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764. *The Chemistry of Fungi. Part XLVII.*[1] *The Constitution of Ergochrysin A, Secalonic Acid A, and Secalonic Acid B*

By J. W. ApSimon, J. A. Corran, N. G. Creasey, W. Marlow, W. B. Whalley, and (in part) K. Y. Sim

Ozonolysis of ergochrysin A, $C_{29}H_{25}O_{12}(CO_2Me)$, one of the pigments of ergot, yields hemiergoflavin-2-carboxylic acid (VIII), pyrolysis forms the benzoate (IV; R = Me), and fusion with alkali gives the acid (IV; R = H) with the biphenyl (V; R^1 = COMe, R^2 = H). Vigorous acetylation of ergochrysin A forms the hemiergoflavin (VI; $R^1 = R^2$ = Ac), which is degraded by acid to carbon dioxide, the acid (IV; R = H), and the hemiergoflavin (VII; R = H).

Tri-*O*-methylergochrysinone A (X), formed by oxidation of tri-*O*-methylergochrysin A (I; $R^2 = R^3$ = H, R^1 = Me), gives the biphenyl (XI) upon degradation with alkali.

Ergochrysin A undergoes mutarotation in pyridine to yield an isomer, isoergochrysin A. These and other observations are rationalised in terms of the structures (I; $R^2 = R^3$ = H, R^1 = Me) for tri-*O*-methylergochrysin A and (I; $R^1 = R^2 = R^3$ = H) or (III) for ergochrysin A.

Constitutions are derived for the closely related colouring matters, secalonic acid A and secalonic acid B.

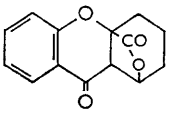
The biosynthesis of the ergot pigments is discussed.

In continuation of our studies [1,2] on the ergot pigments, we have investigated the amorphous residues remaining after the separation of ergoflavin, and have isolated a second, yellow, optically active, crystalline pigment which is another representative of the bis(hexahydroxanthonyl) group of pigments (cf. ergoflavin [1]). Our pigment is almost certainly ergochrysin, which was originally isolated by Bergmann in 1932.[3] Although a direct comparison has not been possible * we propose to regard our compound as ergochrysin and to modify the name to ergochrysin A.† This Paper describes the derivation

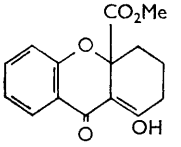
* None of the material isolated by Bergmann is now extant (personal communication to W. B. W. from the late Professor W. Bergmann).

† In addition to ergoflavin [1, 2] and the pigments described in this Paper, other variants upon the bis(hexahydroxanthonyl) theme have been isolated by Professor P. de Mayo and his group.[4] Since it is likely that further compounds of this class will be isolated the problem of nomenclature has become acute. After consultation with the Editor, Professor de Mayo and we have adopted the following system.

Pigments which contain two units having the essential features of (i) (irrespective of the positions of linkage between the two aromatic rings) are termed ergoflavin A, B, C, etc. Since ergoflavin is as yet the only known representative of this group the use of the suffix is not at present employed.



(i)



(ii)

Similarly, pigments which contain one unit of type (i) together with a unit of type (ii) are called ergochrysin A, B, C, etc. Thus, ergochrysin (old nomenclature) [3] becomes ergochrysin A. Ergochrysin B has been isolated and is the subject of a separate Communication.[4]

Finally, those pigments which contain two units of type (ii) are called secalonic acid A, B, C, etc. Thus, secalonic acid (old nomenclature) [11] is now called secalonic acid A. Chrysergonic acid [11] has been shown to be a mixture of secalonic acid A and secalonic acid B (cf. Franck *et al.*,[9] and de Mayo and his co-workers.[4] Secalonic acids B and C have been isolated.[4]

The term chrysergonic acid, when used in the present Paper, refers to the mixture of secalonic acid A and secalonic acid B isolated by Stoll *et al.*[11]

[1] Part XLVI, preceding Paper.
[2] G. Eglinton, F. E. King, G. Lloyd, J. W. Loder, J. R. Marshall, A. Robertson, and W. B. Whalley, *J.*, 1958, 1833.
[3] W. Bergmann, *Ber.*, 1932, **65**, 1486, 1489.
[4] Personal communication from Professor P. de Mayo.

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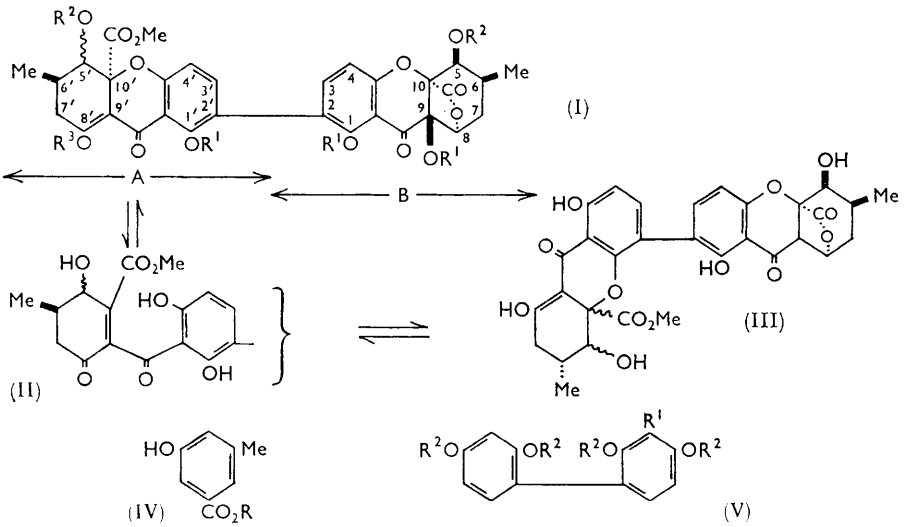
of the structure (I; $R^1 = Me$, $R^2 = R^3 = H$) for tri-*O*-methylergochrysin A, and (I; $R^1 = R^2 = R^3 = H$) or the corresponding angular structure (III) for ergochrysin A. A preliminary account of this work has been published.[5]

The metabolite, $C_{29}H_{25}O_{12}(CO_2Me)$, contains one methoxyl group in an ester residue. Bergmann [3] recorded no methoxyl analysis for his compound but suggested the formula $C_{28}H_{28}O_{12}$. Ergochrysin A and its derivatives retain solvent even more tenaciously than does ergoflavin and must be dried intensively before satisfactory analytical figures are obtainable. The infrared spectrum has peaks at **3521** and **3165** (OH), **1802** (γ-lactone), **1742** (aliphatic ester), together with aromatic absorption at **1618**, **1592**, and **1565** $cm.^{-1}$. The n.m.r. spectrum (in pyridine)s hows a doublet at τ 8·73 ($J = 6$ c./sec., 2 $>$CHMe, 6 protons) and a singlet at τ 6·45 (CO_2CH_3, 3 protons). Ergochrysin A has obvious similarities to ergoflavin,[1] and upon oxidation with potassium permanganate gives (±)-methyl-



succinic acid. Unlike ergoflavin, ergochrysin A exhibits acidic properties, due to the β-diketonic system, and is readily soluble in sodium carbonate solution. The intense red-brown ferric reaction of ergochrysin A is caused by this group; when masked by the formation of the enol ether (I; $R^1 = R^2 = H$, $R^3 = Me$), the intense green ferric reaction of the 1-hydroxyanthone type nucleus is apparent. Pyrolysis of the metabolite yields methyl 3-hydroxy-5-methylbenzoate (IV; R = Me), which is undoubtedly the unidentified substance which Bergmann [3] obtained by the same method. Fusion of ergochrysin A with alkali gave 3-hydroxy-5-methylbenzoic acid (IV; R = H) (cf. Bergmann [3]) together with a substance which, after conversion into the methyl ether, $C_{14}H_8O(OMe)_4$, was identified as 3-acetyl-2,2′,4,4′-tetramethoxybiphenyl (V; $R^2 = Me$, $R^1 = COMe$) (Bergmann [3] obtained 2,2′,4,4′-tetrahydroxybiphenyl by alkali fusion). The general properties of ergochrysin A, namely, *inter alia*, the positive Gibbs test, the formation of a dinitro-derivative (now regarded as the 4,4′-derivative), and the isolation of the biphenyl (V; $R^1 = COMe$, $R^2 = H$), clearly confirmed its similarity to ergoflavin.

