals due to aliphatic methyl groups

mould, although itself too highly coloured for accurate polarimetric measurements, is racemic, since its dihydroderivative gives rise to a series of methyl ethers (see above), all of which are racemic. Also, upon reduction with zinc and acetic acid, followed by acetylation, samples of crystalline isoherqueinone derived by isomerisation of material from different batches of mycelium afforded samples of deoxyherqueinone diacetate with residual rotations of only +2·7° and −3·2°. The highest specific rotation we have recorded for deoxyherqueinone diacetate is +78° (see below).

These conclusions were further confirmed by converting (±)-isoherqueinone into (±)-glycol B, which gave spectra identical with those recorded for the (+)-glycol B already described. Oxidation of (+)-glycol D with silver carbonate absorbed on Celite [16] gave (−)-dihydroisoherqueinone trimethyl ether, which A and B. The latter contained all three of the methoxy-groups present in glycol A, and, since its n.m.r. spectrum revealed coupling between the aromatic methyl group and the adjacent aromatic proton, it could be assigned



structure (10), which is fully in accord with all the analytical and spectral data.

Phenalenone A ($[\alpha]_D$ +131°), which contained only two methoxy-groups, was shown to be converted by methylation with methyl iodide and silver oxide in chloroform into a mixture of phenalenone B, and an isomeric compound designated phenalenone C. Phenalenone A could therefore be assigned either structure

* Two features of the n.m.r. spectra of glycols A, B, C, and D (Table 3) are of special interest. First, the coupling involving the benzylic hydroxy-group suggests that it is very hindered and does not participate in rapid proton exchange; this is in accord with our finding that the glycols are quite resistant to acetylation under ordinary conditions. Secondly, the two benzylic protons are coupled. Long-range coupling of this type, if it implies a W conformation for the centres involved,[15] would indicate that the glycols are epimers with the relative configuration expressed in structure (9).

[15] L. M. Jackman and S. Sternhell, ' Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry,' Pergamon, London, 1969, p. 334.

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

(11; $R^1 = H$, $R^2 = R^3 = Me$) or structure (11; $R^1 = R^2 = Me$, $R^3 = H$), while phenalenone C was to be represented either by structure (12) or by structure (13). Structure (13) could be excluded for phenalenone C since, in its n.m.r. spectrum (Table 4) this compound exhibited no absorption at the very low field which would be expected for the C-9 proton of a phenalenone.[1,17]

TABLE 4

N.m.r. spectra of phenalenones A—E

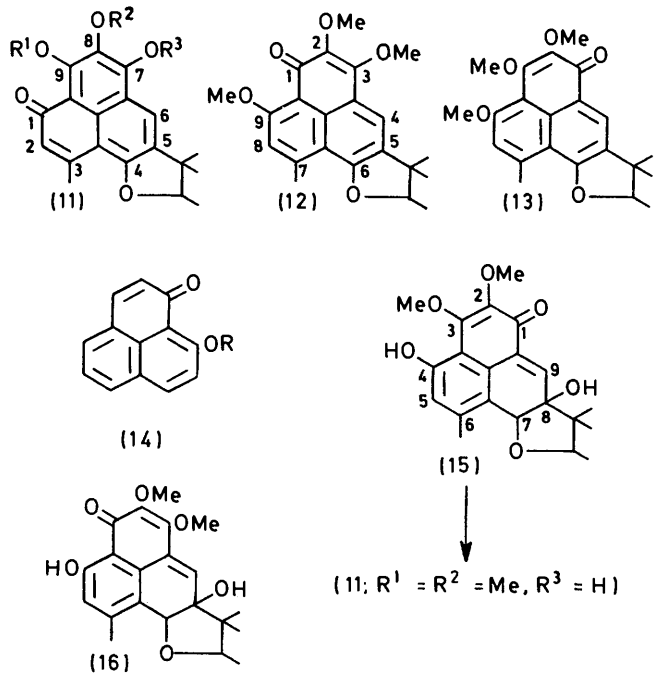
	CMe_2	O·CH·*Me*	Ar-CH_3	Ar-OMe	O·C*H*·Me	Ar-H	Aliphatic $CH_3CO·O·$	Aromatic $CH_3CO·O·$
Phenalenone A (11; $R^1 = H$, $R^2 = R^3 = Me$)	8·69s 8·48s	8·52d *J* 7 Hz	7·32d *J* 1 Hz	5·97s 5·68s	5·68q *J* 7 Hz	C_2 2·97q (*J* 1 Hz) C_6 2·36s		
Phenalenone B (10)	8·69s 8·46s	8·53d *J* 7 Hz	7·53d *J* 1·2 Hz	6·00s 5·91s 5·74s	5·61q *J* 7 Hz	C_2 3·45q (*J* 1·2 Hz) C_6 2·47s		
Phenalenone C (12)	8·70s 8·51s	8·56d *J* 7 Hz	7·30s *	6·02s 5·90s 5·80s	5·74q *J* 7 Hz	C_4 2·57s C_8 2·81s *		
Phenalenone D (11; $R^1 = R^2 = Me$, $R^3 = H$)	8·75s 8·54s	8·50d *J* 6·5 Hz	7·16d *J* 1 Hz	5·97s 5·68s	5·31q *J* 6·5 Hz	C_2 3·09q (*J* 1 Hz) C_6 1·88s		
Phenalenone E (17)	8·52s 8·49s	8·84d *J* 6·5 Hz	7·27s *	6·04s 5·68s	5·98q *J* 6·5 Hz	C_5 3·13s * C_7 1·82d (*J* 1·5 Hz) C_9 1·63d (*J* 1·5 Hz)		
Phenalenone E (17) diacetate	8·49s (6H)	8·93d *J* 6·5 Hz	7·19s *	6·07s 5·74s	4·73q *J* 6·5 Hz	C_5 2·84s * C_7 1·88d (*J* 1·5 Hz) C_9 1·63d (*J* 1·5 Hz)	8·08s	7·48s

* Slightly broadened signal

With the structure of phenalenone C established as (12) it followed that phenalenone A was to be represented by the 9-hydroxyphenalenone structure (11; $R^1 = H$, $R^2 = R^3 = Me$).* In agreement with this conclusion it was found that treatment of phenalenone B (10) with *p*-toluenesulphonic acid in benzene for five minutes on the steam-bath resulted in its demethylation to phenalenone A (11; $R^1 = H$, $R^2 = R^3 = Me$).

When glycol C (9; R = Me) was treated briefly with concentrated hydrochloric acid and dioxan at room temperature the major product was phenalenone C (12) (40% yield). Phenalenones A (11; $R^1 = H$, $R^2 = R^3 = Me$) and B (10) were also obtained in smaller amount.

Phenalenone A (11; $R^1 = H$, $R^2 = R^3 = Me$) could also be obtained from glycol A (9; R = H) by treatment with 6N-hydrochloric acid in dioxan at room temperature. Under these conditions, however, the major product was a compound, designated quinone methide I, to which structure (15) has been assigned on analytical and spectral evidence (see Experimental section). The alternative structure (16), which would also fit the analytical and spectroscopic data, is excluded by the fact that acid-catalysed dehydration of the quinone



methide does not afford phenalenone A (11; $R^1 = H$, $R^2 = R^3 = Me$) [as would be expected of a compound

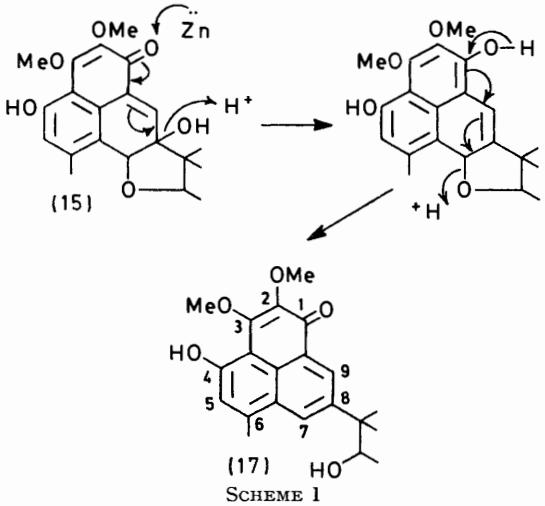
* In view of the reported [18] difficulty in acylating or alkylating 9-hydroxyphenalenone (14; R = H) the ease of methylation and acetylation of phenalenone A was unexpected. However, we have now found that both 9-methoxyphenalenone (14; R = Me) and 9-acetoxyphenalenone (14; R = Ac) can be prepared under mild conditions; it therefore appears that the strongly chelated hydroxy-group of 9-hydroxyphenalenone is more reactive than has previously been supposed. In accord with this is the observation that treatment of atrovenetin (1; $R^1 = R^2 = H$) under mild acetylating conditions gives, in addition to the known triacetate (1; $R^1 = R^2 = Ac$ or **6**; R = Ac) [5] an approximately equal amount of the hitherto undescribed tetra-acetate.

[17] B. Laundon, G. A. Morrison, and J. S. Brooks, *J. Chem. Soc.* (*C*), 1971, 36.

[18] J. D. Loudon and R. K. Razdan, *J. Chem. Soc.*, 1954, 4299.

possessing structure (16)], but affords an isomer of phenalenone A, designated phenalenone D, which must, therefore, be represented by the structure (11; $R^1 = R^2 = Me$, $R^3 = H$).

Confirmation of structure (15) for quinone methide I is provided by its reduction with zinc and acetic acid to give phenalenone E ($[\alpha]_D$ −31°) to which structure (17) is assigned. Such a structure might reasonably arise by the mechanism indicated in Scheme 1. The analytical and spectroscopic data for phenalenone E are fully in accord with the structure assigned. In particular, the n.m.r. spectrum (Table 4) clearly indicates a pair of

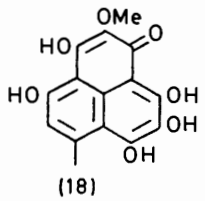


SCHEME 1

meta-coupled aromatic protons, thus proving unequivocally that the ether ring of herqueinone is attached as in structure (2), and excluding from further consideration structures such as (4) in which the ether ring is attached in a different orientation. Phenalenone E (17) gives a diacetate under mild conditions.

When glycol B (9; R = H), which is derived ultimately from the isoherqueinone co-extracted with herqueinone from the mycelium of *P. herquei*, was treated with hydrochloric acid in dioxan under the conditions used to obtain quinone methide I (15) from glycol A, two products were obtained. The minor product was found to be (−)-phenalenone A ($[\alpha]_D$ −121°) (11; $R^1 = H$, $R^2 = R^3 = Me$), enantiomeric with the corresponding material obtained from glycol A, and the major product was a material isomeric with quinone methide I (15), and giving very similar spectra. This latter compound is regarded as an epimer of quinone methide I (15), and is designated quinone methide II. In agreement with this assignment, quinone methide II gave, upon reduction with zinc and acetic acid, (+)-phenalenone E ($[\alpha]_D$ +28°) (17), enantiomeric with the corresponding material obtained starting from glycol A in the herqueinone series.

