A New Synthesis of Rotenoids. Application to 9-Demethylmunduserone, Mundeserone, Rotenonic Acid, Dalpanol, and Rotenone

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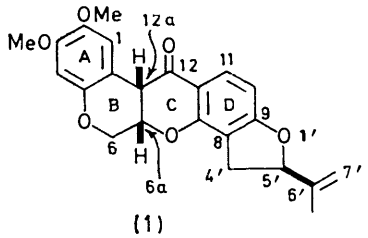
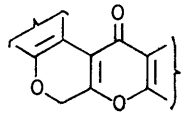
A new synthesis of rotenoids, which involves reaction of a 2'-hydroxyisoflavone with dimethylsulphoxonium methylide followed by rearrangement of the vinylcoumaranone formed, is described. This supplies C-6 by a one carbon entity, as in nature, and unlike other methods attains the correct oxidation level of the B/C ring system without further reduction–oxidation procedures. In illustration, (±)-isorotenone (13) is prepared from isoderritol (11a), and (−)-rotenone (1) from derritol. Total synthesis of the biosynthetically important (±)-9-demethylmunduserone (16), and the natural rotenoid (±)-munduserone (20) is reported using Wanzlick synthesis for the necessary flavonoids. (±)-9-Demethylmunduserone can be dimethylallylated at C-8 to give (±)-rot-2'-enonic acid. Hydrogenation of (−)-rotenone to (−)-rot-2'-enonic acid (17a) and mutarotenone to (±)-rot-2'-enonic acid is re-examined and found to involve two types of 1,2- as well as 1,4-(1'–7')reduction. Following the lines of the biosynthetic pathway, (−)-rot-2'-enonic acid is epoxidised and converted into (−)-dalpanol (18), the apparent immediate precursor of (−)-rotenone in nature. Apart from resolution of (±)-rot-2'-enonic acid, this constitutes a formal total synthesis of (−)-dalpanol.

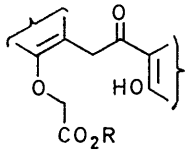
THE synthesis of rotenone (1), its relatives in nature,[1] and their derivatives, raises a number of problems. Known procedures almost invariably produce the B/C ring system at an incorrect oxidation level,† and the 6a,12a-unsaturated products (2) require reduction. Since other functions sensitive to reduction are present,



(1)



(2)



(3)

more than one stage is usually needed to reach the desired oxidation state.[3] 6a,12a-Didehydrorotenoids (2) can be obtained through base catalysed cyclisation of the corresponding derrisic acid or ester (3),[4] and the latter are available (a) from Hoesch reactions[5] using the appropriate nitriles (or from mechanistically related condensations[6]), (b) from 2,2'-dihydroxydeoxybenzoins,[3e,7] or (c) by the hydrolysis of *O*-methoxycarbonylmethyleneisoflavones.[8] Alternatively, the enamines of chroman-3-ones give dehydrorotenoids on reaction with salicoyl chlorides,[9] and the same products are obtained from heating 4-methoxycarbonylchroman-3-ones with *m*-dihydric phenols.[10]

These methods are, in general, restricted in scope, and include steps of low yield. Regiospecificity and other problems are encountered, and methods are unsuitable for preparing radiochemically labelled rotenoids.

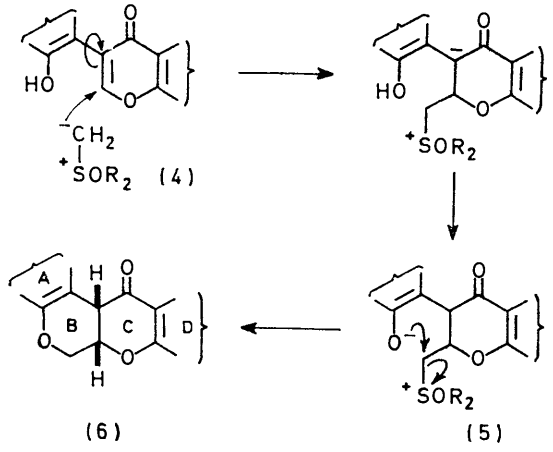
We have now developed a synthesis of rotenoids from 2'-hydroxyisoflavonoids. This is of particular interest since recent work has demonstrated the intermediacy of the latter in the biosynthesis of rotenoids.[11] In the present paper we describe the syntheses of isorotenone ‡ (13) and rotenone (1) from the corresponding 2'-hydroxyisoflavones; the total syntheses of (±)-9-demethylmunduserone (16) and (±)-rotenonic acid (17a); and the synthesis of (6a*S*,12a*S*,5'*R*)-dalpanol (18) from

† The early claim by Offe[2] to have prepared a rotenoid type of ring system without 6a,12a-didehydro-intermediates has never been verified.

‡ For a preliminary communication, see ref. 12.