Acetylation of ergochrysin A at room temperature gave an unstable hexa-acetate which when purification was attempted, was rapidly converted into the penta-acetate (I; $R^3 = H$, $R^1 = R^2 = Ac$) whose n.m.r. spectrum showed signals at τ 2·31—3·07 (aromatic multiplet 4 protons), 6·27 (singlet, CO_2CH_3, 3 protons), 7·77, 7·82, 7·87, 7·91, and 7·97 (singlets 5 O·CO·CH_3), and 8·97 (doublet, $J = 5$ c./sec., 6 protons, 2 $>$CHMe). Vigorous acetylation

[5] J. W. ApSimon, J. A. Corran, N. G. Creasey, W. Marlow, W. B. Whalley, and (in part) K. Y. Sim, *Proc. Chem. Soc.*, **1963**, **313**.

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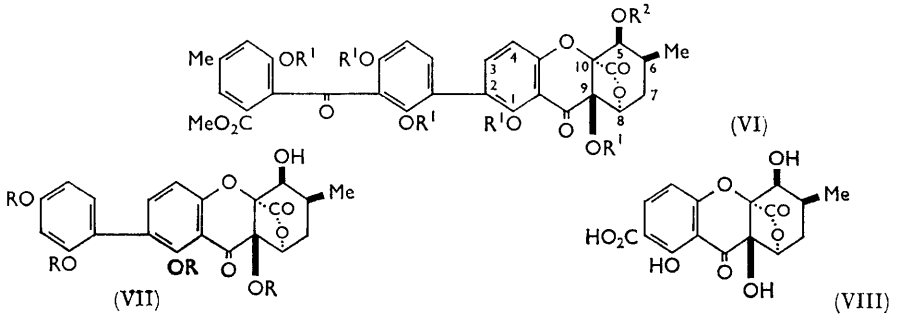
of this product (or of ergochrysin A) gave the benzophenone (VI; $R^1 = R^2 = Ac$), whose constitution was established by the following considerations. The infrared spectrum showed peaks at 1818 (γ-lactone), 1786 (acetate carbonyl), and 1745 (ester carbonyl) cm.$^{-1}$. The n.m.r. spectrum included signals at τ 2·49—3·03 (aromatic multiplet, 6 protons), 4·24 (doublet, J = 6 c./sec., C-8-proton), 4·99 (singlet, AcO–C–*H*, 1 proton), 6·33 (singlet, Ar·CO_2CH_3, 3 protons), 7·62 (singlet, Ar·CH_3, 3 protons), 7·90 (singlet, 2 CH_3·CO·O, 6 protons), 7·98 (singlet, Ar·O·CO·CH_3, 3 protons), 8·03 (singlet, Ar·O·CO·CH_3, 3 protons), 8·42 (singlet, Ar·O·CO·CH_3, 3 protons), 8·98 (doublet, J = 6 c./sec., >CHMe, 3 protons). Degradation of the benzophenone (VI; $R^1 = R^2 = Ac$) with hydrobromic acid gave



carbon dioxide, the acid (IV; R = H), and 2-(2,4-dihydroxyphenyl)hemiergoflavin (VII; R = H) which formed hemieroflavin-2-carboxylic acid (VIII) [1] upon ozonolysis.

In a comparison of the pigments isolated by us and by Professor de Mayo's group it became evident that our ergochrysin A was the substance termed pigment V by them.[4] The identity was confirmed in both laboratories by a comparison of the pigment and the acetate (VI; $R^1 = R^2 = Ac$).

Ozonolysis of ergochrysin A also gave hemiergoflavin-2-carboxylic acid (VIII). The complete structure and absolute stereochemistry of one half of the ergochrysin A molecule was therefore established. The formation of these derivatives in conjunction with the spectral evidence clearly established the structure of the benzophenone as (VI; $R^1 = R^2 = Ac$). Carefully controlled deacetylation of (VI; $R^1 = R^2 = Ac$) gave 2-[2,4-dihydroxy-3-(2-hydroxy-6-methoxycarbonyl-4-methylbenzoyl)phenyl]hemiergoflavin (VI; $R^1 = R^2 = H$), which was methylated to yield (VI; $R^2 = H$, $R^1 = Me$), $\nu_{max.}$ 3521 (OH), 1802 (γ-lactone), 1730 (aryl ester), 1707 and 1675 (ketone), and 1597 and 1575 (aromatic) cm.$^{-1}$. The n.m.r. spectrum included signals at τ 2·29—3·33 (aromatic multiplet, 6 protons), 6·21 6·27, 6·40, and 6·67 (4 aryl methyls, 12 protons), 6·36 (Ar·CO·O·CH_3, 3 protons), 6·56 (9-methoxyl, 3 protons), 7·62 (Ar·CH_3, 3 protons), and 8·82 (doublet, J = 6 c./sec., >CH·CH_3, 3 protons). A small quantity of a second product, $\nu_{max.}$ 3497 (OH), 1799 (γ-lactone), and 1718 (aryl ester) cm.$^{-1}$, had the properties of a xanthone and may be formulated as (XII) or (XIII).

Methylation of 2-(2,4-dihydroxyphenyl)hemiergoflavin (VII; R = H) gave 2-(2,4-dimethoxyphenyl)di-*O*-methylhemieroflavin (VII; R = Me) which was oxidised by the Jones reagent [6] to 2-(2,4-dimethoxyphenyl)di-*O*-methylergoflavone (IX), $\nu_{max.}$ 1808 (γ-lactone), τ 2·43—3·60 (aromatic multiplet, 5 protons), 4·62 (doublet, C-8 proton), 6·19, 6·28, 6·51, and 6·67 (singlets, 4 methoxyls, 12 protons), and 8·73 (doublet, J 5·5 c./sec., >CH·CH_3, 3 protons). In agreement with its structure, degradation of (IX) with base gave oxalic acid with 3-acetyl-4-hydroxy-2,2′,4′-trimethoxybiphenyl. The methyl ether (V; R^1 = COMe, R^2 = Me) was identical with an authentic specimen [6] and with the methyl ether of the product obtained from the alkali fusion of ergochrysin A. The biphenyl (V; R^1 = COMe, R^2 = Me) was further characterised by reduction to 3-ethyl-2,2′,4,4′-

[6] A. Bowers, T. G. Halsall, E. R. H. Jones, and A. J. Lemin, *J.*, 1953, 2548.

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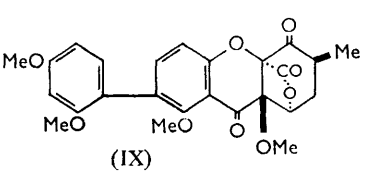
tetramethoxybiphenyl (V; $R^1 = Et$, $R^2 = Me$), which was identical with a synthetic specimen.[7]



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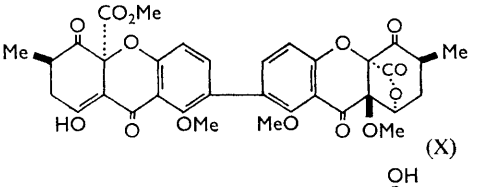

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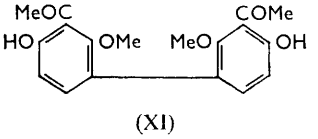

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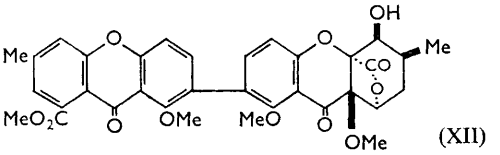

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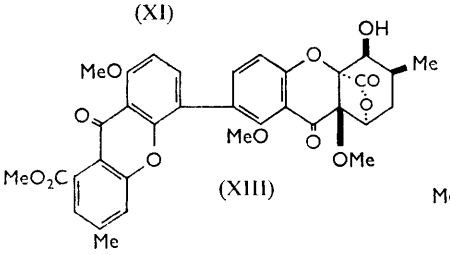

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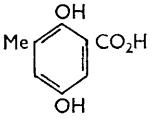