Relationship between Herqueinone and Isoherqueinone.—All the foregoing experimental work provides confirmation that structure (2; $R^1 = Me$, $R^2 = H$) correctly represents herqueinone. The acid-catalysed hydrolysis of herqueinone into xanthoherquein (18) and methyl isopropyl ketone, and its reduction to deoxyherqueinone (1; $R^1 = Me$, $R^2 = H$) with zinc and acetic acid [3,5]



(18)

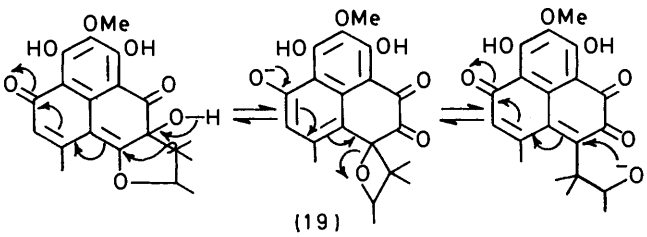
are also readily accommodated by this structure. Structure (2; $R^1 = Me$, $R^2 = H$) is fully consistent with the spectra recorded for herqueinone; the presence of three hydroxy-groups in herqueinone was demonstrated when it was shown by mass spectrometric measurement that three protons were exchanged for deuterium simply by heating under reflux a solution of herqueinone in deuterioethanol.

The obtainment of different enantiomers of phenalenones A (11; $R^1 = H$, $R^2 = R^3 = Me$) and E (17) from glycol A (9; R = H) (derived from herqueinone) on the one hand and glycol B (9; R = H) (derived from isoherqueinone) on the other indicates that herqueinone and isoherqueinone differ in the configuration of the asymmetric centre in the ether ring. Also, since the gross structure (2; $R^1 = Me$, $R^2 = H$) assigned to these compounds possesses only two asymmetric centres, and since herqueinone and isoherqueinone are not enantiomeric, both these compounds must have the same configuration at the tertiary carbinolic centre.

The obtainment of pure crystalline (±)-isoherqueinone by base treatment of a mixture of herqueinone and isoherqueinone (containing about 30% of the latter) is most readily explained by postulating that the herquinone is epimerised at the tertiary carbinolic centre to give *enantio*-isoherqueinone which then combines with the isoherqueinone initially present in the mixture. Confirmation of this view was provided by examination of the mother liquor, which, if the foregoing is correct, ought to be rich in *enantio*-isoherqueinone. First, the material obtained by evaporation of the mother liquor gave by successive reduction and acetylation deoxyherqueinone diacetate of $[\alpha]_D$ +54°, to be compared with the residual specific rotation of +2·7° recorded for the product obtained when essentially racemic crystalline isoherqueinone was similarly treated. Secondly, hydrogenation and methylation of the material obtained from the mother liquor gave (+)-dihydroisoherqueinone dimethyl ether (7; $R^1 = R^2 = Me$, $R^3 = R^4 = H$) ($[\alpha]_D$ +38°) which gave spectra identical with those recorded for the racemic material obtained by similar treatment of crystalline isoherqueinone. Furthermore, lithium aluminium hydride reduction of the optically active material gave (−)-glycol B (9; R = H) ($[\alpha]_D$ −32°) enantiomeric with the corresponding product ($[\alpha]_D$ +43°) derived ultimately from isoherqueinone co-extracted with herqueinone from the mycelium of *P. herquei*.

Results obtained from a batch of mycelial extract which, from its n.m.r. spectrum, contained a preponderance (55%) of isoherqueinone over herqueinone provided further confirmation. The crystalline product obtained by mild base treatment of the mixture was, as before, almost racemic isoherqueinone since it could be converted into deoxyherqueinone diacetate of $[\alpha]_D$ −3·2°. In this case, as expected, the mother liquor was rich in isoherqueinone of natural configuration, from which (−)-deoxyherqueinone diacetate ($[\alpha]_D$ −31°) was prepared.

All the experiments described above were carried out on herqueinone isolated from *P. herquei* (strain I.M.I. 89376), which contained isoherqueinone as an impurity present in variable amount (but not less than 30% by n.m.r. assay). Through the generosity of Professor D. H. R. Barton a small portion of herqueinone which had been extracted from *P. herquei* (strain S.M. 138) by Professor Raistrick and his collaborators during their original work on the mould [3] was made available to us. The n.m.r. spectrum of this material revealed that it contained only about 10% of isoherqueinone. Deoxyherqueinone diacetate derived from it had a specific rotation of +66°, implying that the optically pure material would have $[\alpha]_D$ +82°. Of particular interest was the result of base-catalysed epimerisation of this herqueinone-rich mixture. The first crop of crystalline material was almost pure *enantio*-isoherqueinone; this was shown by converting it into deoxyherqueinone diacetate of $[\alpha]_D$ +78°, which is very close to the theoretical value calculated above. Presumably, *enantio*-isoherqueinone crystallised out in this instance as a result of the high concentration in which it was present in solution after epimerisation of the herqueinone. The presence of some (±)-isoherqueinone in the mother liquor was confirmed by converting the material obtained by evaporating the solvent into partially racemic deoxyherqueinone diacetate of $[\alpha]_D$ +61°.

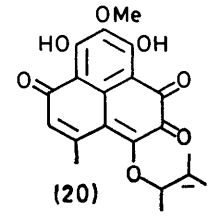


(19)

SCHEME 2

The mechanism of epimerisation of herqueinone into *enantio*-isoherqueinone may be written as illustrated in Scheme 2. Support for this may be adduced from the conversion of herqueinone, under basic conditions, into trimethylherqueinone B (3) the structure of which is analogous to the postulated intermediate (19). An alternative proposal,[10] involving the intermediacy of the tertiary carbanion (20) appears less plausible to us.

Since herqueinone is invariably contaminated with varying amounts of isoherqueinone it follows that when the mixture is converted into derivatives of atrovenetin (1; $R^1 = R^2 = H$), in which the only remaining asymmetric centre is the one in the ether ring, the observed specific rotations of the products will vary, depending on the proportion of isoherqueinone present. Thus, successive reduction and methylation of a herqueinone–isoherqueinone mixture (containing 35% of the latter by n.m.r. assay) affords the orange (1; $R^1 = R^2 = Me$) and yellow (6; R = Me) trimethyl ethers of atrovenetin with $[\alpha]_D$ values of +35° and +27°



(20)

respectively. The same compounds derived from atrovenetin obtained from the mycelium of *P. atrovenetum* (strain S.M. 683) [6] gave specific rotations of +109° and +76° respectively.* It follows from the identical sign of rotation observed for the methyl ethers derived from atrovenetin and from a mixture of herqueinone and isoherqueinone in which the former predominates that the asymmetric centre in the ether ring has the same configuration in both herqueinone and atrovenetin.

The Structure of Norherqueinone.—During the present investigation it has been unequivocally established that herqueinone is simply a monomethyl ether of norherquinone. The additional evidence obtained may be summarised as follows.

The n.m.r. spectrum of norherqueinone is strikingly similar to that of herqueinone and is fully in agreement with structure (2; $R^1 = R^2 = H$). Impurity peaks revealed that the material isolated by us contained *ca.* 15% of herqueinone and *ca.* 10—12% of isonorherqueinone including, possibly, some isoherqueinone. It was converted (as described previously) [5] into atrovenetin triacetate (1; $R^1 = R^2 = Ac$) or (6; R = Ac) (28% yield); the yield of atrovenetin from norherqueinone was probably between 50% and 60% as we have shown that acetylation of atrovenetin under the conditions employed results in the formation of equivalent amounts of tri- and tetra-acetates (see Experimental section).

Further evidence for the relationship between herqueinone and norherqueinone arose from the observation that hydrogenation of norherqueinone followed by

* These specific rotations indicate that the atrovenetin extracted from *P. atrovenetum* has a high degree of configurational homogeneity, since a calculation based on that assumption implies that the herqueinone–isoherqueinone mixture contained 32—34% of isoherqueinone, a figure in reasonable agreement with that estimated from the n.m.r. spectrum of the mixture. The recent report [19] that atrovenetin is a biosynthetic precursor of norherqueinone and herqueinone, however, raises the interesting possibility that some *enantio*-atrovenetin may be formed in *P. herquei* to serve as a precursor for isoherqueinone and isonorherqueinone.

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

methylation of the product with diazomethane under appropriate conditions gave, in an overall yield of 42%, dihydronorherqueinone trimethyl ether (containing *ca.* 5% of the iso-compound by n.m.r. assay) shown to be identical with dihydroherqueinone dimethyl ether (7; $R^1 = R^2 = Me$, $R^3 = R^4 = H$) by direct comparison of spectra, and by its conversion, in 70% yield, into glycol C (9; R = Me) by successive methylation with potassium carbonate and methyl sulphate and reduction with lithium aluminium hydride.

Finally, base-catalysed isomerisation of norherqueinone gave *enantio*-isonorherqueinone which, by successive hydrogenation and methylation, was converted into *enantio*-dihydroisonorherqueinone trimethyl ether ($[\alpha]_D$ +49°). This compound was shown to be the enantiomer of dihydroisoherqueinone dimethyl ether (7; $R^1 = R^2 =$ Me, $R^3 = R^4 = H$) by its reduction with lithium aluminium hydride to (−)-*enantio*-glycol B (9; R = H) ($[\alpha]_D$ −44°), which was compared directly with the sample of lower optical purity ($[\alpha]_D$ −32°) obtained from *enantio*-isoherqueinone (see above) and with the (+)-enantiomer ($[\alpha]_D$ +43°) and (±)-isomer already described.

TABLE 5

Yield of herqueinone and norherqueinone isolated from *P. herquei*

Batch no.	No. of flasks	Volume of culture fluid (l.)	Wt. of dry mycelium (g.)	Wt. of herqueinone (g.)	Wt. of norherqueinone (g.)
1	25	10	106	5·36	2·83
2	50	20	150	3·98	1·05
3	50	20	185	9·03	2·20
4	50	20	220	13·31	—

EXPERIMENTAL

M.p.s were measured on a Kofler block, unless otherwise stated, and are uncorrected. I.r. spectra were recorded on a Unicam SP 1000G spectrophotometer or on a Perkin-Elmer P.E. 125 instrument and refer to KCl discs unless stated otherwise. U.v. spectra were recorded on a Unicam SP800 spectrophotometer, using 95% ethanol as solvent. N.m.r. spectra were measured on a Varian A60A instrument using 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 $G_{F_{254}}$.

Isolation of Herqueinone and Norherqueinone.—The culture of *Penicillium herquei* used in these studies was of strain number I.M.I. 89376. The growth conditions and isolation procedure were the same as those already described,[3] except that the initial growth of cultures was carried out on potato–dextrose agar. Yields of herqueinone and norherqueinone obtained from different batches varied considerably, as indicated in Table 5.

The herqueinone thus obtained was purified by chromatography. A typical procedure was as follows. Herqueinone (batch 4, 1·96 g.) was dissolved in 10% ethyl acetate–90% chloroform (100 ml.) and applied to a column of Kieselgel H (150 g.) and Hyflosupercel (15 g.). Elution with 10% ethyl acetate–90% chloroform separated the material into three main coloured bands: a yellow band of high R_F, a deep red band, and a dark green band of very low R_F. The deep red band was collected and evaporated to give herqueinone (1·8 g.), m.p. 218—222° (capillary), $[\alpha]_D$ +300° (*c* 0·14 in $CHCl_3$). The n.m.r. spectrum of this material in pyridine (Table 1) showed clearly that it contained a high proportion (40%) of isoherqueinone, which could not be removed by chromatography (the material gave only one spot in t.l.c. using a wide range of solvents) or by crystallisation (after two recrystallisations from chloroform the n.m.r. spectrum of the material was virtually unchanged).