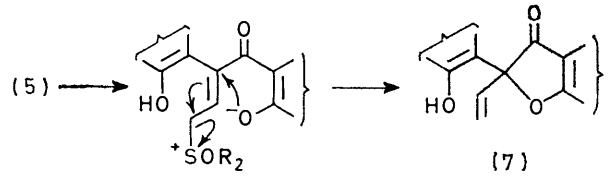
[1] L. Crombie, *Fortschr. Chem. org. Naturstoffe*, 1963, **21**, 275.
[2] H. A. Offe and W. Barkow, *Chem. Ber.*, 1947, **80**, 458.
[3] (*a*) M. Miyano and M. Matsui, *Bull. Agric. Chem. Soc. Japan*, 1958, **22**, 128; *Chem. Ber.*, 1958, **91**, 2044; (*b*) H. Fukami, S. Takahashi, K. Konishi, and M. Nakajima, *Bull. Agric. Chem. Soc. Japan*, 1960, **24**, 123; (*c*) J. R. Herbert, W. D. Ollis, and R. C. Russell, *Proc. Chem. Soc.*, 1960, 177; (*d*) H. Fukami, J. Oda, G. Sakata, and M. Nakajima, *Agric. and Biol. Chem. (Japan)*, 1961, **25**, 252; (*e*) G. Büchi, L. Crombie, P. J. Godin, J. S. Kaltenbronn, K. S. Siddalingaiah, and D. A. Whiting, *J. Chem. Soc.*, 1961, 2843.
[4] (*a*) F. B. LaForge, H. L. Haller, and L. E. Smith, *J. Amer. Chem. Soc.*, 1931, **53**, 4400; (*b*) E. P. Clark, *ibid.*, p. 313; (*c*) S. Takei, S. Miyajima, and M. Ono *Ber.*, 1932, **65**, 1041; (*d*) M. Miyano, *Chem. Ber.*, 1965, **87**, 3962; (*e*) N. Nakatani and M. Matsui, *Agric. and Biol. Chem. (Japan)*, 1968, **32**, 769; 1969, **33**, 110; (*f*) T. Harano, *Bull. Chem. Soc. Japan*, 1970, **43**, 1560.
[5] (*a*) A. Robertson, *J. Chem. Soc.*, 1933, 489, 1163; (*b*) T. S. Kenny, A. Robertson, and S. W. George, *ibid.*, 1939, 1610; (*c*) S. H. Harper, *ibid.*, 1942, 593.
[6] K. Fukui, M. Nakayama, M. Hatanaka, T. Okamoto, and Y. Kawase, *Bull. Chem. Soc. Japan*, 1963, **36**, 397; K. Fukui, M. Nakayama, A. Tanaka, and S. Sasatami, *ibid.*, 1965, **38**, 845.
[7] F. B. LaForge, *J. Amer. Chem. Soc.*, 1933, **55**, 3040.
[8] (*a*) K. Fukui, M. Nakayama, and T. Harano, *Experientia*, 1967, **23**, 613; (*b*) V. Chandrashekar, M. Krishnamurti, and T. R. Seshadri, *Tetrahedron*, 1967, **23**, 2505; *Current Sci.*, 1965, **34**, 479; 1967, **36**, 623; (*c*) K. Fukui, M. Nakayama, and T. Harano, *Bull. Chem. Soc. Japan*, 1969, **42**, 199, 233; (*d*) T. Harano, *ibid.*, 1970, **43**, 1560; (*e*) K. Fukui, M. Nakayama, and T. Harano, *Experientia*, 1969, **25**, 789; (*f*) M. Krishnamurti, Y. R. Sambhy, and T. R. Seshadri, *Indian J. Chem.*, 1971, **9**, 297.
[9] (*a*) M. Miyano, *J. Amer. Chem. Soc.*, 1965, **87**, 3958; (*b*) M. Miyano, *J. Org. Chem.*, 1970, **35**, 246; (*c*) M. Uchiyama, M. Ohhashi, and M. Matsui, *Agric. and Biol. Chem. (Japan)*, 1966, **30**, 1145.
[10] M. Baran-Marsak, J. Massicot, and D. Molko, *Bull. Soc. chim. France*, 1971, 191.
[11] P. M. Dewick, L. Crombie, and D. A. Whiting, *Chem. Comm.*, 1970, 1469.
[12] L. Crombie, P. W. Freeman, and D. A. Whiting, *Chem. Comm.*, 1970, 563.

(6a*S*,12a*S*)-rotenonic acid. The new synthesis is readily adapted to give rotenoids with specific radiochemical labels; these have been employed in a companion study[13] on rotenoid biosynthesis. Knowledge of the course of rotenoid synthesis in nature has influenced the choice of synthetic target, and the design of route, in this *in vitro* work.



SCHEME 1

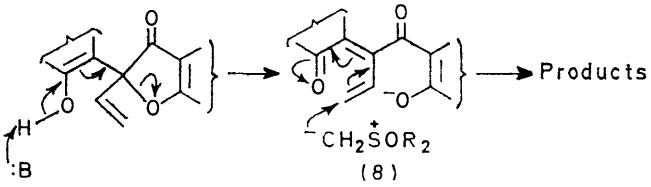
The conversion of isoflavones (4) into rotenoids (6) requires methylene insertion to complete ring B; in nature there is evidence that this process employs *S*-adenosylmethionine.[14] In methylation by this reagent, *e.g.* in ergosterol[15] and tuberculostearic acid,[16] only two hydrogens of the *S*-methyl are retained,[16a] an observation which prompted Lederer to draw an analogy with alkylation by sulphoxonium methylides. This suggestion, although without subsequent experimental support,[17] provided an attractive hypothesis for rotenoid formation in nature (Scheme 1) and provoked studies[18,19] of the reactions of isoflavones with dimethylsulphoxonium methylide. Although the desired Michael addition (4) ⟶ (5) occurs, further reaction (with 2′-hydroxy present) follows Scheme 2, with opening of the chroman-



SCHEME 2

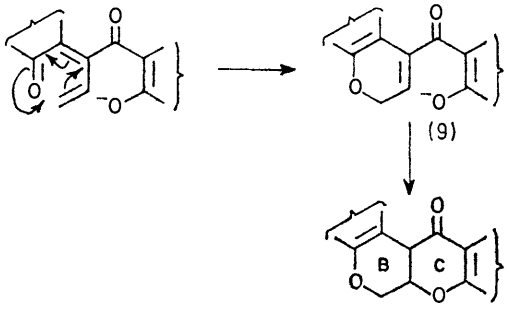
4-one ring and recyclisation to vinylcoumaranone (7), frustrating rotenoid formation.

Vinylcoumaranones (7) are however susceptible to further reaction in base with dimethylsulphoxonium methylide.[19] This reaction, which may also be represented as an allylic displacement, seems most readily rationalised (Scheme 3) in terms of base catalysed iso-



SCHEME 3

merisation of the 2′-hydroxyvinylcoumaranone and Michael addition of the methylide to the new dienone (8). Another possibility (Scheme 4) for rotenoid synthesis now becomes apparent since dienone (8) might (in the absence of ylide) undergo electrocyclic rearrangement to the dehydrorotenol structure (9), and such ketones are known[20] to cyclise to rotenoids in weak base.



SCHEME 4

To test this proposition, isoderritol isoflavone (10) was prepared from isoderritol (11a) [the benzil (11b) was also obtained] and converted into the vinylcoumaranone[19] (12) by treatment with dimethylsulphoxonium methylide in dimethylsulphoxide. The coumaranone (12) was heated at 100° in pyridine for 24 h; the product was shown to be (±)-isorotenone (13) (80% isolated) by comparison with an authentic sample.[21] Scheme (4) is thus realised.

The isomerisation (12) ⟶ (13) was followed in several solvents at 100° using a modification of the Goodhue procedure[22] to assay the rotenoid product. In pyridine, conversion into isorotenone reached 96% after 1 h; in the hydroxylic solvent n-butanol the reaction was slower (*e.g.* 78% in 1 h). The conversion rate was further reduced in ethylene glycol (37% in 1 h) and was slow in dipolar aprotic dimethyl sulphoxide (17% in 1 h). No isorotenone was formed in toluene at 100° after 4 h,