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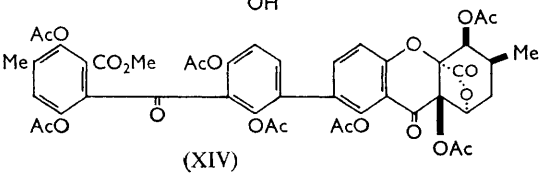
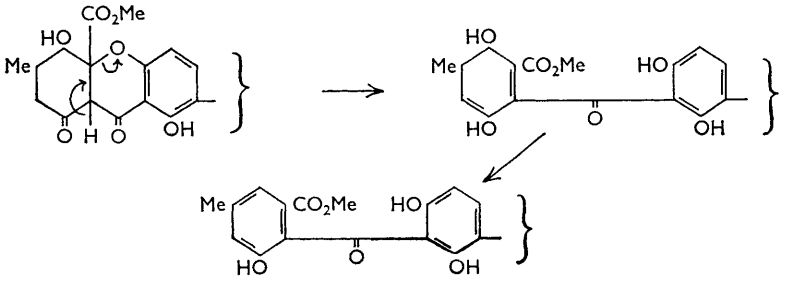


(XIV)

Methylation of ergochrysin A gives 1,1′,9-tri-*O*-methylergochrysin A (I; $R^1 = Me$, $R^2 = R^3 = H$), $\nu_{max.}$ 1802 (γ-lactone), 1730 (ester carbonyl), 1681 (unchelated ketone), and 1595 (β-diketone) cm.$^{-1}$, τ 4·28 (singlet, 1 proton, exchangeable with D_2O, enolic hydroxyl), 2·46 (triplet, $J = 9$ c./sec., one pair of *ortho*-aromatic protons), 3·00 (triplet, $J = 9$ c./sec., one pair of *ortho*-aromatic protons), 6·32, 6·38, 6·44, and 6·57 (singlets, 4 O·CH_3, 12 protons). Since the spectrum shows the presence of two aliphatic *C*-methyl residues and only four aromatic protons, as two pairs of *ortho*-protons, it is clear that the methyl 3-hydroxy-5-methylbenzoate, obtained by pyrolysis of ergochrysin A, and the same residue which constitutes the terminal unit of the benzophenone (VI) must be an artifact. Oxidation of tri-*O*-methylergochrysin A (I; $R^1 = Me$, $R^2 = R^3 = H$) gives 1,1′,9-tri-*O*-methylergochrysinone A (X), $\nu_{max.}$ 1812 (γ-lactone), 1748 (ester carbonyl), 1689 (unchelated carbonyl), and 1600 (β-diketone) cm.$^{-1}$. Degradation of (X) with alkali furnished oxalic acid together with 3,3′-diacetyl-4,4′-dihydroxy-2,2′-dimethoxybiphenyl (XI), previously isolated from the degradation of the corresponding derivatives of ergoflavin.[1,2,7]

These facts may be rationalised in terms of the structure (I; $R^1 = Me$, $R^2 = R^3 = H$) for tri-*O*-methylergochrysin A; thus, ergochrysin A may be represented as (I; $R^1 = R^2 = R^3 = H$) or the equivalent angular structure (III) (see later). On this basis, the genesis of the benzophenone (VI; $R^1 = R^2 = Ac$) is by way of the following sequence:



[7] J. W. ApSimon, N. G. Creasey, W. Marlow, K. Y. Sim, and W. B. Whalley, Part XLVIII, following Paper.

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The presence of the secondary hydroxyl group in the moiety A of ergochrysin A has been substantiated as follows. The n.m.r. spectrum of tri-*O*-methylergochrysin A exhibits a signal (equivalent to 1 proton) in the range τ 4—5, due to the C-8 proton (cf. ergoflavin and its derivatives [1]), whereas the tri-*O*-acetate (I; $R^1 = Me$, $R^2 = R^3 = Ac$) displays three separate signals (equivalent to three protons) in the same region. These signals are assigned to the C-8 proton and to the two methine protons at C-5 and C-5′. The paramagnetic shift of these two protons is characteristic of the secondary alcoholic hydroxyl groups.[8] The position of the 5′-hydroxyl residue has been confirmed as follows. Tri-*O*-methylergochrysinone A (X) was converted by vigorous acetylation into the benzophenone (XIV), which was degraded by hydrobromic acid to 2,5-dihydroxy-3-methylbenzoic acid (XV). The 2-hydroxyl group of this acid corresponds to the 4′-ketone function in (X) and hence with the presence of a secondary alcoholic hydroxyl function at the same position in the parent tri-*O*-methylergochrysin A.

The >CHMe group at C-6 in the ergoflavin moiety of ergochrysin A has the (*S*)-absolute configuration.[1] Since (±)-methylsuccinic acid is produced by the oxidation of ergochrysin A it follows that C-6′ has the opposite, (*R*)-configuration as, *e.g.*, in (I).

In contrast to ergoflavin, ergochrysin A undergoes mutarotation in pyridine solution at room temperature. Ergoflavin is recovered unchanged after boiling with pyridine, but under these conditions ergochrysin is converted into an isomer, isoergochrysin A, which gives (±)-methylsuccinic acid on oxidation, methyl 3-hydroxy-5-methylbenzoate on pyrolysis, the benzophenone (VI; $R^1 = R^2 = Ac$) upon vigorous acetylation, and tri-*O*-methylergochrysin A (I; $R^1 = Me$, $R^2 = R^3 = H$) upon methylation. We originally suggested [5] that this isomerisation involved inversion of the configuration at C-9′. Further examination of ergochrysin A and its derivatives clearly shows that this view is untenable and that ergochrysin A and its derivatives exist largely in the enolic modification. Hence, stable products which are epimeric at C-9′ are unlikely (cf. Franck *et al.*[9]). We now believe that this isomerisation involves a chalcone–flavanone type of interconversion [cf. (I) $\rightleftharpoons$ (II) $\rightleftharpoons$ (III)] which may result in (*a*) inversion of configuration at C-10′, (*b*) a change from a linear structure, type (I), to an angular structure, type (III), or *vice versa*, and (*c*) a combination of (*a*) and (*b*). Thus, whilst the tri-*O*-methyl ether of ergochrysin A is unequivocally defined as (I; $R^1 = Me$, $R^2 = R^3 = H$),* ergochrysin A could be the appropriate stereochemical modification of the linear or angular formula types (I) or (III), respectively. By analogy with ergoflavin we tentatively adopt the linear structure (I; $R^1 = R^2 = R^3 = H$) for ergochrysin A.

Since methanol had been used at various stages during the isolation of ergochrysin A it was possible that the methoxyl group in the metabolite could be an artifact, resulting either from esterification of the corresponding carboxylic acid or from a transesterification process. This possibility was excluded by performing one extraction in which methanol was replaced by ethanol, when ergochrysin A was obtained. The presence of a methoxyl rather than an ethoxyl residue was confirmed by the isolation of methyl 3-hydroxy-5-methylbenzoate upon pyrolysis.

The n.m.r. spectra of ergochrysin A and its derivative indicate that the molecule is non-planar (cf. ergoflavin [1]). Thus, *e.g.*, the four methoxyl signals in the n.m.r. spectrum of tri-*O*-methylergochrysin A may confidently be assigned as follows: (*a*) τ 6·27 (CO_2CH_3) (cf. the signal for the corresponding methyl ester residue in penta-*O*-acetylergochrysin A at τ 6·32), (*b*) τ 6·57 (the 9-methoxyl) (cf. the value, *ca.* τ 6·6, for the same signal in the analogous derivatives of ergoflavin [1]); hence the signals at τ 6·38 and 6·44 must be assigned

* Since methylation of ergochrysin A and of isoergochrysin A yields the same tri-*O*-methyl ether (I; R = Me, $R^2 = R^3 = H$), it is not possible at this stage to know whether this ether corresponds to ergochrysin A or to isoergochrysin A. Until this point has been clarified, and for purposes of nomenclature only, we call this ether tri-*O*-methylergochrysin A.

[8] L. M. Jackman, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," Pergamon Press, London, 1959, p. 55.

[9] B. Franck and E. M. Gottschalk, *Angew. Chem. Internat. Edn.*, 1964, **3**, 441.