TABLE 6

Isomerisation of herqueinone to isoherqueinone

Percentage of isoherqueinone in the herqueinone used as starting material	Deoxyherqueinone diacetate obtained from crystalline isoherqueinone		Deoxyherqueinone diacetate obtained from isoherqueinone present in mother liquors	
	M.p.	$[\alpha]_D$	M.p.	$[\alpha]_D$
10 *	172—174°	+78°	170—172°	+61
35	177—178	+2·4	174—175	+54
55	176—177	−3·2	173—175	−31

* Sample of herqueinone extracted by Raistrick *et al.* from *P herquei* (strain S.M. 138).[3]

In the n.m.r. spectra of all samples of herqueinone obtained as described above, isoherqueinone was the only discernible impurity. The actual percentage of isoherqueinone present in different samples of herqueinone isolated in the present work varied from 34 to 55% as adjudged by n.m.r. spectroscopy. Although the mass spectrum of the purified sample exhibited a peak at $M - 16$, deoxyherqueinone, if present at all, was present only in very small amount. In the n.m.r. spectrum of herqueinone containing 5% of added deoxyherqueinone (in pyridine solution) signals due to the latter at τ 6·01 (s, Ar-OMe), 7·13 (s, Ar-Me), and 8·61 (d, *J* 6·5 Hz, *Me*CH·O) were easily distinguished. The t.l.c. of the mixture in a number of different solvents showed a large separation of the spots due to the two components, while in the t.l.c. of both the crude and purified herqueinone obtained from all the batches of *P. herquei* grown no spot corresponding to deoxyherqueinone was ever observed.

Because of its very low solubility, it was not possible to attempt purification of norherqueinone by chromatography. Instead it was purified, as already described,[3] by fractionation with boiling ethanol and recrystallisation from glacial acetic acid. Norherqueinone thus obtained (m.p. 269° dec.) gave an n.m.r. spectrum (pyridine solution) with peaks virtually superposable on the corresponding absorptions in herqueinone. The presence of *ca.* 15% herqueinone (OMe signal at τ 6·07) and *ca.* 10—12% isonorherqueinone (aliphatic CMe signal at τ 9·11) (including, possibly, some isoherqueinone which gives an identical n.m.r. signal) was indicated by the presence of appropriate impurity peaks. The proportion of isonorherqueinone in crude norherqueinone was similar to that remaining after purification; however, some reduction in the amount of herqueinone was achieved by fractionation with boiling ethanol. The presence of herqueinone in the norherqueinone was revealed also by t.l.c. Neither n.m.r. spectroscopy nor t.l.c. gave any indication that atrovenetin was present as an impurity, despite the appearance of a peak at $M - 16$ in the mass spectrum of norherqueinone. In the n.m.r. spectrum of norherqueinone in pyridine to

which 5% of atrovenetin had been added peaks due to the latter at τ 8·56 and 8·68 were easily distinguished.*

Deuteriation of Herqueinone.—A solution of herqueinone (containing some isoherqueinone) (130 mg.) in 95% deuterioethanol–5% deuterium oxide (5 ml.) was heated under reflux for 7 hr. The hot solution was filtered and upon concentration of the filtrate, orange-red crystals, m.p. 227—228° (capillary), were deposited. The incorporation of two and three atoms of deuterium into different molecules of the substrate was apparent from the appearance in the mass spectrum of the product of new parent peaks at *m/e* 374 and 375, with a large diminution in the relative abundance of the original parent peak at *m/e* 372. The accurate masses of the two new peaks were measured (Found: *m/e*, 374·1338 and 375·1378. $C_{20}H_{18}D_2O_7$ requires *M*, 374·1335 $C_{20}H_{17}D_3O_7$ requires *M*, 375·1393).

A comparison of the n.m.r. spectra of the material before and after deuteriation revealed that some isomerisation to isoherqueinone had occurred under the conditions employed.

Isomerisation of Herqueinone.—In a typical experiment, a solution of herqueinone (1·83 g.) (containing about 35% isoherqueinone) in anhydrous acetone (60 ml.) was heated under reflux for 1 hr. with anhydrous potassium carbonate (2 g.). The acetone was evaporated under reduced pressure and dilute hydrochloric acid was added to the residue which was then extracted with ether. (Substantial losses of material resulted from the formation of a highly persistent ether–water emulsion.) The ether extract was washed with water, dried (Na_2SO_4), and evaporated *in vacuo*. The residue was recrystallised from ethanol to give an almost racemic mixture of isoherqueinone and *enantio*-isoherqueinone (742 mg.), m.p. 240—241° (capillary), undepressed on admixture with an authentic sample, m.p. 243—245° (capillary), originally prepared by Raistrick *et al.*[3] Concentration of the mother liquors gave a second crop of material (128 mg.), m.p. 230—240° (capillary).

The mother liquors were evaporated to dryness to give a non-crystalline residue (110 mg.) which was largely *enantio*-isoherqueinone.

The intense colour of isoherqueinone precluded accurate polarimetric measurements. The degree of optical activity was determined by reducing each sample to deoxyherqueinone with zinc and acetic acid (as already described for herqueinone [3]), followed by acetylation with acetic anhydride and pyridine to afford deoxyherqueinone diacetate, which was purified in the present work by chromatography on Kieselgel G (eluant; 20% ether–80% benzene) and recrystallisation from methanol. The specific rotation of the deoxyherqueinone diacetate could be accurately determined. The results are summarised in Table 6.

Methylation of Deoxyherqueinone.—Herqueinone (150 mg.) (containing *ca.* 33% of isoherqueinone as judged by its n.m.r. spectrum) was reduced with zinc and acetic acid as previously described.[3] The zinc was removed by filtration, and washed with chloroform. To the combined filtrate and chloroform washings, more chloroform was added, and the mixture was repeatedly washed with water. The chloroform solution was dried (Na_2SO_4), and evaporated *in vacuo* to yield deoxyherqueinone as a yellow solid. The deoxyherqueinone thus obtained was dissolved in ethanol (5 ml.) and treated with an excess of ethereal diazomethane at room temperature for 6 hr. The crystalline material obtained after work-up was separated into two major fractions by chromatography on a column of Kieselgel H (20 g.) and Hyflosupercel (2 g.) using 10%-ether–90% benzene as eluant. The fraction of higher R_F, which fluoresced bright yellow under u.v. light gave, after recrystallisation from chloroform–ligroin, partially racemic atrovenetin orange trimethyl ether (23 mg.), m.p. 179—180°, raised by several further recrystallisations to 185—187°, $[\alpha]_D$ +35° (*c* 0·69, in $CHCl_3$). This material gave i.r., u.v., and n.m.r. spectra which were superposable on those of authentic atrovenetin orange trimethyl ether, m.p. 178—179°, $[\alpha]_D$ +109° (*c* 1·2, in $CHCl_3$).

From the chromatographic fraction of lower R_F value, which gave a blue fluorescence under u.v. light, yellow crystals (55 mg.) of partially racemic atrovenetin yellow trimethyl ether were obtained. After one recrystallisation from chloroform–ligroin these were constant-melting at 169—170°, $[\alpha]_D$ +27° (*c* 1·42, in $CHCl_3$). This compound gave i.r., u.v., and n.m.r. spectra which were superposable on those of authentic atrovenetin yellow trimethyl ether, m.p. 168—169°, $[\alpha]_D$ +76° (*c* 1·42, in $CHCl_3$).

Oxidation of Deoxyherqueinone with Chromium Trioxide.—A re-investigation of this reaction gave essentially the same result as previously described.[5b] It was established, however, that the yield of the anhydride (5) obtained is very sensitive to the amount of sulphuric acid present. In a typical experiment, herqueinone (50 mg.) was dissolved in pyridine (0·7 ml.) and glacial acetic acid (4 ml.); after being shaken with acid-washed zinc dust (1 g.) for 30 min., the solution was filtered and sulphuric acid (14 ml.; 12N) was added to the filtrate. Oxidation with chromium trioxide (105 mg.) in water (0·4 ml.) and glacial acetic acid (3·1 ml.) was carried out as previously described.[5b] After work-up, a pure sample of the anhydride (5) (9·6 mg., 22%) was obtained by preparative t.l.c. (20 × 20 cm. plate, 0·5 mm. coating of Kieselgel G), using 4% ethanol–96% benzene as eluant. The material obtained was identical in all respects with an authentic sample of the anhydride obtained in the earlier work.

The above reaction was carried out several times with yields varying from 19 to 22%. However, none of the required product could be detected when the quantity of sulphuric acid solution used was 5 ml. or 20 ml. Similarly, when we used the conditions described by Cason *et al.*,[9] which do not include the addition of sulphuric acid, none of the naphthalic anhydride (5) could be detected.

Conversion of Norherqueinone into Atrovenetin Triacetate (1; $R^1 = R^2 =$ Ac) *or* (6; R = Ac).—Norherqueinone (100 mg.), previously recrystallised from glacial acetic acid and containing *ca.* 15% herqueinone and 12% isonorherqueinone as judged from its n.m.r. spectrum, was dissolved in pyridine (2 ml.) and glacial acetic acid (10 ml.) and reduced with zinc dust in the manner previously described.[5] Acetylation of the deoxynorherqueinone (atrovenetin) produced with acetic anhydride (1 ml.) and pyridine (2 ml.) gave, after chromatography of the product on Kieselgel G, deoxyherqueinone diacetate (14 mg.) which was recrystallised from methanol to yield

* The n.m.r. spectrum of atrovenetin in [$^2H_6$]dimethyl sulphoxide is quite normal: τ 3·17 (1H, s, Ar-H), 5·33 (1H, q, *J* 7 Hz, O–C*H*–Me), 7·26 (3H, s, Ar-CH_3), 8·50 (3H, s, CMe_2), 8·58 (3H, d, *J* 7 Hz, O–CH–*Me*), and 8·74 (3H, s, CMe_2). In pyridine solution, however, the only sharp signals are as follows: τ 8·38 (3H, s, CMe_2), 8·62 (3H, s, CMe_2), and 8·62 (3H, d, *J* 7 Hz, O–CH–*Me*). The signals arising from the aromatic methyl group and the tertiary proton in the ether ring are very broad and ill-defined, presumably as a result of the complex formation already observed between atrovenetin and pyridine.[5b]

yellow needles, m.p. 174—176° (undepressed on admixture with an authentic sample of the same m.p.) and atrovenetin triacetate (31 mg.), which was recrystallised from methanol to give yellow needles, m.p. 181—183° (undepressed on admixture with an authentic sample of the same m.p.). The identities of the products were confirmed by a comparison of their i.r. and u.v. spectra with those of authentic samples. The yield of atrovenetin triacetate represents less than the true yield for the conversion of norherqueinone into atrovenetin since no attempt was made to isolate the atrovenetin tetra-acetate which is formed during the acetylation (see next experiment).

Atrovenetin Tetra-acetate.—Atrovenetin (150 mg.) was treated with acetic anhydride (0·5 ml.) and pyridine (1 ml.) at room temperature for 16 hr.; excess of acetic anhydride was destroyed by the addition of methanol (2 ml.), and the reaction mixture was poured into dilute hydrochloric acid and extracted with chloroform. The chloroform extract was washed with water, dried (Na_2SO_4), and evaporated *in vacuo* to give a yellow gummy solid. The product was separated into two fractions by preparative t.l.c. (20 × 20 cm. plate, 0·5 mm. coating of Kieselgel G) using 30% ether–70% benzene as eluant. The band of higher R_F (green fluorescence under u.v. light) afforded atrovenetin triacetate (90 mg.) as a yellow solid which crystallised from acetone–ethanol as orange cubes, m.p. 187—188°, undepressed on admixture with an authentic specimen of the same m.p. The two specimens also gave superposable n.m.r. spectra.