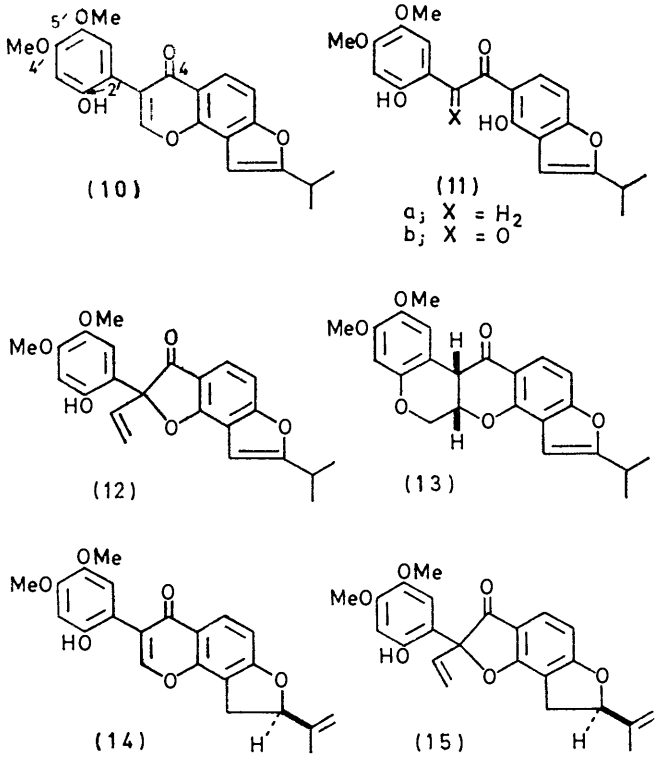
[13] L. Crombie, P. M. Dewick, and D. A. Whiting, *J.C.S. Chem. Comm.*, 1972, 1182, 1183; *J.C.S. Perkin I*, following paper.
[14] L. Crombie, C. L. Green, and D. A. Whiting, *J. Chem. Soc.* (*C*), 1968, 3029.
[15] L. W. Parks, *J. Amer. Chem. Soc.*, 1958, **80**, 2023.
[16] (*a*) E. Lederer, *Biochem. J.*, 1964, **93**, 449; (*b*) K. Bloch, W. L. Lennarz, and G. Scheurerbrandt, *J. Biol. Chem.*, 1962, **237**, 664.
[17] E. Lederer, *Quart. Rev.*, 1969, **23**, 453.
[18] G. A. Caplin, W. D. Ollis, and I. O. Sutherland, *J. Chem. Soc.* (*C*), 1968, 2302.
[19] L. Crombie, J. S. Davies, and D. A. Whiting, *J. Chem. Soc.* (*C*), 1971, 304.
[20] L. Crombie, P. J. Godin, K. S. Siddalingaiah, and D. A. Whiting, *J. Chem. Soc.*, 1961, 2876.
[21] J. J. Boam, R. S. Cahn, and R. F. Phipers, *J. Chem. Soc.*, 1938, 513.
[22] L. D. Goodhue, *J. Assoc. Offic. Analyt. Chemists*, 1936, **19**, 118.

although all the vinylcoumaranone had reacted, by undetermined pathways.

A parallel sequence was then carried out with derritol isoflavone [23] (14). Reaction with dimethylsulphoxonium methylide made available the vinylcoumaranone (15) as a mixture of diastereoisomers, rearranging in pyridine at 100° to 'mutarotenone', a mixture of rotenone (1) and its 6a,12a-epimer. Fractional crystallisation of this mixture yields [20,21] natural (6a*S*,12a*S*,5′*R*)-rotenone (1).

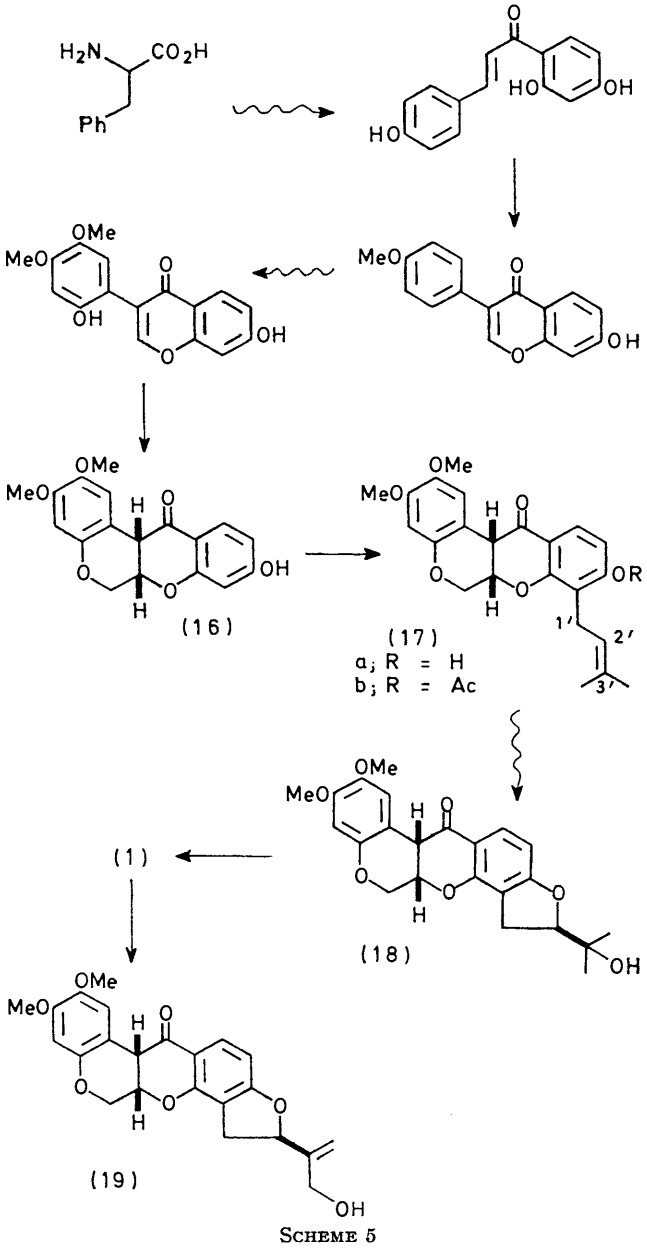
This method is adaptable to the production of [6-^{3}H]-rotenoids [13] since trimethylsulphoxonium iodide can readily be labelled by exchange with alkaline tritiated water and then provides tritiated ylide for use in the above synthesis.

Biosynthetic studies [13] on the formation of the rotenoid amorphigenin (19) in germinating seeds of *Amorpha fruticosa*, provide evidence for the biological sequence outlined in Scheme 5. A key role is occupied by 9-demethylmunduserone (16), which, if not diverted by methylation to munduserone (20), is the precursor of rotenoids with 2,3-dimethoxylation in ring A and resorcinol oxygenation in ring D, *e.g.* rotenonic acid (17a), dalpanol (18), rotenone (1), and amorphigenin (19). At the start of this work, 9-demethylmunduserone was not known either in nature or from synthesis, and we undertook a total synthesis of the racemic form, which



would use the 2′,7-dihydroxy-4,5-dimethoxyisoflavone (21a) as intermediate, paralleling biosynthesis. As a preliminary the methods for isoflavone synthesis were tested by preparing 2′-hydroxy-4′,5′,7-trimethoxyisoflavone (21b).

7-Methoxychromanone (23a) was prepared (in improved yield over previous methods [24]) by cyclisation of



SCHEME 5

(*m*-methoxyphenoxy)propionic acid (22a) with polyphosphoric acid. Base-catalysed reaction with 4,5-dimethoxy-*o*-benzoquinone, following the method of Wanzlick and Weber-Schilling [25] gave 4′,5′-dihydroxy-2′,7-dimethoxyisoflavone (21c). Complete methylation

[23] M. B. Thomas, Ph.D. Thesis, University College, Cardiff, 1965.