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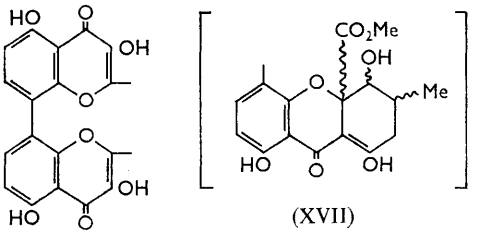
to the 1- and 1′-methoxyls (though not necessarily in that order). Consequently, as in ergoflavin,[1] these methoxyls must be shielded by the adjacent aromatic ring, whence it follows that the dihedral angle between the moieties (A) and (B) is large.

In addition to the pigments ergoflavin, ergochrysin A, and those to be reported by Professor de Mayo's group,[4] others have been isolated from ergot. Thus Kraft [10] obtained a pigment, secalonic acid, to which he assigned the formula $C_{14}H_{14}O_6$. This was revised to $C_{28}H_{28}O_{14}$ by Bergman [3] and to $C_{31}H_{30\text{-}32}O_{14}$ by Stoll *et al.*,[11] who also obtained chrysergonic acid, $C_{32}H_{30\text{-}32}O_{14}$. Franck, Thiele, and Reschke [12] initially claimed that secalonic acid (now called secalonic acid A) and chrysergonic acid were the same compound, $C_{28}H_{24\text{-}28}O_{10}(CO_2Me)$, and advanced the partial formula (XVI), in which the 3,5-dihydroxychromone system was invoked to account for the acidity (pK_{DMF} 8·5) of the metabolite.

In view of the obvious similarities between ergochrysin A, secalonic acid A, and chrysergonic acid, *e.g.*, (*a*) the similar molecular formulæ,[11] (*b*) the mutarotation exhibited by the three pigments in pyridine,[11] and (*c*) the formation of methylsuccinic acid and of 2,2′,4,4′-tetrahydroxybiphenyl upon fusion with alkali,[11] we were prompted to speculate upon the structures of secalonic acid A and chrysergonic acid. We were intrigued by the possibility, which has been confirmed in the sequel, that these two metabolites were diastereoisomers of the molecular formula, $C_{28}H_{24}O_{10}(CO_2Me)_2$, type (XVII), comprising two units of the moiety (A) in ergochrysin A (I). Through the courtesy of Dr. J. Renz, of Sandoz Ltd., who placed the remainder of his original isolates at our disposal, we were quickly able to confirm our speculation. A preliminary report of our conclusions has been published.[5]



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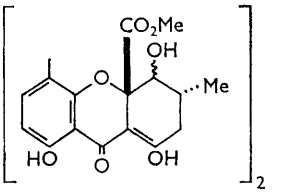
(XVII)



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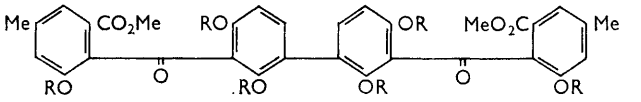
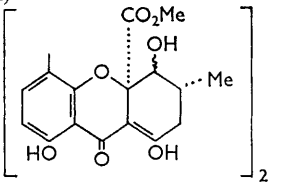


(XVIII)



(XX)

The specimen of secalonic acid provided by Dr. Renz was a homogeneous compound (R_F 0·44) having the expected formula, $C_{28}H_{24}O_{10}(CO_2Me)_2$, devoid of lactonic functions, $\nu_{max.}$ 3584 (OH), 1748 (aliphatic ester), and 1626 (ketone) cm.$^{-1}$, and was apparently identical with secalonic acid A (cf. ref. 9). Although we originally regarded chrysergonic acid as an homogeneous material, further investigation using the method of Franck *et al.*,[9] has shown it to be a mixture of secalonic acid A and secalonic acid B (*ca.* 2 : 1) (cf. Franck *et al.*[9]). This does not, however, invalidate our conclusions, and our derivation of the formula $C_{28}H_{24}O_{10}(CO_2Me)$ for secalonic acid B. Secalonic acid A and secalonic acid B are not carboxylic acids, but acidic β-diketones, devoid of lactonic functions. Both pigments exhibit intense red-brown ferric reactions in alcohol, characteristic of the β-diketonic system. However, when this is masked by formation (diazomethane) of the enol ether, the intense green ferric reaction of the 1-hydroxyxanthone type nucleus is readily apparent

[10] F. Kraft, *Arch. Pharm.*, 1906, **244**, 336.
[11] A. Stoll, J. Renz, and A. Brack, *Helv. Chim. Acta*, 1952, **35**, 2022.
[12] B. Franck, O. W. Thiele, and T. Reschke, *Chem. Ber.*, 1962, **95**, 1328.

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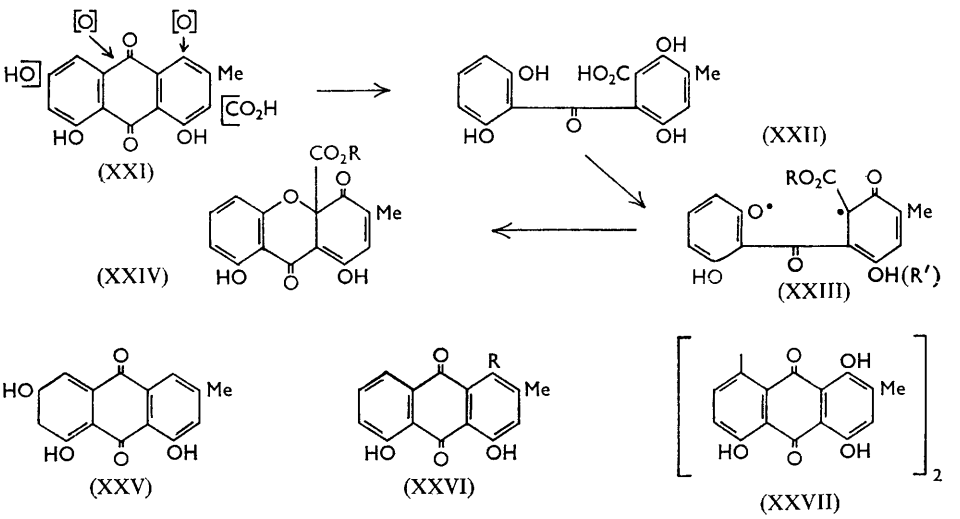
(cf. ergochrysin A). When pyrolysed, both pigments yield methyl 3-hydroxy-5-methylbenzoate (cf. ergochrysin A), and upon vigorous acetylation give (quantitatively) the same optically inactive bis(benzophenone) (XVIII; R = Ac) (cf. ergochrysin A), which contains all the carbon atoms of the original metabolite (contrast Stoll *et al.*[11]). The optical inactivity of (XVIII; R = Ac) was confirmed by an examination of the optical rotatory dispersion curve.

The structure of this bis(benzophenone) follows from the spectral and analytical evidence, and by analogy with the benzophenone (VI; $R^1 = R^2 =$ Ac) derived similarly from ergochrysin A. Thus, the infrared spectrum has $\nu_{max.}$ 1779 (aromatic carbonyl) and 1727 (aromatic ester carbonyl), whilst the n.m.r. spectrum shows signals at τ 2·36—2·90 (aromatic multiplet, 8 protons), 6·28 (singlet, $2CH_3{\cdot}O{\cdot}CO$, 6 protons), 7·56 (singlet, $2Ar{\cdot}CH_3$, 6 protons), 7·99, 8·07, and 8·17 (singlets, each being $2Ar{\cdot}O{\cdot}CO{\cdot}CH_3$, total 18 protons), giving a total proton count of 38 as required by the structure (XVIII; R = Ac). Controlled deacetylation of this bis(benzophenone) gave the parent compound (XVIII; R = H) which was methylated to yield 2,2′,4,4′-tetramethoxy-3,3′-di-(2-methoxy-6-methoxycarbonyl-4-methylbenzoyl)biphenyl (XVIII; R = Me), $\nu_{max.}$ 1732 (ester carbonyl), 1658 (the benzophenone carbonyl), 1603, 1587, and 1571 (aromatic) cm.$^{-1}$. The n.m.r. spectrum indicated a total proton count of 38 as required, giving signals at τ 2·52—3·35 (aromatic multiplet, 8 protons), 6·23 (singlet, $2Ar{\cdot}CO_2CH_3$, 6 protons), 6·31, 6·38, and 6·68 (singlets, each being $2O{\cdot}CH_3$, total 18 protons), and 7·62 (singlet, $2Ar{\cdot}CH_3$, 6 protons). The products obtained by Stoll *et al.*[11] by acetylation of secalonic acid A and chrysergonic acid were obviously impure specimens of the benzophenone (XVIII; R = Ac), but the reason for the report that these compounds had no acetyl groups is obscure.