From the band of lower R_F (bright yellow fluorescence under u.v. light) there was obtained *atrovenetin tetra-acetate* (100 mg.) as a yellow solid which was recrystallised from methanol as bright yellow crystals, m.p. 193—194°, $[\alpha]_D$ +34° (*c*, 1·62 in $CHCl_3$) (Found: C, 63·25; H, 5·15. $C_{27}H_{26}O_{10}$ requires C, 63·5; H, 5·15%), $\lambda_{max.}$ 211, 276, 343, 420, and 442 nm. (log ε 4·52, 4·61, 4·02, 4·27, and 4·21); $\nu_{max.}$ (Nujol) 1590, 1625, and 1775 cm.$^{-1}$; τ 3·00 (1H, s, Ar-H), 5·32 (1H, q, *J* 6·5 Hz, O–C*H*–Me), 7·15 (3H, s, Ar-CH_3), 7·51, 7·66, 7·68, 7·70 (each 3H, s, 4 × OAc), 8·53 (3H, d, *J* 6·5 Hz, O–CH–Me), 8·55 (3H, s, CMe_2), and 8·75 (3H, s, CMe_2).

Dihydroherqueinone Monomethyl Ether (7; $R^1 = R^3 = R^4 = H$, $R^2 = Me$).[4]—In a typical experiment, a slurry of herqueinone (1·24 g.) (containing isoherqueinone as an impurity) in ethyl acetate (80 ml.) was hydrogenated over 10% palladised charcoal (300 mg.). Uptake of hydrogen ceased after 3 hr, when 1 molar equivalent had been absorbed and all the organic material had passed into solution. The catalyst was removed by filtration and the filtrate was treated with ethereal diazomethane (*ca.* 0·2N; 20 ml.) at 0 °C for 2½ hr. Excess of diazomethane was destroyed by addition of a few drops of glacial acetic acid; the solvent was evaporated *in vacuo* to afford a crystalline residue (1·14 g.). This was chromatographed on a column of Kieselgel G (56 g.) using 1% ethanol–99% benzene as eluant to afford dihydroherqueinone monomethyl ether (707 mg., 52%) as yellow crystals, m.p. 172—174°, after one recrystallisation from ligroin (b.p. 60—80°), $\nu_{max.}$ 3440, 3340 (OH), 1600 (H-bonded CO), and 1570 cm.$^{-1}$; $\lambda_{max.}$ 235, 269, 282, 291, 364 (infl.), and 400 nm. (log ε 4·59, 4·16, 4·16, 4·17, 3·79, and 3·92). The n.m.r. spectrum of this material (Table 2) exhibited signals, arising from dihydroisoherqueinone monomethyl ether present as an impurity. The m.p. of the product depends on the relative proportions of the two isomers.

Dihydroherqueinone Monomethyl Ether Diacetate (7; $R^1 = R^3 = Ac$, $R^2 = Me$, $R^4 = H$).—Dihydroherqueinone monomethyl ether (70 mg.) (containing some dihydroisoherqueinone monomethyl ether) was treated overnight at room temperature with acetic anhydride (0·5 ml.) and pyridine (1 ml.). Excess of acetic anhydride was destroyed by the addition of methanol and the reaction mixture was poured into dilute hydrochloric acid and extracted with chloroform. The chloroform extract was washed successively with dilute hydrochloric acid and water, and evaporated *in vacuo* to give a yellow gum (73 mg.), which was applied to a plate coated with Kieselgel G (20 × 20 cm., 0·5 mm. coating) and eluted with 6% ether–94% chloroform. From the colourless band which fluoresced bright blue under u.v. light *dihydroherqueinone monomethyl ether diacetate* (33 mg.) (containing no more than 5% of the corresponding compound in the iso-series as indicated by its n.m.r. spectrum) was obtained as a colourless gum which could not be crystallised (Found: *m/e* 472·1727. $C_{25}H_{29}O_9$ requires *M*, 472·1733), $\lambda_{max.}$ 231, 260, and 359 nm. (log ε 4·58, 4·38, and 3·93); $\nu_{max.}$ (5% soln. in $CHCl_3$) 1670, 1767, and 3510 cm.$^{-1}$.

Dihydroherqueinone Monomethyl Ether Triacetate (7; $R^2 = Me$, $R^1 = R^3 = R^4 = Ac$).—Dihydroherqueinone monomethyl ether (59 mg.) (containing some dihydroisoherqueinone monomethyl ether) was heated for 15 min. at 110° with toluene-*p*-sulphonic acid monohydrate (15 mg.) and acetic anhydride (1 ml.). The reaction mixture was cooled and poured into water, and the products of the reaction were obtained as a yellow gum by extraction with chloroform. This material was chromatographed on four Kieselgel G plates (20 × 20 cm., *ca.* 0·2 mm. thickness). After eight developments with 12% ether–88% benzene two blue fluorescent bands were discernible. Although these overlapped somewhat, it was possible to obtain *dihydroherqueinone monomethyl ether triacetate* from the band of higher R_F as a yellow gum (21 mg.), in a homogeneous state, as judged by its n.m.r. spectrum (Found: *m/e*, 514·1831. $C_{27}H_{30}O_{10}$ requires *M*, 514·1839), $\lambda_{max.}$ 228, 259, 336 (infl.), and 358 nm. (log ε 4·60, 4·28, 3·76, and 3·88); $\nu_{max.}$ ($CHCl_3$) 1680, 1735, and 1768 cm.$^{-1}$.

The material isolated from the band of lower R_F exhibited n.m.r. signals which indicated that it was a mixture of dihydroherqueinone monomethyl ether triacetate and dihydroisoherqueinone monomethyl ether triacetate.

Dihydroherqueinone Dimethyl Ether (7; $R^1 = R^2 = Me$, $R^3 = R^4 = H$).—(*a*) Dihydroherqueinone monomethyl ether (80 mg.) (containing some dihydroisoherqueinone monomethyl ether), dissolved in ethyl acetate (3 ml.), was treated for 3 hr. with ethereal diazomethane (*ca.* 4 molar equivalents) to give, after work-up, a semi-crystalline product which was purified by preparative t.l.c. (20 × 20 cm. plate, 0·5 mm. coating of Kieselgel G; 8% ether–92% benzene). *Dihydroherqueinone dimethyl ether* appeared as a yellow band (green-yellow fluorescence under u.v. light) from which it was obtained by extraction with acetone. After recrystallisation from methanol the material had m.p. 151—154°, $[\alpha]_D$ −37° (*c* 1·22 in $CHCl_3$); from its n.m.r. spectrum it was clear that dihydroisoherqueinone dimethyl ether was present as an impurity (Found: C, 65·5; H, 6·15; *m/e*, 402·1659. $C_{22}H_{26}O_7$ requires C, 65·65; H, 6·5%; *M*, 402·1678), $\lambda_{max.}$ 229, 275, and 379 nm. (log ε 4·62, 4·38, and 3·74); $\nu_{max.}$ 1668, 3320, and 3430 cm.$^{-1}$.

(*b*) Herqueinone (5 g.) (containing isoherqueinone) was hydrogenated in ethyl acetate (100 ml.) using 10% Pd–C

as catalyst. Uptake ceased after 9½ hr. when one molecular equivalent of hydrogen had been absorbed. The catalyst was removed by filtration, and excess ethereal diazomethane was added to the filtrate which was left overnight at room temperature. Excess of diazomethane was destroyed by the addition of acetic acid, and the reaction mixture was filtered and evaporated to dryness. Chromatography of the residue on a column of Kieselgel H (230 g.) and Hyflosupercel (23 g.) using 8% ether–92% benzene as eluant gave a mixture (1·66 g.), m.p. 166—176° of dihydroherqueinone dimethyl ether and dihydroisoherqueinone dimethyl ether.

(*c*) Crude norherqueinone (5 g.) was extracted with boiling ethanol (50 ml.) and the insoluble material (3·8 g.) was taken up in dimethylformamide (20 ml.) and hydrogenated over 10% Pd–C (600 mg.) which had been previously saturated with hydrogen. One molecular equivalent of hydrogen (240 ml.) was absorbed during 10 hr., after which no further uptake of hydrogen occurred. The catalyst was removed by filtration and the filtrate was diluted with ether and added to an ice-cold solution of diazomethane (*ca.* 3 g.) in ether (170 ml.) with swirling, during 5 min. The reaction mixture was left overnight at room temperature, filtered, and evaporated *in vacuo* to give a red gum, which was chromatographed on a column of Kieselgel H (200 g.) and Hyflosupercel (20 g.) using 8% ether–92% benzene as eluant to give dihydroherqueinone dimethyl ether (1·81 g.). One recrystallisation from ether gave pale yellow crystals (1·26 g.), m.p. 155—156°, undepressed on admixture with material obtained as described in (*a*) above. Two further recrystallisations from methanol gave very pale yellow rods, m.p. 157—158°, unchanged by further recrystallisation, $[\alpha]_D$ −35° (*c* 0·8 in $CHCl_3$). The n.m.r. spectrum of this material, which was superposable on that of the product obtained in (*a*) above, revealed that it contained only *ca.* 5% of dihydroisoherqueinone dimethyl ether.

Dihydroherqueinone Dimethyl Ether Monoacetate (7; $R^1 = R^2 = Me$, $R^3 = Ac$, $R^4 = H$).—Dihydroherqueinone dimethyl ether (50 mg.) (containing *ca.* 40% dihydroisoherqueinone dimethyl ether as adjudged by its n.m.r. spectrum) was acetylated overnight at room temperature with acetic anhydride (0·5 ml.) and pyridine (1 ml.). Work-up in the usual way gave a yellow gum, which was subjected to preparative t.l.c. (20 × 20 cm. plate, 0·5 mm. coating of Kieselgel G); the plate was developed three times with 10% ether–90% benzene. *Dihydroherqueinone dimethyl ether monoacetate* was obtained as a clear gum (46 mg.) by extraction with acetone of a pale yellow band which fluoresced blue under u.v. light. The material could not be crystallised, and its n.m.r. spectrum revealed that it contained *ca.* 40% dihydroisoherqueinone dimethyl ether monoacetate as an impurity (Found: *m/e*, 444·1770. $C_{24}H_{28}O_8$ requires *M*, 444·1784), $\lambda_{max.}$ 233, 262, 337 (infl.), and 350 nm. (log ε 4·54, 4·20, 3·77, and 3·82); $\nu_{max.}$ ($CHCl_3$) 1570, 1620, 1670, 1760, and 3550 $cm.^{-1}$.