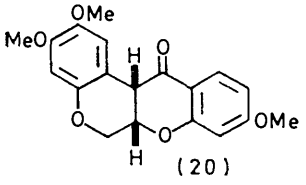
[24] G. B. Bachman and H. A. Levine, *J. Amer. Chem. Soc.*, 1948, **70**, 599; J. Oberlin and P. Pfeiffer, *Ber.*, 1924, **57**, 208; W. H. Perkin, J. N. Ray, and R. Robinson, *J. Chem. Soc.*, 1926, 941; J. D. Loudon, and R. K. Razdan, *ibid.*, 1954, 4299.

[25] C. A. Weber-Schilling and H. W. Wanzlick, *Tetrahedron Letters*, 1969, 2345; *Chem. Ber.*, 1971, **104**, 1518.

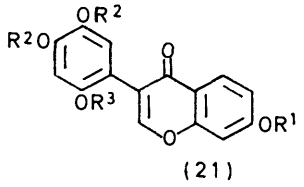
to tetramethoxyisoflavone (21d) was followed by selective demethylation to the desired isoflavone (21b).

Reaction between the isoflavone (21b) and dimethylsulphoxonium methylide gave the new 2-vinylcoumaran-3-one (25) clearly characterised by its spectra; heating the coumaranone in pyridine at 100° afforded (±)-munduserone [23] (20), m.p. 171—172°, with i.r., u.v., and mass spectroscopic details in good agreement with published data [26] and the expected n.m.r. spectrum.[27] This constitutes a new and convenient total synthesis of (±)-munduserone.

A by-product in coumaranone formation was identified as the aroylbenzofuran (24a); a parallel reaction has been reported.[19]

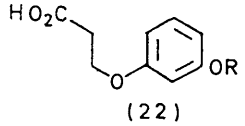


(20)



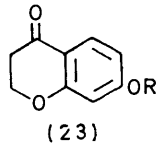
(21)

a; $R^1 = R^3 = H, R^2 = Me$
b; $R^3 = H, R^1 = R^2 = Me$
c; $R^1 = R^3 = Me, R^2 = H$
d; $R^1 = R^2 = R^3 = Me$
e; $R^3 = Me, R^2 = H, R^1 = CH_2Ph$
f; $R^2 = R^3 = Me, R^1 = CH_2Ph$
g; $R^1 = R^3 = Ac, R^2 = Me$
h; $R^1 = CH_2Ph, R^3 = Ac, R^2 = Me$
i; $R^1 = CH_2Ph, R^3 = H, R^2 = Me$
j; $R^1 = R^3 = CH_2Ph, R^2 = Me$



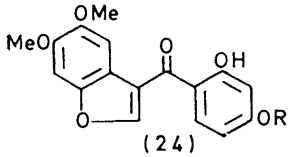
(22)

a; R = Me
b; R = H



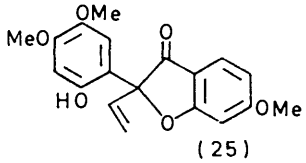
(23)

a; R = Me
b; R = CH_2Ph



(24)

a; R = Me
b; R = H



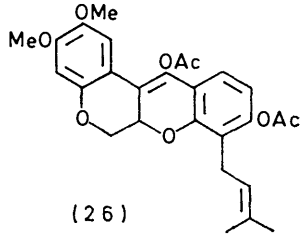
(25)

For preparation of the isoflavone (21a) with a free 7-hydroxy-group, 7-benzyloxychroman-4-one [28] (23b) was treated with 4,5-dimethoxy-*o*-benzoquinone to yield 7-benzyloxy-4′,5′-dihydroxy-2′-methoxyisoflavone (21e). Methylation gave 7-benzyloxy-2′,4′,5′-trimethoxyisoflavone [29] (21f) and 2′-demethylation with aluminium chloride in acetonitrile was accompanied by debenzylation, finally producing 2′,7-dihydroxy-4′5′-dimethoxyisoflavone [8a,d] (21a). This isoflavone was allowed to react with dimethylsulphoxonium methylide and the intermediate coumaranone rearranged in pyridine to provide (±)-9-demethylmunduserone (16). This new rotenoid, $C_{18}H_{16}O_6$, M^+ 328, showed the expected [26] fragment ions *m/e* 192 (100%), 191 (40), 177 (29), and 137 (5), and the n.m.r. spectrum was very similar to that of munduserone. Confirmation of the structure (16) was completed by methylation with diazomethane to give (±)-munduserone, identical with the above specimen. A second, minor product in the methylide reaction was again obtained, the aroylbenzofuran (24b), arising from reaction of the isoflavone with base.[19]

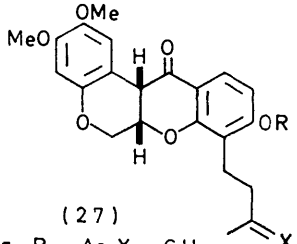
With this synthesis, the rotenoid (16) became available both in unlabelled and tritiated forms; the latter was used to establish the role allocated to (16) in the biosynthetic Scheme 5.

This last methylide conversion of an isoflavone into a rotenoid proceeded in poor yield; this is thought to be occasioned by the free 7-hydroxy-group, which on ionisation in the basic medium reduces the electrophilicity of the carbonyl function. To avoid this problem an alternative route involving the protected 7-benzyloxy-4′,5′-dimethoxy-2′-hydroxyisoflavone (21i) was explored. The latter was prepared from the diacetylisoflavone (21g) by selective deacylation–benzylation to the monobenzyl ether (21h) [the dibenzylether (21j) was obtained as a side product], and subsequent 2′-deacetylation. Reaction of the benzyloxyisoflavone (21i) with dimethylsulphoxonium methylide gave benzyl 9-demethylmunduserone, debenzylated by aluminium chloride to 9-demethylmunduserone (chromatographic identification). The overall yield was still very low, and the route excessively lengthy.

Synthesis of 8-prenylated rotenoids, following the sequence (Scheme 5) disclosed in the biosynthetic work, was now examined. The first objective became 8-prenylation of 9-demethylmunduserone (16) to yield rotenonic



(26)



(27)

a; R = Ac, X = CH_2
b; R = H, X = CH_2
c; R = Ac, X = O

acid (17a). The latter has been known for many years in the (6a*S*,12a*S*)-form as it can be obtained by hydrogenolysis of rotenone in pyridine over palladium on

[26] (*a*) W. D. Ollis, C. A. Rhodes, and I. O. Sutherland, *Tetrahedron*, 1967, **23**, 4741; (*b*) N. Finch and W. D. Ollis, *Proc. Chem. Soc.*, 1960, 176; (*c*) R. I. Reed and J. M. Wilson, *J. Chem. Soc.*, 1963, 5949.