The formation of the benzophenone (XVIII; R = Ac) is analogous to the conversion of ergochrysin A into (VI; $R^1 = R^2 =$ Ac). It thus follows that secalonic acid A and secalonic acid B are diastereoisomers of formula (XVII); the two C_{15} residues are linked in the 4,4′-positions, in contrast to ergoflavin [1] and ergochrysin A. The position of this



linkage is based upon the use of the Gibbs test, which in our hands (cf. Franck *et al.*[11]) has consistently and reproducibly given a negative reaction ($\lambda_{max.}$ ~480 mμ) using the method of King *et al.*[13] However, Professor P. de Mayo has obtained a positive reaction ($\lambda_{max.}$ ~675 mμ) when using specimens of secalonic acids B and C isolated in his own laboratory and specimens supplied by us.[4] This discrepancy may be due to minor variations

[13] F. E. King, T. J. King, and L. C. Manning, *J.*, 1957, 563.

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in experimental technique and/or reagents, which cause the opening of the oxygen heterocyclic ring with consequent vitiation of the test. Until contrary evidence is available, we provisionally retain the 4,4′-mode linkage of the two moieties.

Franck *et al.*[9] isolated (+)-methylsuccinic acid from the terminal C ring of secalonic acid A. Thus, the configuration at C-6 and C-6′ in this metabolite and at C-6′ in ergochrysin A are the same. These authors also deduced the absolute configurations (XIX) and (XX) at C-10 and C-10′ for secalonic acids A and B, respectively. On this basis it is possible to suggest the absolute configuration at C-10′ in ergochrysin A. Thus, the molecular rotation $[\phi]$ of ergoflavin (all rotations in pyridine) is +536°. Therefore, the contribution to $[\phi]$ from each half of the molecule (assuming no serious interaction) is +268°. Ergochrysin has $[\phi] = -425°$, whence it follows that $[\phi]$ for the moiety (A) in (I) is −692°. Secalonic acid A has $[\phi] = -1270°$, *i.e.*, approximately $2 \times -692 = -1384°$. Since the major contribution to $[\phi]$ may be ascribed to the asymmetry of C-10′, it seems likely that the absolute stereochemistry of this centre in ergochrysin is the same as that in secalonic acid A, *i.e.*, as in (I).

No experimental evidence is yet available concerning the mode of biosynthesis of the ergot pigments, but we believe that the co-occurrence [12] of ergoflavin and the anthraquinone endocrocin (XXI) has biogenetic significance. Thus, this quinone is most probably acetate or malonate derived (cf. Gatenbeck [14]), and the formation from it (or one of its precursors) of a hemiergoflavin-type unit can be envisaged as proceeding by an unexceptional and acceptable sequence of the type (XXI) ⟶ (XXIV). Dimerisation, by oxidative coupling, of the unit type (XXIV) and its various obvious minor structural modifications would then furnish ergoflavin and its congeners, although the various stages in this sequence do not necessarily proceed in this order.

Whilst there is evidence,[15] in certain cases, that the benzophenone type of intermediate (XXII) is derived by the condensation of two preformed benzenoid ring systems rather than from an anthraquinone,[16,17] this possible modification of the biogenetic pathway does not invalidate our general thesis. There is a striking similarity between the sequence of structures exhibited by the acetate-derived anthraquinoid pigments flavoskyrin (XXV), chrysophanol (XXVI; R = H), islandicin (XXVI; R = OH), and iridoskyrin (XXVII), which co-occur as metabolites of *Penicillium islandicum*, and that invoked in our suggested biogenetic route to the ergot pigments.

Experimental

Ergochrysin A.—The amorphous, yellow material (20 g.) obtained during the extraction of ergoflavin was dissolved in ether, and after 24 hr. insoluble material was collected. The filtrate was evaporated to a gum, which, after solution in hot methanol (50—100 ml.), deposited a bright yellow semicrystalline solid (12 g.) on cooling. This material was dissolved in a large volume of hot acetone and the solution concentrated to small bulk. Hot methanol was again added and the solution concentrated until crystals appeared. On cooling, ergochrysin A (4 g.) separated as deep yellow prisms, or prismatic rods, m. p. 220° (decomp.).

This material (1 g.) was dissolved in boiling methanol (200 ml.) and the solution evaporated to *ca.*, 40 ml.; on cooling, golden-yellow prisms, m. p. 215—220° (decomp.) separated. Recrystallisation was also achieved by dissolving ergochrysin A in acetone, concentrating to a small volume, and adding hot alcohol or chloroform; deep yellow prisms, m. p. 225° (decomp.), separated from the alcoholic solution, whilst from chloroform a pale yellow prismatic variety, m. p. 215° (decomp.), was obtained. These materials were solvated, and after intensive drying at 160°/0·1 mm. had m. p. 285—290° (decomp.).

Various *samples* were prepared for analysis: (*a*) ergochrysin A, from acetone–alcohol, dried for 6 hr. at 160°, m. p. 285° (decomp.); (*b*) similar sample, dried for 24 hr. at 160°, m. p. 292°

[14] S. Gatenbeck, *Acta Chem. Scand.*, 1960, **14**, 102, 230, 296.
[15] Personal communication from Professor C. H. Hassall.
[16] S. Gatenbeck, *Svensk kem. Tidskr.*, 1960, **72**, 188.
[17] T. Money, *Nature*, 1963, **199**, 592.

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(decomp.); (*c*) ergochrysin A, from acetone–chloroform, dried for 6 hr. at 160°, m. p. 286° (decomp.), $[\alpha]_D^{20}$ −37·6° (*c* 0·710 in acetone), $[\alpha]_D^{20}$ −65·4° (*c* 1·03 in pyridine; immediate reading), $\lambda_{max.}$ 244, 269, and 338 mμ (log ε 4·25, 4·29, and 4·25 [Found: (*a*) C, 59·5, 59·6; H, 4·7, 4·8; O, 35·0; OMe, 5·1, 5·4. (*b*) C, 59·4, 59·9; H, 4·8, 5·1; O, 35·0; OMe, 5·1. (*c*) C, 59·3; H, 5·0; O, 36·5; OMe, 5·2. $C_{30}H_{25}O_{13}$(OMe) requires C, 59·6; H, 4·5; O, 35·4; OMe, 5·0%]. Ergochrysin A is very sparingly soluble in the usual organic solvents, exhibits an intense red-brown ferric reaction in alcohol, and a positive Gibbs test ($\lambda_{max.}$ ~620 mμ). Chromatography [9] on thin layers of Kieselgel (Merck) impregnated with 6·3% of oxalic acid, using a 9 : 1 mixture of chloroform and methyl propyl ketone, gave only one spot, R_F 0·53.

Acetylation of ergochrysin A (0·4 g.) at room temperature during 3 days in acetic anhydride (15 ml.) and pyridine (1 ml.), followed by decomposition with water (100 ml.) during 5 hr., gave *penta*-O-*acetylergochrysin A* as an amorphous solid (0·3 g.) having an intense red-brown ferric reaction in ethanol, m. p. 180—185° $[\alpha]_D^{24}$ −24·6° (*c* 2·03 in acetone) (Found: C, 58·3; H, 4·5. $C_{41}H_{38}O_{19}$ requires C, 58·9; H, 4·6%).

4,4′-Dinitroergochrysin A.—Ergochrysin A (2 g.) was dissolved in concentrated nitric acid (50 ml.), and after 20 min. the solution was poured on to ice (50 g.), to give the *product*, yellow prisms, m. p. 302° (decomp.) (from acetone–methanol) [Found: C, 51·0; H, 3·8; N, 3·9; OMe, 4·4. $C_{30}H_{23}N_2O_{17}$(OMe) requires C, 51·9; H, 3·6; N, 3·9; OMe, 4·3%].