Dihydroherqueinone Dimethyl Ether Diacetate (7; $R^1 = R^2 = Me$, $R^3 = R^4 = Ac$).—Dihydroherqueinone dimethyl ether (50 mg.) (containing some dihydroisoherqueinone dimethyl ether) was acetylated with acetic anhydride (1 ml.) and toluene-*p*-sulphonic acid (16 mg.) at 110° for 10 min. Work-up in the usual way (see dihydroherqueinone monomethyl ether triacetate) gave a yellow gum which was purified by preparative t.l.c. (20 × 20 cm. plate, 0·5 mm. coating of Kieselgel G); the plate was developed with 4% ethyl acetate–96% benzene. The major fraction, which appeared as a pale yellow band with a light blue fluorescence under u.v. light, was extracted with acetone. The initially gummy material crystallised on standing with a few drops of methanol. One recrystallisation from methanol gave *dihydroherqueinone dimethyl ether diacetate* (25 mg.) as colourless prisms, m.p. 193—195°, $[\alpha]_D$ −144° (*c*, 1·24 in $CHCl_3$). The n.m.r. spectrum of the material revealed the presence of a small amount of dihydroisoherqueinone dimethyl ether diacetate (Found: C, 64·1; H, 6·15, *m/e*, 486·1894. $C_{26}H_{30}O_9$ requires C, 64·2; H, 6·2%; *M*, 486·1890), $\lambda_{max.}$ 232, 263, and 352 nm. (log ε 4·69, 4·33, and 4·00); $\nu_{max.}$ 1680, 1735, and 1760 $cm.^{-1}$.

Dihydroherqueinone Trimethyl Ether (7; $R^1 = R^2 = R^3 = Me$, $R^4 = H$).—(*a*) Dihydroherqueinone dimethyl ether (270 mg.) (containing some dihydroisoherqueinone dimethyl ether), dimethyl sulphate (0·1 ml.), and anhydrous potassium carbonate (2 g.) were heated with anhydrous acetone under reflux for 1 hr. After addition of further portions of dimethyl sulphate (0·1 ml.) and anhydrous potassium carbonate (2 g.), refluxing was continued for a further 2 hr. The reaction mixture was filtered, the acetone was removed from the filtrate by distillation *in vacuo*, and the residual dimethyl sulphate was destroyed by stirring the mixture with dilute sodium hydroxide for 10 min. After neutralisation of the base with dilute hydrochloric acid, the products of the reaction were isolated as a yellow gum by extraction with chloroform. The material was purified by chromatography on a column of Kieselgel H using 1% ethanol–99% benzene as eluant. In this way *dihydroherqueinone trimethyl ether* (containing some dihydroisoherqueinone trimethyl ether as an impurity as judged by its n.m.r. spectrum) was obtained in almost quantitative yield as a yellow gum which could not be crystallised (Found: C, 66·1; H, 6·9; *m/e*, 416·1836. $C_{23}H_{28}O_7$ requires C, 66·35; H, 6·8%; *M*, 416·1835), $\lambda_{max.}$ 230, 273, and 366 nm. (log ε 4·41, 4·17, and 3·60); $\nu_{max.}$ ($CHCl_3$) 1665 and 3530 $cm.^{-1}$.

(*b*) Glycol C (9; R = Me) (50 mg.) and a deposition of silver carbonate on Celite (1·4 g.) [16] were heated in benzene under reflux. A portion (3 ml.) of the solvent was distilled out of the mixture and the remaining reaction mixture was heated under reflux for 4 days, more benzene being added daily to maintain a total volume of *ca.* 6 ml.; after addition of a further portion (400 mg.) of the silver carbonate–Celite mixture the heating was continued for a further four days. The reaction mixture was filtered and the filtrate was evaporated *in vacuo* to give a pale yellow gum which was purified by preparative t.l.c. (20 × 20 cm. plate, 0·5 mm. coating of Kieselgel G_{F254}; 30% ether–70% benzene). Extraction of the fast-moving band which fluoresced bright green in u.v. light with acetone gave dihydroherqueinone trimethyl ether (17 mg.) as a colourless gum which could not be crystallised. The n.m.r. spectrum of this material was identical with the set of signals attributed to dihydroherqueinone trimethyl ether in the n.m.r. spectrum of the mixture obtained as described above in (*a*).

Unchanged glycol C (identified by m.p. and mixed m.p.) was obtained from a band of lower R_F which did not fluoresce in u.v. light.

Dihydroherqueinone Trimethyl Ether Acetate (7; $R^1 = R^2 = R^3 = Me$, $R^4 = Ac$).—Acetylation of dihydroherqueinone trimethyl ether (55 mg.) (containing *ca.* 15% dihydroisoherqueinone trimethyl ether) with acetic anhydride

(1 ml.) and toluene-*p*-sulphonic acid (15 mg.) at 110° for 10 min. gave, after work-up in the usual way (see dihydroherqueinone monomethyl ether triacetate) a pale yellow gum from which a chromatographically homogeneous fraction was obtained by preparative t.l.c. (20 × 20 cm. plate, 0·5 mm. coating of Kieselgel G) using 4% ethanol–96% benzene as eluant (eluting twice). This material, initially a gum (42 mg.), crystallised very slowly when left with a few drops of methanol for several weeks. Recrystallisation from methanol gave *dihydroherqueinone trimethyl ether acetate* (containing *ca.* 15% dihydroisoherqueinone trimethyl ether acetate as an impurity, as judged by its n.m.r. spectrum) as colourless crystals, m.p. 136—139° (Found: *m/e*, 458·1916. $C_{25}H_{30}O_8$ requires *M*, 458·1941), $\lambda_{max.}$ 227, 274, and 273 nm. (log ε 4·65, 4·42, and 3·85); $\nu_{max.}$ (10% soln. in $CHCl_3$) 1680 and 1730 cm.$^{-1}$ (no absorption above 3100 cm.$^{-1}$).

(±)-*Dihydroisoherqueinone Monomethyl Ether* (7; R^1 = R^3 = R^4 = H, R^2 = Me).—(±)-Isoherqueinone (102 mg.), obtained by base treatment of a herqueinone–isoherqueinone mixture (containing 55% of the iso-compound by n.m.r. assay) extracted from the mycelium of *P. herquei*, was converted into its dihydro-derivative by hydrogenation in ethyl acetate using 10% palladised charcoal as catalyst. The dihydro-compound was methylated at 0° for 90 min. with ethereal diazomethane (4 ml., 0·4 molar solution). After work-up, the crystalline product was purified by preparative t.l.c. (20 × 20 cm. plate, 1 mm. coating of Kieselgel G; 1% ethanol–99% benzene). In this way virtually racemic *dihydroiosherqueinone monomethyl ether* (42 mg.) was obtained. The material was constant melting at 192—194° after being recrystallised once from chloroform–ligroin and twice from cyclohexane. As obtained, the material was, in fact, slightly dextrorotatory, $[\alpha]_D$ +1·4° (*c* 2·3 in $CHCl_3$), indicating that the (±)-isoherqueinone contained a small amount of isoherqueinone of natural configuration (Found: C, 65·3; H, 6·3; *m/e*, 388·1525. $C_{21}H_{24}O_7$ requires C, 64·95; H, 6·25%; *M*, 388·1522), $\lambda_{max.}$ 233, 269, 282, 292, 366 (infl.), and 402 nm. (log ε 4·62, 4·10, 4·10, 4·11, 3·67, and 3·83); $\nu_{max.}$ 1600, 1620, 3350, 3420, and 3490 cm.$^{-1}$. The n.m.r. spectrum of this material (Table 2) exhibited no bands which could be assigned to impurities.

(+)-*Dihydroisoherqueinone Monomethyl Ether* (7; R^1 = R^3 = R^4 = H, R^2 = Me).—Herqueinone (5 g.) (containing some isoherqueinone) was reduced and methylated (using *ca.* 1·3 equivalents of diazomethane) as already described in the preparation of dihydroherqueinone monomethyl ether. Chromatography of the product on a column of Kieselgel H (300 g.) and Hyflosupercel (30 g.) using 1% ethanol–99% benzene as eluant gave, from the leading fraction, (+)-*dihydroisoherqueinone monomethyl ether* (307 mg.) as yellow crystals, which were recrystallised from hexane as green-yellow needles (220 mg.), m.p. 179—181°, $[\alpha]_D$ +20° (*c* 1·45 in $CHCl_3$). The u.v., i.r., and n.m.r. spectra of this material were identical with those of the racemic modification described in the previous experiment.

Later chromatographic fractions were combined and further methylated with an excess of diazomethane as already described in the preparation of dihydroherqueinone dimethyl ether to give a mixture of the dimethyl ethers of herqueinone and isoherqueinone, as indicated by the n.m.r. spectrum of the product.

(−)-*Dihydroisoherqueinone Monomethyl Ether Diacetate* (7; R^1 = R^3 = Ac, R^2 = Me, R^4 = H).—(+)-Dihydroisoherqueinone monomethyl ether (43 mg.) was treated overnight at room temperature with acetic anhydride (0·5 ml.) and pyridine (1 ml.). The reaction mixture was worked up in the usual way and the product was purified by preparative t.l.c. (20 × 20 cm. plate, with a 0·5 mm. coating of Kieselgel G; 15% ether–85% benzene) to give, after two recrystallisations from aqueous methanol, *dihydroisoherqueinone monomethyl ether diacetate* (27 mg.), m.p. 177—177·5°, $[\alpha]_D$ −41° (*c* 2·33 in $CHCl_3$) (Found: C, 63·8; H, 5·90. $C_{25}H_{28}O_9$ requires C, 63·55; H, 5·95%), $\lambda_{max.}$ 230, 260, and 360 nm. (log ε 4·63, 4·38, and 4·08); $\nu_{max.}$ (Nujol) 1657, 1775, and 3470 cm.$^{-1}$.

(±)-*Dihydroisoherqueinone Dimethyl Ether* (7; R^1 = R^2 = Me, R^3 = R^4 = H) *and* (±)-*Dihydroisoherqueinone Trimethyl Ether* (7; R^1 = R^2 = R^3 = Me, R^4 = H).—(±)-Isoherqueinone (450 mg.) was hydrogenated in ethyl acetate (40 ml.) over pre-saturated 10% palladised charcoal (400 mg.). Uptake of hydrogen ceased after 1 hr. when *ca.* 1 molecular equivalent of hydrogen had been absorbed. After removal of the catalyst by filtration, the reaction mixture was reduced in bulk (to *ca.* 10 ml.) by evaporation *in vacuo*, and a solution of diazomethane (*ca.* 8 molar equivalents) in a mixture of ether and ethanol (20 ml.) was added. The reaction mixture was left at room temperature for 2 hr., and then worked up to give a yellow crystalline product. This was separated into two major fractions by chromatography on a column of Kieselgel H (50 g.) and Hyflosupercel (5 g.) using 8% ether–92% benzene as eluant. The material of higher R_F was recrystallised from acetone to yield (±)-*dihydroisoherqueinone dimethyl ether* (149 mg.), m.p. 213—216°, $[\alpha]_D$ 0° (*c* 1·5 in $CHCl_3$) (Found: C, 65·85; H, 6·5; *m/e*, 402·1674. $C_{22}H_{26}O_7$ requires C, 65·65; H, 6·5%; *M*, 402·1678), $\lambda_{max.}$ 229, 277, and 381 nm. (log ε 4·62, 4·41, and 3·76); $\nu_{max.}$ ($CHCl_3$) 1628, 1665, 3380, and 3500 cm.$^{-1}$.

The derived *monoacetate* (7; R^1 = R^2 = Me, R^3 = Ac, R^4 = H) prepared by treatment with acetic anhydride–pyridine at room temperature gave colourless crystals from methanol, m.p. 177—178° (Found: C, 64·9; H, 6·45. $C_{24}H_{28}O_8$ requires C, 64·85; H, 6·35%), $\lambda_{max.}$ 209, 238, and 325 nm. (log ε 4·63, 4·26, and 3·94); $\nu_{max.}$ (Nujol) 1668, 1768, and 3480 cm.$^{-1}$.