[27] L. Crombie and J. W. Lown, *J. Chem. Soc.*, 1962, 775; D. J. Adam, L. Crombie, and D. A. Whiting, *J. Chem. Soc.* (*C*), 1966, 542.

[28] P. Naylor, G. R. Ramage, and F. Schofield, *J. Chem. Soc.*, 1958, 1190; A. O. Fitton and G. R. Ramage, *ibid.*, 1962, 4870.

[29] A. Fukui and M. Nakayama, *Bull. Chem. Soc. Japan*, 1965, **38**, 1803.

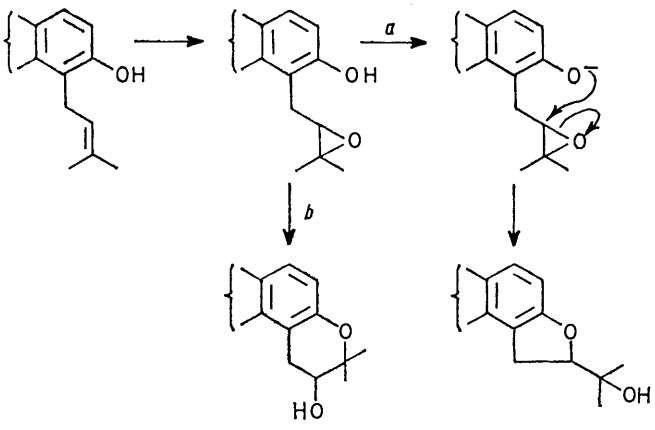
barium sulphate.[21,30] Since prenylation of the rotenoid (16) would afford (±)-rotenonic acid, an authentic specimen of the latter was prepared.

Hydrogenolysis of (—)-rotenone by the reported method afforded (6a*S*,12a*S*)-rotenonic acid, giving an acetyl derivative (17b) with acetic anhydride in aqueous alkali. This acetate was readily hydrolysed under acidic conditions without racemisation, to the parent (6a*S*,12a*S*)-rotenonic acid. Acetylation with acetic anhydride–pyridine mixtures gave the enoldiacetate (26), characterised by a stilbene-like u.v. chromophore, and the absence in the n.m.r. of shielding effects by a 12-carbonyl group. In one preparation of rotenonic acid, using hydrogenation over palladium catalyst on carbon support, the whole alkali-soluble product was acetylated. Monoacetylrotenonic acid (17b) was separated by crystallisation, and a second product was then obtained, which proved to be the isomeric (6a*S*,12a*S*)-rot-3′-enonic acid acetate (27a). The n.m.r. spectrum of this isomer showed only one unsaturated methyl, τ 8·13 (s), vinyl methylene, 5·32, 5·40, and coupled benzylic, 7·30, and allylic, 7·85 methylene protons. Other spectral details resemble those of the acetate of rotenonic acid (17b); compound (17a) is now referred to as rot-2′-enonic acid. The new isomer, rot-3′-enonic acid (27b), was obtained on acid hydrolysis of its acetate. Structure (27a) was confirmed by oxidative cleavage with osmium tetroxide–sodium metaperiodate, when the expected methyl ketone (27c) was obtained, $\nu_{max.}$ 1766, 1716, and 1686 cm^{-1}, τ 7·90 (CH_3CO) and 7·70 (CH_2CO); on alkaline deuteriation both these n.m.r. signals disappeared. The course of hydrogenolysis of rotenone can thus involve 1,4-addition (O-1′–C-7′) giving rot-2′-enonic acid, and two types of 1,2-addition giving rot-3′-enonic acid (O-1′–C-5′) and dihydrorotenone (C-6′–C-7′).

(6a*S*,12a*S*)-Rot-2′-enonic acid was much more resistant to racemisation in bases (ethanolic sodium acetate, potassium carbonate–acetone, or pyridine) than rotenone;[20,21] stronger bases induced considerable decomposition, and yields of racemate were poor. (±)-Rot-2′-enonic acid was best prepared by hydrogenolysis of 'mutarotenone', a mixture[20,21] of (6a*S*,12a*S*,5′R)- and (6a*R*,12a*R*,5′*R*)-stereoisomers of rotenone.

With (±)-rot-2′-enonic acid in hand, its synthesis from (±)-9-demethylmunduserone was studied, using the Lewis acid catalysed condensation[31] with 3,3-dimethylallyl alcohol. Since only small amounts of the rotenoid were available the course of the condensation was followed by isotope dilution. (±)-9-Demethylmunduserone (3·90 mg)was treated with [1,1-$^3H_2$]-3,3-dimethylallyl alcohol (1·08 mg, 0·172 mCi) * and boron trifluoride–ether in methylene chloride, at 5°. The product was diluted with inactive (±)-rot-2′-enonic acid and recrystallised repeatedly; after 12 recrystallisations constant activity was attained, as shown by four further recrystallisations. The total activity retained showed a 23% yield of (±)-rot-2′-enonic acid in the synthesis.

Further investigations into *in vitro* transformations of rot-2′-enonic acid to parallel those of Scheme 5 have been carried out; these have used the optically active form, obtained from rotenone as described above. Here we report the formation of (—)-dalpanol (18), according to Scheme 6, involving epoxidation of the dimethylallyl substituent followed by intramolecular epoxide opening by the phenolic hydroxy-group. Two courses are open in such a reaction (Scheme 6, *a* and *b*), and studies with analogues in the coumarin field[32] suggest that path *b* is favoured by acid catalysed ring opening, but under neutral or alkaline conditions dihydrofurans (path *a*) are the major products. Thus, (6a*S*,12a*S*)-rot-2′-enonic acid was allowed to react with *m*-chloroperbenzoic acid in chloroform, in the presence of aqueous sodium carbonate. (—)-Dalpanol (18), $[\alpha]_D$ —132° (*c* 2, $CHCl_3$), was obtained, identical with the natural product.[33] Diastereoisomeric



SCHEME 6

(6a*S*,12a*S*,5′*S*)-dalpanol is presumably also formed in the reaction but was not isolated. But for the optical resolution of (±)-rot-2′-enonic acid, which has not yet been undertaken, this constitutes a total synthesis of (—)-dalpanol.

EXPERIMENTAL

Except where otherwise stated, the following generalisations apply. M.p.s were determined using a hot stage microscope. Optical rotations were measured with a half shadow polarimeter. U.v. data were recorded for ethanol solutions ($\log_{10}$ ε follows $\lambda_{max.}$ in parentheses). I.r. spectra were obtained for chloroform solutions. N.m.r. spectra were determined at 60 MHz in deuteriochloroform, using tetramethylsilane as internal standard. All hydroxylic protons were located by deuterium exchange. Molecular weights were measured by mass spectrometry. All

* We thank Mr. G. W. Kilbee for this sample.

[30] (*a*) H. L. Haller and P. S. Schaffer, *J. Amer. Chem. Soc.*, 1933, **55**, 3944; (*b*) F. B. LaForge and L. E. Smith, *ibid.*, 1929, **51**, 2574; (*c*) F. B. LaForge and H. L. Haller, *ibid.*, 1932, **54**, 810.