Oxidation of Ergochrysin A with Potassium Permanganate.—A solution of potassium permanganate (10 g.) in water (250 ml.) was added during 6 hr. to ergochrysin A (2 g.) dissolved in acetone (150 ml.). Next day the solution was clarified with sulphur dioxide and the acetone removed *in vacuo*. Exhaustive extraction of the aqueous liquor with ether gave a semi-solid which was chromatographed in benzene on silica, to give (±)-methylsuccinic acid (80 mg.), m. p. 105°, identical with an authentic specimen [Found: C, 45·4; H, 6·2; *C*-Me, 10·3. Calc. for $C_4H_5O_4$(Me): C, 45·5; H, 6·1; *C*-Me, 11·2%]. The optical rotatory dispersion curve showed that it was optically inactive.

Pyrolysis of Ergochrysin A.—An intimate mixture of purified sand (30 g.) and ergochrysin A (1 g.) was divided into 8 equal portions. Each portion was heated to redness in a Pyrex tube (15 × 2 cm.). Purification of a benzene solution of the distillate on a silica column (18 × 1 cm.) gave methyl 5-hydroxy-3-methylbenzoate (30 mg.) which separated from benzene–light petroleum (b. p. 40—60°) in needles, m. p. 92°, identical (m. p., mixed m. p., infrared) with an authentic specimen [Found: C, 65·6; H, 6·1; OMe, 18·5%; *M* (Rast), 160. Calc. for $C_8H_7O_2$(OMe): C, 65·1; H, 6·0; OMe, 18·7%; *M*, 166].

Alkali Fusion of Ergochrysin A.—Ergochrysin A (5 g.) was added during 15 min. to molten potassium hydroxide (35 g.) at 190° in a nickel crucible. The frothing melt was stirred at 190—200° for 10 min., cooled, dissolved in water (500 ml.), acidified, and exhaustively extracted with ether. The extract was separated into neutral, phenolic, and acidic fractions. The neutral fraction was negligible; the phenolic material could not be satisfactorily purified, but after methylation followed by chromatography it gave 3-*acetyl*-2,2′,4,4′-*tetramethoxybiphenyl* in prisms (10 mg.), m. p. 112° (from methanol), identical with an authentic specimen [7] [Found: C, 69·0; H, 6·9; OMe, 35·0. $C_{14}H_8O$(OMe)$_4$ requires C, 68·4; H, 6·3; OMe, 39·2%]. Chromatography of the acidic fraction in benzene on alumina, followed by elution with chloroform–acetone (9 : 1), gave oxalic acid and 5-hydroxy-3-methylbenzoic acid, m. p. and mixed m. p. 207°, having the requisite infrared spectrum. Methylation with diazomethane gave methyl 5-hydroxy-3-methylbenzoate, m. p. and mixed m. p. 92°, having the requisite infrared spectrum.

Acetylation of Ergochrysin A.—(*a*) A solution of ergochrysin A (1 g.) in acetic anhydride (20 ml.) containing pyridine (1 ml.) was heated on a steam-bath for 4 hr. and refluxed for a further 2 hr. After removal of the solvent *in vacuo* the residue gave, from acetone–methanol, 2-[2,4-*diacetoxy*-3-(2-*acetoxy*-4-*methyl*-6-*methoxycarbonylbenzoyl*)*phenyl*]-1,5,9′-*tri*-O-*acetylhemiergoflavin* (0·7 g.), needles, m. p. 234°, $[\alpha]_D^{20}$ +58·6° (*c* 0·512 in acetone), $[\alpha]_D^{20}$ +14·5° (*c* 1·00 in pyridine) [Found: C, 59·9; H, 4·6; OMe, 3·7. $C_{42}H_{35}O_{18}$(OMe) requires C, 60·1; H, 4·5; OMe, 3·6%]. This acetate has a negative ferric reaction in alcohol.

(*b*) The same acetate (0·6 g.) was obtained when a mixture of ergochrysin A (1 g.), sodium acetate (0·5 g.), and acetic anhydride (5 ml.) was refluxed for 5 hr.

Acid Degradation of 2-[2,4-*Diacetoxy*-3-(2-*acetoxy*-4-*methyl*-6-*methoxycarbonylbenzoyl*)*phenyl*]-1,5,9′-*tri*-O-*acetylhemiergoflavin*.—A mixture of this acetate (0·5 g.), acetic acid (2 ml.), and 48% hydrobromic acid (5 ml.) was refluxed for 1 hr. On cooling, orange-brown needles separated. The solid product was collected, washed with water, and triturated with 2N-sodium

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hydrogen carbonate for 20 min. The residue was washed, dried, and purified from ethyl acetate–light petroleum, to give 2-(2,4-*dihydroxyphenyl*)*hemiergoflavin* in clusters of yellow needles (0·22 g.), m. p. 195°, or from aqueous alcohol, in yellow plates, m. p. 225°, $[\alpha]_D^{20}$ +66·5 °(*c* 1·125 in 95% alcohol), $\lambda_{max.}$ 255, 284, and 394 mμ (log ε 4·18, 4·20, and 3·41) (Found: C, 59·9; H, 4·6. $C_{21}H_{18}O_9$ requires C, 60·8; H, 4·4%). This substance, which has an intense green ferric reaction in alcohol, crystallises with difficulty, is difficult to desolvate, and consequently does not analyse satisfactorily.

2-(2,4-*Diacetoxyphenyl*)-1,5,9′-*tri*-O-*acetylhemiergoflavin* separated from acetone–methanol in yellow needles, m. p. 190—191°, $[\alpha]_D^{26}$ +42·3° (*c* 2·075 in acetone) (Found: C, 59·8; H, 4·6. $C_{31}H_{28}O_{14}$ requires C, 59·6; H, 4·5%).

Prepared in the usual manner, 2-(2,4-*dimethoxyphenyl*)-1,9-*di*-O-*methylhemiergoflavin* formed needles, m. p. 152°, or prisms, m. p. 190° (from methanol), $[\alpha]_D^{22}$ −9·6° (*c* 3·64 in acetone), $[\alpha]_D^{20}$ +16·5° (*c* 1·00 in 95% ethanol) [Found: C, 64·3; H, 5·5; OMe, 26·9. $C_{21}H_{14}O_5(OMe)_4$ requires C, 63·8; H, 5·5; OMe, 26·4%]. The p-*nitrobenzoate* formed rosettes of pale yellow needles, m. p. 174—176° (from acetone) [Found: C, 62·5; H, 5·0; N, 2·5; OMe, 20·5. $C_{28}H_{17}NO_8(OMe)_4$ requires C, 62·0; H, 4·7; N, 2·3; OMe, 20·0%]. Prepared by the pyridine–acetic anhydride method, 2-(2,4-*dimethoxyphenyl*)-5-O-*acetyl*-1,9-*di*-O-*methylhemiergoflavin* separated from acetone–methanol or chloroform–light petroleum in yellow needles, m. p. 195°, $[\alpha]_D^{20}$ −59·8° (*c* 1·375 in acetone) (Found: C, 62·3; H, 5·5; OMe, 24·5. $C_{23}H_{16}O_6(OMe)_4$ requires C, 63·3; H, 5·5; OMe, 24·2%].

The sodium hydrogen carbonate extract was acidified, extracted with ether, and the crystalline residue sublimed, to yield 5-hydroxy-3-methylbenzoic acid (75 mg.), needles, m. p. and mixed m. p. 211° (Found: C, 63·6; H, 5·4. Calc. for $C_8H_8O_3$: C, 63·2; H, 5·3%). This acid was further characterised by conversion into 5-methoxy-3-methylbenzoic acid which formed needles, m. p. 133° (from benzene–light petroleum), identical with an authentic specimen [Found: C, 65·3; H, 6·1; OMe, 18·9. Calc. for $C_8H_7O_2(OMe)$: C, 65·1; H, 6·0; OMe, 18·7%].

In a repetition, this degradation was performed in a stream of nitrogen. The effluent gas was passed through three traps; the first contained water (to remove acetic acid), and the second and third contained saturated baryta solution. The third trap was replaced at intervals until no more precipitate formed. The weight of $BaCO_3$ formed was 0·207 g. = 46·2 mg. of CO_2 ≡ 98% of 1 mol.