The material of lower R_F was recrystallised twice from acetone to give (±)-*dihydroisoherqueinone trimethyl ether* (48 mg.) as bright yellow crystals, m.p. 186—188° (Found: C, 66·4; H, 6·6. $C_{23}H_{28}O_7$ requires C, 66·35; H, 6·8%), $\lambda_{max.}$ 231, 274, 343 (infl.), and 373 nm. (log ε 4·57, 4·40, 3·61, and 3·80); $\nu_{max.}$ 1600, 1663, and 3460 cm.$^{-1}$.

(+)-(enantio)-*Dihydroisoherqueinone Dimethyl Ether* (7; R^1 = R^2 = Me, R^3 = R^4 = H).—(*a*) The residue (300 mg.) obtained by evaporating the mother liquor arising from the preparation of (±)-isoherqueinone by base treatment of a herqueinone-rich mixture of herqueinone and isoherqueinone was hydrogenated and methylated as described in the preceding experiment. Chromatography of the product on a column of Kieselgel H (50 g.) and Hyflosupercel (5 g.) gave (+)-*enantio*-dihydroisoherqueinone dimethyl ether (62 mg.), which was recrystallised from methanol, m.p. 198—202°, $[\alpha]_D$ +38° (*c*, 1·28 in $CHCl_3$). The material gave i.r. ($CHCl_3$ soln.), u.v., and n.m.r. spectra which were superposable on those of the (±)-isomer. From its reduction to (−)-*enantio*-glycol B (9; R = H) of $[\alpha]_D$ −32° (q.v.) it would appear to have an optical purity of *ca.* 75%.

(*b*) A mixture of norherqueinone and isonorherqueinone

(1·7 g.), but containing no more than 10% of the latter as judged by its n.m.r. spectrum was treated with mild base as previously described [3] to give, after one recrystallisation from methanol, *enantio*-isonorherqueinone (340 mg.), the n.m.r. spectrum of which was exactly superposable on the signals assigned to the minor component of the starting material. A portion (200 mg.) of the product was hydrogenated in dimethylformamide (5 ml.) over pre-saturated 10% palladised charcoal (200 mg.). Uptake of hydrogen ceased after one molar equivalent had been absorbed. After removal of the catalyst by filtration, the reaction mixture was added to an excess of ethereal diazomethane and left at room temperature for 5 hr. The yellow gum obtained by work-up of the reaction mixture was purified by preparative t.l.c. (two 20 × 20 cm. plates, 0·5 mm. coating of Kieselgel G); the plates were developed twice with 10% ether–90% benzene. From a band of high R_F which fluoresced bright yellow in u.v. light there was obtained (+)-*enantio*-dihydroisoherqueinone dimethyl ether (53 mg.) as almost colourless crystals, m.p. (after one recrystallisation from methanol) 198—199°, $[\alpha]_D$ +49° (*c* 1·15, in $CHCl_3$). The i.r. and u.v. spectra of material obtained in this way were superposable on those of the material described in the preceding paragraph. Reduction of this material gave *enantio*-glycol B (9; R = H) of $[\alpha]_D$ −44° (q.v.), implying a high degree of optical purity.

(−)-*Dihydroisoherqueinone Trimethyl Ether* (7; $R^1 = R^2 = R^3 =$ Me, $R^4 =$ H).—(+)-Glycol D (50 mg.) was oxidised with silver carbonate–Celite (1·4 g.) in benzene (9 ml. initially, reduced to 6 ml. by distillation so as to remove any moisture azeotropically). After 60 hr. the oxidation appeared to be complete (t.l.c.). Work-up gave (−)-*dihydroisoherqueinone trimethyl ether* (35 mg.) as a colourless gum which crystallised when left standing with methanol. Recrystallisation from aqueous ethanol gave colourless needles, m.p. 121—122°, $[\alpha]_D$ −20° (*c* 0·61, in $CHCl_3$). The i.r. and n.m.r. spectra of this material were superposable on those of (±)-dihydroisoherqueinone trimethyl ether (m.p. 186—187°) obtained by methylation of (±)-dihydroisoherqueinone (see above).

2,3-*Dihydro*-4,9-*dihydroxyphenalen*-1-*one* (8; R = H) *and* 4,9-*Dihydroxyphenalen*-1-*one*.—2,3-Dihydro-4,9-dimethoxyphenalen-1-one (155 mg.) [1] was heated under reflux with pyridine hydrochloride (2·7 g.) for 16 min. The reaction mixture was poured into water and the products were extracted with chloroform. After the chloroform extract had been washed successively with dilute hydrochloric acid and water, it was dried (Na_2SO_4) and evaporated *in vacuo*. Chromatography of the residue on a column of Kieselgel G (15 g.), using 2% methanol–98% chloroform as eluant, gave two major fractions. The first of these, which fluoresced blue under u.v. light was recrystallised from chloroform–ligroin (b.p. 60—80°) to give 2,3-*dihydro*-4,9-*dihydroxyphenalen*-1-*one* (82 mg.), m.p. 234—238° (Found: C, 72·5; H, 4·65. $C_{13}H_{10}O_3$ requires C, 72·9; H, 4·7%), $\lambda_{max.}$ 232, 275, 278 (infl.), and 360 nm. (log ε 4·30, 3·75, 3·72, and 3·91); $\nu_{max.}$ (Nujol) 3400 (broad) and 1620 cm.$^{-1}$; τ 2·16 (1H, d, *J* 9 Hz, 7-H), 2·46 (d, *J* 9 Hz, 6-H), 3·03 (1H, d, *J* 9 Hz, 5-H or 8-H), 3·05 (1H, d, *J* 9 Hz, 8-H or 5-H), 6·79 (2H, m, 2-methylene), 7·05 (2H, m, 3-methylene), and −3·95 (1H, s, 9-OH).

Treatment with acetic anhydride and pyridine overnight gave the derived *diacetate*, which recrystallised from methanol as colourless needles, m.p. 154—156° (Found: *m/e*, 298·0838. $C_{17}H_{14}O_5$ requires *M*, 298·0841), $\lambda_{max.}$ 218, 250, and 325 nm. (log ε 4·62, 4·31, and 3·75); $\nu_{max.}$ 1685 and 1753 cm.$^{-1}$; τ 1·95 (1H, d, *J* 9 Hz, 7-H), 2·21 (1H, d, *J* 9 Hz, 6-H), 2·72 (1H, d, *J* 9 Hz, 5-H or 8-H), 2·78 (1H, d, *J* 9 Hz, 8-H or 5-H), 6·77 (2H, m, 2-methylene), 7·09 (2H, m, 3-methylene), 7·55 (3H, s, Ar-OAc), and 7·58 (3H, s, Ar-OAc).

The second fraction, which fluoresced green under u.v. light, was sublimed at 200 °C (0·07 mm. Hg) to give 4,9-*dihydroxyphenalen*-1-*one* as pale orange crystals (33 mg.), which did not melt below 320° (Found: *m/e*, 212·0464. $C_{13}H_8O_3$ requires *M*, 212·0473), $\lambda_{max.}$ 232, 252, 263, 277, 287, 309 (infl.), 382 (infl.), 404, 419, 426, 450, 455 (infl.), 471 (infl.), 494 (infl.) nm. (log ε 4·25, 3·91, 3·90, 3·89, 3·78, 3·40, 3·91, 3·98, 3·99, 3·00, 3·83, 3·82, 3·75, and 3·27); $\nu_{max.}$ 1570, 1625, and 2500—3500 cm.$^{-1}$ (broad absorption).

9-*Methoxyphenalen*-1-*one* (14; R = Me).—(*a*) A solution of 9-hydroxyphenalenone [17] (22 mg.) in dry acetone (10 ml.) was heated under reflux with anhydrous potassium carbonate (1 g.) and dimethyl sulphate (0·5 ml.) for 1½ hr. After filtration, the solvent was evaporated *in vacuo* to give 9-*methoxyphenalen*-1-*one* as a yellow gum which slowly crystallised (Found: *m/e*, 210·0678. $C_{14}H_{10}O_2$ requires *M*, 210·0681), $\lambda_{max.}$ 234, 262, 350, and 412 nm. (log ε 4·30, 4·19, 4·26, and 3·97); $\nu_{max.}$ ($CHCl_3$) 1618, and 1643 cm.$^{-1}$; τ 5·86 (3H, s, OMe). Attempts to recrystallise the sample were unsuccessful and caused some decomposition, as revealed by t.l.c.

(*b*) A solution of 9-hydroxyphenalenone (20 mg.) in chloroform (3 ml.) was stirred vigorously at room temperature for 1½ hr. with dry, freshly prepared, silver oxide (200 mg.) and methyl iodide (1·1 ml.). Work-up as described in the preceding experiment gave a yellow gum which was shown by t.l.c. to be mainly 9-methoxyphenalenone together with a small amount of unchanged starting material.

9-*Acetoxyphenalen*-1-*one* (14; R = Ac).—Treatment of 9-hydroxyphenalenone (22 mg.) with acetic anhydride (0·25 ml.) and pyridine (0·5 ml.) at room temperature for 16 hr. gave, after work-up in the usual way, a gum, which was separated by preparative t.l.c. (20 × 20 cm. plate, with a 0·5 mm. coating of Kieselgel G) using benzene as eluant into unchanged starting material (8 mg.) and 9-*acetoxyphenalen*-1-*one* (10 mg.) which gave yellow crystals, m.p. 105—106° from methanol (Found: *m/e*, 238·0619. $C_{15}H_{10}O_3$ requires *M*, 238·0630), $\lambda_{max.}$ 238, 257, 355, 382, and 439 nm. (log ε 4·14, 4·18, 4·08, 3·75, and 3·42); $\nu_{max.}$ (Nujol) 1624 and 1750 cm.$^{-1}$.

(+)-*Glycol A* (9; R = H) *and* (+)-*Glycol B* (9; R = H).—(*a*) A mixture of dihydroherqueinone dimethyl ether and dihydroisoherqueinone dimethyl ether (1·02 g.) in dry ether (35 ml.) was stirred at room temperature for 30 min. with a suspension of lithium aluminium hydride (200 mg.) in ether (5 ml.). After excess of lithium aluminium hydride had been destroyed by the addition of ethyl acetate, the reaction was worked up by the addition of water followed by enough dilute hydrochloric acid to clarify the aqueous phase; the organic layer was then separated, washed several times with water, dried (Na_2SO_4), and evaporated *in vacuo* to give a pale yellow gum which slowly crystallised. T.l.c. revealed that the mixture consisted of two colourless components, which did not fluoresce under u.v. light but which became bright red when the chromatographic plate was sprayed with a 1 : 1 mixture

of conc. nitric and sulphuric acids. Separation of the two products was achieved by chromatography on a column of Kieselgel H (200 g.) and Hyflosupercel (20 g.) using 15% ether–85% benzene as eluant. The band of higher R_F gave, after recrystallisation from ether–ligroin (b.p. 40—60°), (+)-*glycol B* (305 mg.) as colourless needles, m.p. 172—175°; a further recrystallisation gave material constant-melting at 177—178°, $[\alpha]_D$ +43° (*c* 0·93, in $CHCl_3$) (Found: C, 65·4; H, 7·1; *m/e*, 404·1826. $C_{22}H_{28}O_7$ requires C, 65·35; H, 7·0%; *M*, 404·1835), $\lambda_{max.}$ 246, 312, and 332 (infl.) nm. (log ε 4·63, 3·87, and 3·64); $\nu_{max.}$ 1580, 1607, 1629, 3340, and 3480 cm.$^{-1}$. A second crop (23 mg.), m.p. 167—174° was obtained by concentration of the mother liquors.