[31] F. Bohlmann and K. M. Kleine, *Chem. Ber.*, 1966, **99**, 885; A. C. Jain, P. Lal, and T. R. Seshadri, *Tetrahedron*, 1970, 2631.

[32] *Inter alia* F. Bohlmann and H. Franke, *Chem. Ber.*, 1971, **104**, 3229; R. P. H. Murray, M. Sutcliffe, and P. H. McCabe, *Tetrahedron*, 1971, **27**, 4901; L. Crombie, D. E. Games, N. J. Haskins, and G. F. Reed, *J.C.S. Perkin I*, 1972, 2247, 2248, 2256.

[33] D. Adinarayana, R. V. M. Campbell, L. Crombie, M. Radhakrishniah, and J. Rajasekhara Rao, *J. Chem. Soc.* (*C*), 1971, 29.

compounds mentioned in this section had u.v., i.r., and n.m.r. spectra in agreement with their structure, although these details are not all described. T.l.c. used silica Gel G; visualisation was effected with iodine vapour or aqueous hydrogen iodide. Preparative work (p.l.c.) employed silica gel HF_{254}. B.E.M.P. refers to benzene–ethyl acetate–methanol–light petroleum (b.p. 60—80°) (6 : 4 : 1 : 5). Laporte ' H ' alumina was used in column chromatography.

Isoderritol and Isoderritol isoflavone were prepared by published methods,[19] m.p. 145—146 and 183—183·5° respectively. In the latter preparations, a bright yellow crystalline compound was isolated by p.l.c. of the mother liquors, and proved to be 1-(*2-hydroxy-4,5-dimethoxyphenyl*)-2-(*4-hydroxy-2-isopropylbenzo*[b]*furan-5-yl*)*ethane*-1,2-*dione* (11b), m.p. 173—174° (Found: C, 65·35; H, 5·35%; *M*, 384·1197. $C_{21}H_{20}O_7$ requires C, 65·25; H, 5·2%; *M*, 384·1209), $\lambda_{max.}$ 240 (5·4), 249infl. (4·48), 284 (4·26), and 356 nm (3·99), $\nu_{max.}$ 1631, 1516, and 1467 cm^{-1}, τ −2·22 and −1·87 (chelated OH), 2·59 (1H, d, *J* 9 Hz), 3·17, 3·36, and 3·44 (all 1H, s), 6·05 and 6·30 (both 3H, s), 8·65 (6H, d, *J* 7 Hz).

Isorotenone from Isoderritol Isoflavone.—A solution of dimethylsulphoxonium methylide was prepared under nitrogen by stirring together oil-free sodium hydride (72 mg, 3 mmol) and trimethylsulphoxonium iodide (660 mg, 3 mmol) in dimethyl sulphoxide (15 cm^3) for 20 min. Isoderritol isoflavone (1 g, 2·54 mmol) in dimethyl sulphoxide (10 cm^3) was added, and stirring continued for 3 h at room temperature. The mixture was diluted with water (100 cm^3), acidified, and extracted with ethyl acetate. The extracts were washed, dried, and evaporated. The residue crystallised from methanol to provide the vinylcoumaranone (12) (490 mg, 46%), m.p. 143—144° (lit.,[19] m.p. 143—144°). Methylation with methyl iodide in acetone over dry potassium carbonate gave 7-*isopropyl*-2-(*2,4,5-trimethoxyphenyl*)-2-*vinylbenzo*[1,2-b:3,4-b′]*difuran*-3(2H)-*one* (12), m.p. 103—104° (Found: *M*, 408·150. $C_{24}H_{24}O_6$ requires *M*, 408·157). The vinylcoumaranone (100 mg) in pyridine (2 cm^3) was sealed in a glass vessel and heated at 100° overnight. The pyridine was evaporated and the residue purified by p.l.c. [silica gel G, ethyl acetate–benzene (4 : 1)] to afford (±)-isorotenone (13) (80 mg, 80%), m.p. 162—163°, undepressed by mixing with an authentic sample.[19]

The Course of 2-*Vinylcoumaran*-3-*one* (12) *Isomerisation; Time and Solvent Variations.*—In a typical experiment the vinylcoumaranone (12) (10 mg) was heated with the dry solvent (0·5 cm^3) at 100°, in a sealed vial incorporating a septum for sample withdrawal. Aliquot portions (25 mm^3) were removed at appropriate intervals, diluted in acetone (5 cm^3), and mixed with Goodhue reagent [5 cm^3; 0·1% alcoholic sodium nitrite–4·0% aqueous potassium hydroxide, (7 : 1)]. After 5 min 9N-sulphuric acid (12·5 cm^3) was added. The mixture was shaken and diluted with acetone to 25 cm^3. After 30 min the visible spectrum was recorded, and the absorbance at 548 nm ($\lambda_{max.}$) measured. The concentration of isorotenone formed was calculated from a calibration curve. The starting vinylcoumaranone, in the same test, did not give rise to significant absorption at or near 548 nm. The results are in the Table.

Conversion into isorotenone (13) of coumaranone (12) in various solvents

Pyridine								
t/min	2	2	10	22	33	45	63	3600
Conversion (%)	8	20	28	54	66	88	99	96
n-Butanol								
t/min	1	3	5	8	15	25	65	200
Conversion (%)	4	12	16	22	36	56	78	85
Ethylene glycol								
t/min	5	15	20	45	60	120	240	
Conversion (%)	7	11	18	32	37	43	52	
Dimethyl sulphoxide								
t/min	10	20	30	60	180	360		
Conversion (%)	4	6	9	17	18	12		
Toluene								
t/min	120	240						
Conversion (%)	0	0						

Preparation of Mutarotenone from Derritol Isoflavone.—Derritol, m.p. 159—161°, and derritol isoflavone, m.p. 178—179°, were prepared by established methods.[23] A solution of dimethylsulphoxonium methylide was prepared from oil-free sodium hydride (30 mg, 1·25 mmol), trimethylsulphoxonium iodide (275 mg, 1·25 mmol), and dimethyl sulphoxide (4 cm^3). Derritol isoflavone (400 mg, 1·02 mmol) in dimethyl sulphoxide (15 cm^3) was added and the mixture was stirred under dry nitrogen for 3 h. The mixture was poured into water, acidified, and extracted with ethyl acetate. The extracts were washed with water, dried, and evaporated. The product was purified by p.l.c. [B.E.M.P.; chloroform–isopropanol (10 : 1)], but the diastereoisomeric vinylcoumaranones (15) (100 mg) failed to crystallise. It was heated in dry pyridine (1 cm^3) at 100° for 48 h. Two products were isolated by p.l.c. (chloroform) and crystallisation: (i) didehydrorotenone (2 mg), m.p. 224—225°, and (ii) mutarotenone, m.p. 144—145°, (26 mg, 26% from the coumaranones). Both were identified by m.p., mixed m.p., and spectral comparison with authentic specimens.