Oxidation of 2-(2,4-*Dihydroxyphenyl*)*hemiergoflavin*.—(*a*) A solution of 2-(2,4-dihydroxyphenyl)hemiergoflavin (1·5 g.) in acetone (100 ml.) was oxidised by the addition of a solution of potassium permanganate (7·5 g.) in water (175 ml.) during 6 hr. After isolation in the usual way, the crude oxidation product was dissolved in chloroform–acetone (9 : 1) and chromatographed on silica, using the same solvent system as eluent. Two products were isolated: (i) hemiergoflavin-2-carboxylic acid (25 mg.), needles, m. p. 247°, identical (m. p., mixed m. p., infrared) with a specimen derived from ergoflavin, and (ii) (−)-methylsuccinic acid, needles (90 mg.), m. p. 110—111° (from benzene–ether) (Found: C, 46·5; H, 6·1. Calc. for $C_5H_8O_4$: C, 45·5; H, 6·1%). The optical comparison with an authentic specimen of (−)-methylsuccinic acid was made by a determination of the optical rotatory dispersion curve.

(*b*) Ozonolysis of 2-(2,4-dihydroxyphenyl)hemiergoflavin (0·7 g.) by the method used for the ozonolysis of ergoflavin gave hemiergoflavin-2-carboxylic acid (54 mg.), identical (m. p., mixed m. p., infrared, rotation) with the previously isolated specimens.

Ozonolysis of Ergochrysin A.—Ozonised oxygen was passed through a solution of ergochrysin A (2 g.) in ethyl acetate (200 ml.) at 0° for 3¼ hr. The solvent was removed under reduced pressure and the product isolated as previously described,[1] to yield hemiergoflavin-2-carboxylic acid (52 mg.), identified by m. p., mixed m. p., rotation, and infrared spectrum.

2-[2,4-*Dimethoxy*-3-(2-*methoxy*-6-*methoxycarbonyl*-4-*methylbenzoyl*)*phenyl*]-1,9-*di*-O-*methylhemiergoflavin*.—The hexa-acetate (VI; $R^1 = R^2 =$ Ac) (0·2 g.) was dissolved in methanol (15 ml.). Three drops of 50% w/w methanolic potassium hydroxide were added with stirring. After 10 sec., the solution was diluted with water (50 ml.), cooled, and acidified with hydrochloric acid. The dried precipitate was an amorphous, yellow powder which did not readily crystallise. Methylation of this (0·55 g.) occurred during 4 hr. in boiling acetone containing methyl sulphate (1 g.) and potassium carbonate (2 g.), to yield the *product* in pale yellow prisms (0·4 g.), m. p. 250—253°, $[\alpha]_D^{20}$ −7·3° (*c* 2·20 in acetone), $\lambda_{max.}$ 252 and 319 (infl.) mμ (log ε 4·53 and 3·88) [Found: C, 64·0; H, 5·6; OMe, 26·7. $C_{30}H_{18}O_7(OMe)_6$ requires C, 63·9; H, 5·4; OMe, 27·5%].

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During the purification of this methyl ether a small quantity (10 mg.) of a *xanthone* was obtained in lemon-yellow prisms, m. p. 298—299° (from acetone–methanol) [Found: C, 64·3; H, 4·9; OMe, 20·3. $C_{30}H_{18}O_8(OMe)_4$ requires C, 64·8; H, 4·8; OMe, 19·7%].

Prepared quantitatively by the pyridine–acetic anhydride method, 2-[2,4-*dimethoxy*-3-(2-*methoxy*-6-*methoxycarbonyl*-4-*methylbenzoyl*)*phenyl*]-5-O-*acetyl*-1,9-*di*-O-*methylhemiergoflavin* formed needles, m. p. 214° (from methanol) [Found: C, 63·9; H, 5·4; OMe, 26·3. $C_{32}H_{20}O_8(OMe)_6$ requires C, 63·5; H, 5·3; OMe, 25·9%].

2-(2,4-*Dimethoxyphenyl*)-1,9-*di*-O-*methylhemiergoflavinone*.—A stirred solution of 2-(2,4-dimethoxyphenyl)-1,9-di-*O*-methylhemiergoflavin (1 g.) in acetone (50 ml.) was oxidised by the addition of the Jones reagent [6] (3·4 ml.). Next day the *product* was isolated in the usual manner and purified from methanol, to yield yellow prisms (0·7 g.), m. p. 158°, $[\alpha]_D^{20}$ +152° (*c* 5·45 in acetone) [Found: C, 64·2; H, 5·1; OMe, 27·0. $C_{21}H_{12}O_5(OMe)_4$ requires C, 64·1; H, 5·1; OMe, 26·5%]. This ketone gives no ferric reaction in alcohol but gives an immediate precipitate with Brady's reagent.

A mixture of this ketone (0·5 g.) and 10% sodium hydroxide solution (20 ml.) was heated on a steam-bath for 105 min. The clear solution was cooled to 0° and acidified with 50% sulphuric acid. The mixture was extracted with ether and the extracts washed with 2N-sodium hydrogen carbonate. On evaporation, the ethereal solution gave a yellow oil which was purified from methanol, to give the optically inactive 3-*acetyl*-4-*hydroxy*-2,2′,4′-*trimethoxybiphenyl* (0·4 g.), yellow plates, m. p. 94° [Found: C, 67·9; H, 6·1; OMe, 29·9. $C_{14}H_9O_2(OMe)_3$ requires C, 67·6; H, 6·0; OMe, 30·8%]. The acidic fraction from this degradation gave oxalic acid (0·14 g.), identical with an authentic specimen. Methylation of this ketone (0·15 g.) by the usual process gave 3-acetyl-2,2′,4,4′-tetramethoxybiphenyl in needles (0·12 g.), m. p. 116° (from methanol), identical with an authentic specimen [7] [Found: C, 68·7; H, 6·3; OMe, 36·3. Calc. for $C_{14}H_8O(OMe)_4$: C, 68·4; H, 6·3; OMe, 39·2%].

3-*Ethyl*-2,2′,4,4′-*tetramethoxybiphenyl*.—A mixture of 3-acetyl-4-hydroxy-2,2′,4′-trimethoxybiphenyl (0·25 g.), 100% hydrazine hydrate (0·35 ml.), and diethylene glycol (10 ml.) was refluxed for ½ hr. The mixture was cooled, treated with solid potassium hydroxide (0·35 g.), and maintained at 150° for a further ½ hr. The temperature was raised to 210° and the condenser removed for ½ hr. The condenser was replaced and refluxing continued at 210° for a further 1 hr. After cooling, dilution with water (25 ml.), and acidification with 2N-sulphuric acid, the product was extracted with ether. After removal of the ether the crude product was dissolved in benzene and chromatographed on silica, using benzene as eluent, to give a straw-coloured oil (0·1 g.) which could not be induced to crystallise but was methylated directly to yield the *product*, prisms (50 mg.), m. p. 83° (from light petroleum) [Found: C, 71·2; H, 7·4; OMe, 40·8. $C_{14}H_{10}(OMe)_4$ requires C, 71·5; H, 7·3; OMe, 41·0%], identical (m. p. mixed m. p., infrared) with a synthetic specimen.[7]

1,1′,9-*Tri*-O-*methylergochrysin A*.—A solution of ergochrysin A (1 g.) in acetone (40 ml.) containing dimethyl sulphate (2 ml.) and potassium carbonate (3 g.) was refluxed for 4 hr. The *product* was isolated in the usual manner and separated from 95% alcohol during several days, in pale yellow needles (0·5 g.), m. p. 176—179° with subsequent re-solidification and re-melting at 259—260°, $[\alpha]_D^{24}$ −18·5° (*c* 1·15 in acetone), $\lambda_{max.}$ 255 and 319 mμ (log ε 4·44 and 3·20) [Found: C, 59·7; H, 5·3; OMe, 18·6. $C_{30}H_{22}O_{10}(OMe)_4$ requires C, 61·1; H, 5·1; OMe, 18·5%]. This ester exhibits an intense red-brown ferric reaction in alcohol. Prepared quantitatively by the pyridine–acetic anhydride method, 5,5′,8′-*tri*-O-*acetyl*-1,1′,9-*tri*-O-*methylergochrysin A* formed needles, m. p. 216° (from methanol) [Found: C, 60·5; H, 5·0; OMe, 16·3. $C_{36}H_{28}O_{13}(OMe)_4$ requires C, 60·6; H, 5·1; OMe, 15·7%].