From the band of lower R_F there was obtained, after recrystallisation from ether–ligroin (b.p. 40—60°), (+)-*glycol A* (411 mg.) as pale yellow plates, m.p. 151—152°, $[\alpha]_D$ +64° (*c* 0·93, in $CHCl_3$) (Found: C, 65·25; H, 7·0. $C_{22}H_{28}O_7$ requires C, 65·35; H, 7·0%), $\lambda_{max.}$ 247, 312, and 332 (infl.) nm. (log ε 4·70, 3·95, and 3·74); $\nu_{max.}$ 1576, 1607, 1631, and 3360 cm.$^{-1}$. A second crop (29 mg.), m.p. 135—145°, was obtained by concentration of the mother liquors.

(*b*) Reduction of a mixture of dihydroherqueinone dimethyl ether and dihydroisoherqueinone dimethyl ether (35 mg.) was also achieved by stirring the mixture in glacial acetic acid (3 ml.) with acid-washed zinc dust (1 g.) for 2 hr. The zinc was removed by filtration and the filtrate was added to chloroform, which was washed several times with water, dried, and evaporated under reduced pressure to give a mixture of products. T.l.c. of the mixture indicated the presence of both glycol A and glycol B. (+)-Glycol A, m.p. 148—151°, undepressed on admixture with material obtained as described above, and having an i.r. spectrum superposable on that of the authentic material, was isolated from the mixture by preparative t.l.c. (20 × 20 cm. plate, 0·5 mm. coating of Kieselgel G_{F254}; 4% ethanol–96% benzene).

(±)-*Glycol B* (9; R = H).—(±)-Dihydroisoherqueinone dimethyl ether (50 mg.) in dry tetrahydrofuran (2 ml.) was stirred at room temperature while a suspension of lithium aluminium hydride (50 mg.) in tetrahydrofuran (5 ml.) was added dropwise. The reaction mixture became colourless, and stirring was continued for a further 5 min. The reaction mixture was worked up in the usual way (see preceding hydride reduction) to give a pale yellow gum which was chromatographed on a column of Kieselgel H (30 g.) and Hyflosupercel (3 g.), using 15% ether–85% benzene as eluant, to give, after recrystallisation from ether–ligroin (b.p. 40—60°) (±)-*glycol B* (40 mg.) as colourless needles, constant-melting at 174—175°, $[\alpha]_D$ 0° (*c* 2·3 in $CHCl_3$) (Found: C, 65·45; H, 6·8; *m/e*, 404·1826. $C_{22}H_{28}O_7$ requires C, 65·35; H, 7·0%; *M*, 404·1835). The i.r. ($CHCl_3$ solution), n.m.r., and mass spectra of this material were superposable on those of an authentic sample of (+)-glycol B, m.p. 177—178°, $[\alpha]_D$ +43°. The optically active and racemic materials gave no melting-point depression on admixture.

(−)-enantio-*Glycol B* (9; R = H).—(+)-*enantio*-Dihydroisoherqueinone dimethyl ether (35 mg.), $[\alpha]_D$ +49° (derived from *enantio*-isonorherqueinone), was reduced with lithium aluminium hydride in ether as described above. The crude product was purified by preparative t.l.c. (20 × 20 cm. plate; 0·5 mm. coating of Kieselgel G) to give (−)-enantio-*glycol B* (34 mg.) which was recyrstallised from ether–ligroin (b.p. 40—60°) as colourless needles, constant-melting at 167—169°, $[\alpha]_D$ −44° (*c* 0·94 in $CHCl_3$) (Found: C, 65·75; H, 6·95. $C_{22}H_{28}O_7$ requires C, 65·35; H, 7·0%). The material gave i.r., u.v., and n.m.r. spectra superposable on those of (+)-glycol B, $[\alpha]_D$ +43°. m.p. 177—178°.

In another experiment, a sample of (+)-*enantio*-dihydroisoherqueinone dimethyl ether, $[\alpha]_D$ +38° (derived from partially racemic *enantio*-isoherqueinone) gave (−)-glycol B with a specific rotation of −32° (*c* 1·15 in $CHCl_3$).

(+)-*Glycol C* (9; R = Me) *and* (+)-*Glycol D* (9; R = Me). —(*a*) A mixture of dihydroherqueinone trimethyl ether and dihydroisoherqueinone trimethyl ether (1 g.) in dry ether (7 ml.) was added dropwise to a suspension of lithium aluminium hydride (200 mg.) in ether (30 ml.). The reaction mixture was stirred at room temperature for 30 min. and was then worked up in the usual way to give a yellow gum, which by t.l.c. appeared to consist of two main components. Chromatography on a column of Kieselgel H (110 g.) and Hyflosupercel (11 g.), using 2% ethanol–98% benzene as eluant afforded, from the early fractions, (+)-glycol D as a gum containing some yellow impurities. After these had been removed by extraction with ligroin (b.p. 60—80°) the gum slowly crystallised. Two recrystallisations from ligroin (b.p. 60—80°) gave (+)-*glycol D* in a pure state as colourless crystals (150 mg.) constant-melting at 152—153°, $[\alpha]_D$ +17° (*c* 3·57, in $CHCl_3$) (Found: C, 66·4; H, 7·3; *m/e* 418·1992. $C_{23}H_{30}O_7$ requires C, 66·0; H, 7·25%; *M*, 418·1991), $\lambda_{max.}$ 245, 301 (infl.), 310, 333 (infl.) nm. (log ε 4·82, 3·93, 3·98, and 3·55); $\nu_{max.}$ 1578, 1592, 1610, and 3480 cm.$^{-1}$. The later chromatographic fractions were shown by t.l.c. to consist mainly of another compound contaminated by a small amount of (+)-glycol D. Rechromatography of these later fractions on a column of Kieselgel H (55 g.) and Hyflosupercel (5 g.) using 20% ether–80% benzene as eluant gave a pale yellow gum (553 mg.) which crystallised on trituration with ligroin (b.p. 60—80°). Recrystallisation from ligroin (b.p. 60—80°) gave (+)-*glycol C* (420 mg.) as colourless needles, m.p. 141—142°, $[\alpha]_D$ +59° (*c* 1·18, in $CHCl_3$) (Found: C, 65·9; H, 7·15; *m/e*, 418·1988. $C_{23}H_{30}O_7$ requires C, 66·0; H, 7·25%; *M*, 418·1991), $\lambda_{max.}$ 245, 301 (infl.), 309, and 330 (infl.) nm. (log ε 4·70, 3·93, 3·97, and 3·67); $\nu_{max.}$ 1579, 1592, 1610, and 3460 cm.$^{-1}$.

(*b*) In another experiment, dihydroherqueinone dimethyl ether (400 mg.), obtained by successive hydrogenation and methylation of norherqueinone [see preparation (*b*) for dihydroherqueinone dimethyl ether] and known from its n.m.r. spectrum to contain only *ca.* 5% of the corresponding compound in the iso-series, was methylated in the manner already described. The dihydroherqueinone trimethyl ether thus obtained was reduced with lithium aluminium hydride as described in the preceding experiment to give (+)-glycol C (291 mg.) as colourless needles; the identity of this material with that of the compound arising ultimately from herqueinone was established by m.p., mixed m.p., and comparison of i.r. and n.m.r. spectra.

Acid Treatment of (+)-*Glycol A* (9; R = H).—(*a*) To a solution of (+)-glycol A (440 mg.) in dioxan (15 ml.) was added hydrochloric acid (10 ml.; 6N). The initially colourless solution soon became deep red and after being stirred at room temperature for 2 hr. it was shown by t.l.c. that no starting material remained. The reaction mixture was neutralised with dilute sodium hydroxide and extracted with ethyl acetate. The ethyl acetate was

washed with water, dried (Na_2SO_4), and evaporated under reduced pressure. The resulting gum was separated into two components by chromatography on a column of Kieselgel H (73 g.) and Hyflosupercel (7 g.) using 15% ethanol–85% benzene as eluant. *Phenalenone A* (11; R^1 = H, R^2 = R^3 = Me) was isolated from the faster-running orange band (which fluoresced bright green in u.v. light) as orange crystals (146 mg.). Recrystallisation from ligroin (b.p. 60—80°) gave the material as orange needles (120 mg.), m.p. 150—151°, $[\alpha]_D$ +131° (*c* 1·00 in $CHCl_3$). Concentration of the mother liquor gave a second crop (16 mg.), m.p. 145—147° (Found: C, 71·1; H, 6·1; *m/e*, 354·1483. $C_{21}H_{22}O_5$ requires C, 71·15; H, 6·25%; *M*, 354·1467), $\lambda_{max.}$ 215, 252, 270 (infl.), 356 (infl.), 378, 453 (infl.), and 472 nm. (log ε 4·51, 4·32, 3·90, 4·17, 3·96, 3·91, and 3·98); $\nu_{max.}$ 1540, 1620, and 3400 $cm.^{-1}$. Treatment of phenalenone A (30 mg.) with acetic anhydride (0·5 ml.) and pyridine (1 ml.) at room temperature for 12 hr. gave, after work-up in the usual way, a yellow gum which was separated by preparative t.l.c. (20 × 20 cm. plate, 0·5 mm. coating of Kieselgel G; 10% ether–90% benzene) into unchanged starting material (18 mg.), m.p. 149—150° and the derived *acetate*, which could not be crystallised (Found: *m/e*, 396·1558. $C_{23}H_{24}O_6$ requires *M*, 396·1573), $\nu_{max.}$ ($CHCl_3$) 1560, 1585, 1625, and 1765 $cm.^{-1}$.

From the slower-moving dark orange band (which did not fluoresce in u.v. light) *quinone methide I* (15) was obtained, after recrystallisation from a mixture of chloroform and ligroin (b.p. 60—80°), as yellow needles (248 mg.), m.p. 166—167°, $[\alpha]_D$ −520° (*c* 0·99, in $CHCl_3$) (Found: C, 67·5; H, 6·6; *m/e*, 372·1572. $C_{21}H_{24}O_6$ requires C, 67·75; H, 6·45%; *M*, 372·1573), $\lambda_{max.}$ 229, 240 (infl.), 305, 310 (infl.), and 405 nm. (log ε 4·43, 4·19, 4·27, 4·25, and 3·68); $\nu_{max.}$ 1590, 1620, 1640, 3360, and 3480 $cm.^{-1}$; τ −2·35 (1H, s, 4-OH), 3·01 (1H, s, 5-H or 9-H), 3·30 (1H, s, 9-H or 5-H) 4·92 (1H, s, 7-H), 5·84 (3H, s, Ar-OMe), 6·16 (3H, s, Ar-OMe), 6·53 [1H, q, *J* 6 Hz, C*H*(Me)O], 7·50 (1H, s, 8-OH), 7·58 (3H, s, 6-CH_3), 8·79 (3H, s, CMe_2), 8·90 (3H, d, *J* 6 Hz, *Me*–CH–O–), and 8·94 (3H, s, CMe_2).