7-*Methoxychroman*-4-*one* (23a).—3-(3-Methoxyphenoxy)-propionic acid (25 g; prepared, m.p. 78—80°, from 3-chloropropionic acid and *m*-methoxyphenol) was heated with polyphosphoric acid [250 g; freshly prepared from phosphorus pentoxide (125 g) and phosphoric acid (83 cm^3)] at 100° for 1 h. The red viscous product was poured over crushed ice (1 kg) and the mixture was extracted with chloroform. The extracts were washed with aqueous sodium hydrogen carbonate and water, and dried. Evaporation of the chloroform, and distillation of the residual oil, b.p. 108° at 5 mmHg, gave 7-methoxychroman-4-one (10·4 g, 46%), m.p. 46—47° (from light petroleum), (lit.,[24] m.p. 52—54°).

2′,4′,5′,7-*Tetramethoxyisoflavone* (21d).—4,5-Dimethoxy-*o*-benzoquinone (3 g) and 7-methoxychroman-4-one (2·4 g) in dry dimethyl sulphoxide (50 cm^3) were stirred together under dry nitrogen. Sodium hydride (400 mg) in dry dimethyl sulphoxide (10 cm^3) was added, and the mixture was stirred for 2 h. Conc. hydrochloric acid (8 cm^3), ice (100 g), and saturated aqueous potassium chloride (50 cm^3) were added in turn. The precipitated solid was collected in ethyl acetate. The organic solution was washed with water, dried, and evaporated. The residue crystallised from methanol to yield 4′,5′-dihydroxy-2′,7-dimethoxyisoflavone (1·92 g, 40%), m.p. 208—209° (lit.,[25] 209—210°).

Methylation of this compound (2·2 g) in acetone (60 cm³) over potassium carbonate (10 g) was effected with methyl iodide (5 cm³, 11·3 g) by heating under reflux overnight. Work-up gave 2′,4′,5′,7-tetramethoxyisoflavone (1·85 g, 76%), m.p. 191° (from methanol) (lit.,[25] 192°).

2′-Hydroxy-4′,5′,7-trimethoxyisoflavone (21b).—2′,4′,5′,7-Tetramethoxyisoflavone (1·8 g), anhydrous aluminium chloride (14 g), and acetonitrile (60 cm³) were heated under reflux with stirring for 16 h. The solvent was evaporated and the residue was treated with 10% aqueous hydrochloric acid (50 cm³) and crushed ice (100 g). The precipitate was filtered off, washed with water, and crystallised from methanol to form *2′-hydroxy-4′,5′,7-trimethoxyisoflavone* (0·96 g, 55%), dimorphic yellow needles, m.p. 180—181 and 195—196° (Found: C, 65·75; H, 5·1. $C_{18}H_{16}O_6$ requires C, 65·85; H, 4·9%), $\lambda_{max.}$ 221 (4·45), 247infl. (4·28), 266 (4·22), and 299 nm (4·26), $\nu_{max.}$ (KBr) 1619 (CO) cm⁻¹, τ ([$^2H_6$]Me_2SO) 0·95 (1H, OH), 1·63 (1H, s, 2-H), 1·89 (1H, d, *J* 11 Hz, 5-H), 2·80 (1H, d, *J* 2 Hz, 8-H), 2·87 (1H, dd, *J* 11, 2 Hz, 6-H), 3·08 (1H, s, 6′-H), 3·37 (1H, s, 3′-H), and 6·07, 6·20, 6·27 (all 3H, s, OMe).

Preparation of the 2-Vinylcoumaran-3-one (25).—Trimethylsulphoxonium iodide (264 mg), sodium hydride (30 mg), and dimethyl sulphoxide (5 cm³) were mixed under dry nitrogen for 15 min. 2′-Hydroxy-4′,5′,7-trimethoxyisoflavone (375 mg) was added, and the reaction was allowed to proceed for 90 min. The mixture was diluted with water, acidified, and extracted with ethyl acetate (2 × 500 cm³). The extracts were washed with water, dried, concentrated, and applied to p.l.c. plates. After elution with B.E.M.P. the major band was extracted to provide *2-(2-hydroxy-4,5-dimethoxyphenyl)-6-methoxy-2-vinylbenzo*[b]*furan-3*(2H)*-one* (25) (45 mg, 16%), m.p. 155—156° (from methanol) (Found: *M*, 342·1098. $C_{19}H_{18}O_6$ requires *M*, 342·1103), $\lambda_{max.}$ 233 (4·28), 270 (4·09), 293 (3·99), and 313 nm (3·91), $\nu_{max.}$ (KBr) 1682 (C=O) and 1622 cm⁻¹, τ (100 MHz) 0·86 (1H, s, OH), 2·38 (1H, d, *J* 9·5 Hz, 4-H), 2·92 (1H, s, 6′-H), 3·26 (1H, dd, *J* 9·5, 2 Hz, 5-H), 3·29 (1H, d, *J* 2 Hz, 7-H), 3·40 (1H, s, 3′-H), 3·69 (1H, 9, *J* 17·5, 10 Hz, C*H*=CH_2), 4·52 and 4·64 (2H, J_{AB} 2 Hz, CH=CH_2), 6·07, 6·17, and 6·18 (all 3H, s, OMe).

(±)-*Munduserone* (20).—The vinylcoumaranone was prepared as in the preceding experiment but without p.l.c. purification, and dissolved in pyridine (1 cm³). The solution was heated at 100° overnight, when the solvent was evaporated and the residue separated by p.l.c. to afford (±)-munduserone (48 mg, 18% from isoflavone), m.p. 171—172° (lit., m.p. 172°) (Found: *M*, 342·1162. Calc. for $C_{19}H_{18}O_6$: *M*, 342·1103). A second product was obtained from the p.l.c., and identified as *5,6-dimethoxy-3-(2-hydroxy-4-methoxybenzoyl)benzo*[b]*furan* (24a) (7 mg, 2·5%), m.p. 163° (Found: *M*, 328·0953. $C_{18}H_{16}O_6$ requires *M*, 328·0947), $\lambda_{max.}$ 245 (4·19), 293 (4·21), and 325 nm (4·06), $\nu_{max.}$ 1624, 1590, and 1493 cm⁻¹, τ (100 MHz) 1·97 (1H, s, 2-H), 2·16 (1H, d, *J* 9 Hz, 6′-H), 2·51 (1H, s, 4-H), 2·89 (1H, s, 7-H), 3·45 (1H, m, 3′-H), 3·50 (1H, dd, *J* 9, 3 Hz, 5′-H), and 6·05 (6H) and 6·13 (3H) (3 × OMe).