1,1′,9-*Tri*-O-*methylergochrysinone A*.—Oxidation of 1,1′,9-tri-*O*-methylergochrysin A (0·5 g.) in acetone (25 ml.) with the Jones reagent [6] (1·5 ml.) gave 1,1′,9-tri-*O*-methylergochrysinone A (0·4 g.) which could not be induced to crystallise. A mixture of this material (0·4 g.) and 10% sodium hydroxide solution (20 ml.) was heated on a steam-bath for 1½ hr. in a stream of nitrogen. After isolation in the usual manner, the phenolic fraction was chromatographed from benzene–chloroform (5 : 1) on silica, to give 3,3′-diacetyl-4,4′-dihydroxy-2,2′-dimethoxybiphenyl (17 mg.), identical (m. p., mixed m. p., infrared) with an authentic specimen. Oxalic acid (30 mg.) was isolated from the aqueous hydrolysate.

Acetylation of 1,1′,9-tri-*O*-methylergochrysinone A (0·5 g.) in boiling acetic anhydride (5 ml.) containing sodium acetate (0·15 g.), during 2½ hr., gave a non-crystalline acetate (0·38 g.) which gave no ferric reaction in alcohol and had $\nu_{max.}$ 1812 (γ-lactone), 1776 (ester), and 1689

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(aromatic ketone) cm.$^{-1}$. This crude acetate was refluxed for 1 hr. with a mixture of 48% hydrobromic acid (5 ml.) and acetic acid (2 ml.). The brown solution was diluted with water (100 ml.) and exhaustively extracted with ether. The extracts were washed with water, and extracted with 2N-sodium hydrogen carbonate. The alkaline washings were acidified, extracted with ether (4 × 50 ml.), and the combined extracts dried and evaporated. Removal of the ether left a glass which was dissolved in chloroform and chromatographed on silica using chloroform as eluent. Evaporation of the eluate furnished 2,5-dihydroxy-3-methylbenzoic acid which on sublimation gave needles, m. p. 220—222° (0·02 g.) (Found: C, 57·4; H, 4·9. Calc. for $C_8H_8O_4$: C, 57·2; H, 4·8%), identical (m. p., mixed m. p., infrared) with an authentic specimen, and exhibiting an intense green ferric reaction in alcohol.

Methylation of this acid (30 mg.) by the dimethyl sulphate–acetone–potassium carbonate method, followed by hydrolysis of the crude ester, gave 2,5-dimethoxy-3-methylbenzoic acid (17 mg.), needles, m. p. 80°, identical with an authentic specimen [Found: C, 60·9; H, 6·2; OMe, 32·3. Calc. for $C_8H_6O_2(OMe)_2$: C, 61·2; H, 6·1; OMe, 31·7%].

Isoergochrysin A.—A solution of ergochrysin A (1 g.) in pyridine (10 ml.) was refluxed for ½ hr., the solvent was removed *in vacuo*, and the residual yellow glass was dissolved in hot ethanol (10 ml.). During 2—3 days, *isoergochrysin A* separated in yellow prisms which were recrystallised from acetone–methanol to give stout, yellow prisms (0·45 g.), m. p. 255—259° (decomp.), $[\alpha]_D^{20}$ +58·6° (*c* 0·512 in pyridine), $\lambda_{max.}$ 212, 264, and 334 mμ (log ε 4·44, 4·35, and 4·25) [Found: C, 59·0; H, 5·1; OMe, 5·0. $C_{30}H_{25}O_{13}(OMe)$ requires C, 59·6; H, 4·5; OMe, 5·0%]. Chromatography [9] on thin layers of Kieselgel (Merck) impregnated with 6·3% of oxalic acid, using a 9 : 1 mixture of chloroform and methyl propyl ketone, gave only one spot, R_F 0·60. Isoergochrysin A exhibits an intense red-brown ferric reaction in alcohol.

Oxidation of isoergochrysin A (cf. ergochrysin A) yields (±)-methylsuccinic acid. Methylation of isoergochrysin A (cf. ergochrysin A) gives 1,1′,9-tri-*O*-methylergochrysin A having the same m. p., mixed m. p., infrared spectrum, and optical rotation as the specimen prepared directly from ergochrysin A. Vigorous acetylation of isoergochrysin A (cf. ergochrysin A) yields the benzophenone (VI; $R^1 = R^2 =$ Ac), identical with the product obtained directly from ergochrysin A.

Secalonic Acid A.—This compound formed pale yellow needles, m. p. 242—245° (decomp.) (from dioxan) (Found: C, 60·1; H, 4·8. Calc. for $C_{32}H_{30}O_{14}$: C, 60·2; H, 4·7%), having an intense red-brown ferric reaction in alcohol and R_F 0·44 under the conditions used for ergochrysin A.

Pyrolysis of secalonic acid A (300 mg.) at atmospheric pressure gave methyl 5-hydroxy-3-methylbenzoate which was chromatographed on silica from light petroleum to give needles (10 mg.), m. p. 92—93°, identical (m. p. mixed m. p., infrared) with an authentic specimen [Found: OMe, 18·9. Calc. for $C_8H_7O_2(OMe)$: OMe, 18·7%].

A mixture of secalonic acid A (0·2 g.) acetic anhydride (2·5 ml.), and sodium acetate (0·75 mg.) was refluxed for 2½ hr. After isolation in the usual way 2,2′,4,4′-*tetra-acetoxy*-3,3′-(2-*acetoxy*-6-*methoxycarbonyl*-4-*methylbenzoyl*)*biphenyl* (0·23 g.) formed prisms, m. p. 205° (from acetone–methanol), $[\alpha]_D^{20}$ 0° (*c* 7·00 in $CHCl_3$). The optical rotatory dispersion curve was parallel to the wavelength axis [Found: C, 61·4; H, 4·4; OMe, 7·1. $C_{42}H_{32}O_{16}(OMe)_2$ requires C, 61·8; H, 4·5; OMe, 7·3%]. Franck *et al.*[12] quote m. p. 150° (decomp.), $[\alpha]_D$ −43·3° (in methanol). Stoll *et al.*[11] record m. p. 205—206°, $[\alpha]_D^{20}$ +10° ±4° (in pyridine).

Chrysergonic Acid.—This formed lemon-yellow needles, m. p. 265—269° (from dioxan) (Found: C, 60·1; H, 4·8. Calc. for $C_{32}H_{30}O_{14}$: C, 60·2; H, 4·7%). Thin-layer chromatography on Kieselgel showed spots at R_F 0·40 and 0·64 in a ratio of *ca.* 2 : 1.[1]

Pyrolysis of chrysergonic acid (500 mg.) gave methyl 5-hydroxy-3-methylbenzoate (25 mg.), m. p. 92°, identical with an authentic specimen. When acetylated using vigorous conditions, chrysergonic acid was converted quantitatively into 2,2′,4,4′-tetra-acetoxy-3,3′-(2-acetoxy-6-methoxycarbonyl-4-methylbenzoyl)biphenyl, identical with the specimen prepared from secalonic acid A, m. p. 204°, $[\alpha]_D^{20}$ 0° (*c* 10·0 in $CHCl_3$) [Found: C, 61·1; H, 4·6; OMe, 7·0. Calc. for $C_{42}H_{32}O_{16}(OMe)_2$: C, 61·8; H, 4·5; OMe, 7·3%].

A solution of this acetate (230 mg.) in methanol (15 ml.) was treated with 50% w/w methanolic potassium hydroxide solution (0·1 ml.). Two minutes later the solution was diluted with water (30 ml.) and acidified. The pale yellow semicrystalline precipitate, which gave an intense green ferric reaction in alcohol, was methylated in boiling acetone (40 ml.) containing potassium carbonate (2 g.) and dimethyl sulphate (1 ml.) during 2½ hr. On isolation, 2,2′,4,4′-*tetramethoxy*-3,3′-(2-*methoxy*-6-*methoxycarbonyl*-4-*methylbenzoyl*)*biphenyl* formed plates (92 mg.),

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m. p. 217° (from methanol) [Found: C, 66·2; H, 5·4; OMe, 35·9. $C_{30}H_{14}O_4(OMe)_8$ requires C, 66·5; H, 5·5; OMe, 36·2%].

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