(*b*) A solution of glycol A (70 mg.) in dioxan (1 ml.) was shaken with concentrated hydrochloric acid (15 ml.) at room temperature for 8 min. The reaction mixture was neutralised with dilute sodium hydroxide and extracted with chloroform. The chloroform extract was washed with water, dried (Na_2SO_4) and evaporated under reduced pressure to give a yellow gum, which was shown by t.l.c. to be a mixture of two components. These were separated by preparative t.l.c. (20 × 20 cm., 0·5 mm. coating of Kieselgel G) using 30% ether–70% benzene as eluant. The material of higher R_F value (10 mg.) was identical with phenalenone A (m.p., mixed m.p.) while the material of lower R_F value (36 mg.) gave, after recrystallisation from ligroin, *phenalenone B* (10), m.p. 109—100°, (Found: C, 71·6; H, 6·55; *m/e*, 368·1620. $C_{22}H_{24}O_5$ requires C, 71·7; H, 6·55%; *M*, 368·1624), $\lambda_{max.}$ 213, 257 (infl.). 277, 337, 350, 374, and 440 nm. (log ε 4·53, 4·23, 4·43, 3·32, 3·94, 3·96, and 4·00); $\nu_{max.}$ 1560, 1610, and 1638 $cm.^{-1}$.

(*c*) A solution of glycol A (50 mg.) in dry benzene (8 ml.) was heated on a water-bath with toluene-*p*-sulphonic acid (25 mg.) for 2 min.; it was then cooled to room temperature, diluted with water, and extracted with benzene. The benzene extract was washed with water, dried (Na_2SO_4) and evaporated under reduced pressure. Preparative t.l.c. (20 × 20 cm. plate, with a 0·5 mm. coating of Kieselgel G), using 30% ether–70% benzene as eluant gave phenalenone A (31 mg.), m.p. 147—149° after recrystallisation from ligroin and phenalenone B (15 mg.), m.p. 108—110° after recrystallisation from the same solvent. The m.p.s of both products were undepressed on admixture with authentic specimens.

Acid Treatment of (+)-Glycol B (9; R = H).—A solution of (+)-glycol B (101 mg.) in dioxan (3 ml.) was stirred at room temperature for 2 hr. with hydrochloric acid (2 ml.; 6N). The reaction mixture was worked up as described in the acid treatment of (+)-glycol A [preceding experiment, method (*a*)] to give a yellow gum which was separated into two components by chromatography on a column of Kieselgel H (35 g.) and Hyflosupercel (3·5 g.) using ether–benzene (3 : 17) as eluant. The product of higher R_F (24 mg.) gave, after recrystallisation from ligroin, (−)-enantio-*phenalenone A* as orange needles, m.p. 147—151°, $[\alpha]_D$ −121° (*c* 0·86, in $CHCl_3$) (Found: C, 71·05; H, 6·1; *m/e*, 354·1453. $C_{21}H_{22}O_5$ requires C, 71·15; H, 6·25%; *M*, 354·1567). On admixture with (+)-phenalenone A (m.p. 150—151°) obtained from (+)-glycol A as described above the m.p. was depressed by 15°. Both enantiomers gave superposable i.r., n.m.r., u.v., and mass spectra; their c.d. curves were enantiomeric.

The band of lower R_F gave, after removal of solvent, a yellow gum (60 mg.) which crystallised on trituration with ligroin and was recrystallised from a mixture of chloroform and ligroin to give *quinone methide II* (15) as yellow rosettes, m.p. 154—155° (depressed to 144° on admixture with quinone methide I), $[\alpha]_D$ −84° (*c* 1·10, in $CHCl_3$) (Found: C, 68·0; H, 6·45; *m/e*, 372·1572. $C_{21}H_{24}O_6$ requires C, 67·75; H, 6·45%; *M*, 372·1573), $\lambda_{max.}$ 227, 305, 310 (infl.), and 403 nm. (log ε 4·55, 4·37, 4·36, and 3·90); $\nu_{max.}$ 1585, 1610, 1640, and 3400 $cm.^{-1}$; τ −2·48 (1H, s, 4-OH), 3·09 (1H, s, 5-H or 9-H), 3·37 (1H, s, 9-H or 5-H), 5·13 (1H, s, 7-H), 5·83 (3H, s, Ar-OMe), 6·16 (3H, s, Ar-OMe), 6·16 [1H, q, *J* 6 Hz, C*H*(Me)O], 7·05 (1H, s, 8-OH), 7·53 (3H, s, 6-CH_3), 8·88 (3H, s, CMe_2), 8·94 (3H, d, *J* 6 Hz, *Me*–CH–O–), and 9·47 (3H, s, CMe_2).

Acid-catalysed Dehydration of Quinone Methide I (15).—A solution of quinone methide I (35 mg.) in benzene (4 ml.) was heated with toluene-*p*-sulphonic acid (20 mg.) at 100° for 5 min. The reaction mixture was cooled, diluted with more benzene, washed with water, dried (Na_2SO_4) and evaporated *in vacuo* to yield a yellow gum. Chromatography on a column of Kieselgel H (17 g.) and Hyflosupercel (1·7 g.) using ether–benzene (1 : 9) as eluant gave *phenalenone D* (11; R^1 = R^2 = Me, R^3 = H) (15 mg.) which crystallised from ligroin as yellow crystals, m.p. 121—124° (Found: C, 71·25; H, 6·1; *m/e*, 354·1456. $C_{21}H_{22}O_5$ requires C, 71·15; H, 6·25%; *M*, 354·1467), $\lambda_{max.}$ 214, 231, 241, 268 (infl.), 281 (infl.), 370, 411, 420 (infl.), and 445 (infl.) nm. (log ε 4·54, 4·39, 4·37, 4·01, 3·89, 4·16, 4·10, 4·08, and 4·00); $\nu_{max.}$ 1585 and 1615 $cm.^{-1}$.

Methylation of Phenalenone A (11; R^1 = H, R^2 = R^3 = Me).—Freshly prepared silver oxide (100 mg.) and methyl iodide (0·5 ml.) were added to a stirred solution of phenalenone A (35 mg.) in chloroform (2 ml.). After 60 min. more silver oxide (40 mg.) and methyl iodide (0·2 ml.) were added; similar quantities were added thereafter at 90 min. intervals. After 5½ hr., when t.l.c. revealed that the starting material had been consumed and that two products had been formed, the solution was filtered and evaporated *in vacuo*. Preparative t.l.c. (20 × 20 cm. plate, with a 0·5 mm. coating of Kieselgel G), using chloroform as eluant, gave, from the band of higher

R_F, phenalenone B (10) (9·5 mg.), m.p. 109—110° (undepressed on admixture with an authentic sample, m.p. 108—110°), and from the band of lower R_F value, *phenalenone C* (12) which gave orange crystals (24 mg.), m.p. 152—153°, $[\alpha]_D$ −11° (*c* 0·74, in $CHCl_3$) from chloroform–ligroin (Found: C, 71·7; H, 6·6; *m/e*, 368·1617. $C_{22}H_{24}O_5$ requires C, 71·7; H, 6·55%; *M*, 368·1624), $\lambda_{max.}$ 249, 271 (infl.), 354, 370 (infl.), 442, and 464 (infl.) nm. (log ε 4·31, 4·13, 4·17, 4·06, 3·89, and 3·86); $\nu_{max.}$ 1540, 1580, and 1620 $cm.^{-1}$.

Demethylation of Phenalenone B (10).—A solution of phenalenone B (15 mg.) in dry benzene (8 ml.) was heated on a water-bath with toluene-*p*-sulphonic acid (25 mg.) for 5 min. The reaction mixture was worked up as described in procedure (*c*) for the acid treatment of (+)-glycol A to give phenalenone A (11; R^1 = H, R^2 = R^3 = Me) (12 mg.), m.p. 148—149°, undepressed on admixture with an authentic specimen.

Reduction of Quinone Methide I (15) *with Zinc and Acetic Acid.*—A solution of quinone methide I (60 mg.) in glacial acetic acid (3 ml.) was shaken with acid-washed zinc dust (1 g.) at room temperature for 20 min. The initially yellow solution quickly became colourless, but when the solution was filtered and the solid residue washed with chloroform the combined filtrate and washings again became yellow. The chloroform solution was washed with water until the washings were neutral, dried, and evaporated *in vacuo*. The crystalline residue was purified by preparative t.l.c. (20 × 20 cm. plate, with a 0·5 mm. coating of Kieselgel G), using methanol–chloroform (1 : 9) as eluant. From the major yellow band, which fluoresced yellow in u.v. light, *phenalenone E* (17) was obtained, after recrystallisation from ether, as yellow needles (42 mg.), m.p. 140—141°, $[\alpha]_D$ −31° (*c* 0·94, in $CHCl_3$) (Found: C, 70·7; H, 6·5; *m/e*, 356·1609. $C_{21}H_{24}O_5$ requires C, 70·75; H, 6·8%; *M*, 356·1624), $\lambda_{max.}$ 242, 260 (infl.), 348, 415, and 438 nm. (log ε 4·49, 4·12, 4·24, 4·00, and 3·97); $\nu_{max.}$ 1568, 1592, 1633, 3440, and 3500 $cm.^{-1}$.

Treatment of (−)-phenalenone E (48 mg.) with acetic anhydride (0·5 ml.) and pyridine (1 ml.) at room temperature for 40 hr. gave, after work-up in the usual way, a yellow gum which was purified by preparative t.l.c. (20 × 20 cm. plate, with a 0·5 mm. coating of Kieselgel G) using ether–benzene (3 : 10) as eluant. In this way, *phenalenone E diacetate* (40 mg.) was obtained, m.p., after successive recrystallisation from methanol and ether–ligroin, 139—141° (Found: C, 68·5; H, 6·35; *m/e*, 440·1826. $C_{25}H_{28}O_7$ requires C, 68·15; H, 6·4%; *M*, 440·1835), $\lambda_{max.}$ 240, 260, 342 (infl.), 352, and 392 (infl.) nm. (log ε 4·45, 4·30, 4·01, 4·18, and 3·73); $\nu_{max.}$ 1620, 1730, and 1768 $cm.^{-1}$.

Reduction of Quinone Methide II (15) *with Zinc and Acetic Acid.*—Reduction of quinone methide II (97 mg.) with zinc and acetic acid in the same way as described above for quinone methide I gave (+)-enantio-*phenalenone E* (17) which crystallised from ether as yellow needles (38 mg.), m.p. 138—139°, $[\alpha]_D$ +28° (*c* 0·77, in $CHCl_3$) (Found: C, 71·0; H, 6·45. $C_{21}H_{24}O_5$ requires C, 70·75; H, 6·8%). The enantiomers of phenalenone E gave superposable n.m.r., u.v., i.r., and mass spectra, and a mixture of the two showed no depression in m.p.

We thank Professor D. H. R. Barton for presenting us with samples of compounds in the atrovenetin and herqueinone series prepared in the earlier work,[5] Dr. R. Thomas for providing us with a culture of *P. herquei* (strain I.M.I. 89376), and Professor W. Klyne and Dr. M. Scopes for measuring the c.d. curves of some of the compounds described in this paper. Acknowledgment is also made to the S.R.C. for the award of a research studentship to J. S. B.

[1/1554 *Received, Augus 26th,* 1971]