Preparation of 7-Benzyloxy-4′,5′-dihydroxy-2′-methoxyisoflavone (21e).—7-Hydroxy- and 7-benzyloxy-chromanone, m.p. 146—147 and 102—103°, were prepared by known routes.[28] The latter (1·71 g) with 4,5-dimethoxy-*o*-benzoquinone (1·50 g) in dry dimethyl sulphoxide (25 cm³) was stirred under nitrogen while sodium hydride (176 mg) in dimethyl sulphoxide (5 cm³) was added. The reaction was continued for 2 h and the product was isolated as in the parallel reaction above; crystallisation from ethanol gave *7-benzyloxy-4′,5′-dihydroxy-2′-methoxyisoflavone* (21e) (1·88 g, 71%), m.p. 183—184° (Found: C, 70·9; H, 4·95. $C_{23}H_{18}O_6$ requires C, 70·75; H, 4·65%), $\lambda_{max.}$ 218 (4·57), 237$_{infl}$ (4·43), 249 (4·39), 267 (4·18), and 298 nm (4·28), $\nu_{max.}$ (KBr) 3500, 1635, 1613, and 1570 cm⁻¹, τ ([$^2H_6$]Me_2SO) 1·17br (2H, OH), 1·81 (1H, s, 2-H), 1·92 (1H, d, *J* 9·5 Hz, 5-H), 2·53 (5H, s, Ph), 2·76 (1H, s, 8-H), 2·82 (1H, d, *J* 9·5 Hz, 6-H), 3·25 and 3·42 (both 1H, s, 6′- and 3′-H), 4·73 (2H, s, OCH_2), and 6·37 (3H, s, OMe).

2′,7-Dihydroxy-4′,5′-dimethoxyisoflavone (21a).—7-Benzyloxy-4′,5′-dihydroxy-2′-methoxyisoflavone (1 g), anhydrous potassium carbonate (3 g), and methyl iodide (3 cm³) in acetone (50 cm³) were refluxed together with stirring overnight. After removal of both solids and solvent, the residue was dissolved in chloroform. The chloroform solution was washed with aqueous alkali and water, dried, and evaporated. The residue was crystallised from methanol to provide 7-benzyloxy-2′,4′,5′-trimethoxyisoflavone (0·86 g, 80%), m.p. 144—145° (lit.,[29] m.p. 143—144°). This product (1·2 g) was treated in acetonitrile (30 cm³) with anhydrous aluminium chloride (4 g) at reflux temperature with stirring for 16 h. After evaporation of the solvent, the residue was acidified (ice cooling). The precipitate was filtered off, washed, and recrystallised from methanol. 2′,7-Dihydroxy-4′,5′-dimethoxyisoflavone (0·54 g, 60%) was obtained, m.p. 235—236° (lit.,[8a,c] 236—237°).

9-Demethylmunduserone (16).—Trimethylsulphoxonium iodide (1·32 g) and sodium hydride (150 mg) were stirred together in dry dimethylsulphoxide (10 cm³) under nitrogen, for 30 min, when 2′,7-dihydroxy-4′,5′-dimethoxyisoflavone (1·62 g) in dimethyl sulphoxide (5 cm³) was added. The reaction was continued for 90 min. The mixture was poured into ice–water, and acidified. The precipitate was collected into ethyl acetate (2 × 250 cm³) and the organic solution was washed, dried, and evaporated. The residue was purified by p.l.c., using chloroform–light petroleum (100 : 1), B.E.M.P., and chloroform–isopropanol (10 : 1), but could not be crystallised. The amorphous product (90 mg, 5% from isoflavone) was heated overnight at 100° in dry pyridine (3 ml). After evaporation of the solvent, and p.l.c. first with B.E.M.P., then with chloroform–isopropanol, (±)-*9-demethylmunduserone* (16) was obtained (70 mg, 4% from isoflavone, 78% from vinyl coumaranone; in repetition, the best yield attained was 14% from isoflavone). (±)-9-Demethylmunduserone was dimorphic, m.p. 149—150 and 203—204° (Found: *M*, 328·0944. $C_{18}H_{16}O_6$ requires *M*, 328·0947), $\lambda_{max.}$ 202 (4·61), 233 (4·14), 282 (4·15), and 317 nm (3·90), $\nu_{max.}$ (KBr) 3480, 3200, 1665, 1620, and 1518 cm⁻¹, τ (100 MHz) 2·11 (1H, d, *J* 8·5 Hz, 11-H), 3·05 (1H, s, 9-OH), 3·20 (1H, s, 1-H), 3·44 (1H, dd, *J* 8·5, 2 Hz, 10-H), 3·51 (2H, m, 4- and 8-H), 5·06 (1H, dd, 6a-H), 5·37 (1H, dd, *J* 12, 3 Hz, 6-H_a), 5·81 (1H, d, *J* 12 Hz, 6-H_b), 6·13 (1H, d, *J* 5 Hz, 12a-H), and 6·21 and 6·25 (both 3H, OMe). On methylation with diazomethane, (±)-munduserone was prepared, m.p. 171—172°, identical with the above sample.

A second product was obtained with 9-demethylmunduserone, and isolated during p.l.c. It proved to be *5,6-dimethoxy-3-(2,4-dihydroxybenzoyl)benzo*[b]*furan* (24b) (9·5 mg, 0·6%), m.p. 93—94° (from methanol) (Found: *M*, 314·0799. $C_{17}H_{14}O_6$ requires *M*, 314·0790, $\lambda_{max.}$ 245 (4·18), 296 (4·20), and 327infl. nm (4·07), $\nu_{max.}$ (KBr) 3500—3100, 1622, 1612, 1549, and 1493 cm⁻¹, τ (100 MHz) −2·52 (1H, s, OH), 1·96 (1H, s, 2-H), 2·16 (1H, d, *J* 8 Hz, 6′-H), 2·50

(1H, s, 4-H), 2·87 (1H, s, 7-H), 3·49 (1H, s, 3′-H), 3·54 (1H, d, *J* 8 Hz, 5′-H), and 6·04 (6H, s, 2 × OMe).

Alternative Route to 9-Demethylmunduserone.—2′,7-Diacetoxy-4′,5′-dimethoxyisoflavone (100 mg), m.p. 151—152° (lit.,[8a,c] m.p. 152—153°), potassium iodide (150 mg), anhydrous potassium carbonate (600 mg), and benzyl chloride (0·1 cm³) were heated together under reflux with acetone (20 cm³) for 18 h. Conc. hydrochloric acid (10 cm³) was added and the mixture was heated for 2 h more, when the solvents were evaporated. The oily residue crystallised from methanol to yield two products: (i) 7-benzyloxy-4′,5′-dimethoxy-2′-hydroxyisoflavone (33 mg, 32%), m.p. 173—174° (lit.,[8a,c] 172—173°), and (ii) 2′,7-dibenzyloxy-4′,5′-dimethoxyisoflavone (10 mg), m.p. 136°. Treatment of the former with dimethylsulphoxonium methylide [prepared as before, from trimethylsulphoxonium iodide (22 mg)] over 2·5 h gave, after the usual isolation procedure and p.l.c., a crystalline product (2 mg), m.p. 102—103°, probably 9-benzyloxy-2,3-dimethoxy-6a,12a-dihydrorotoxen-12(6*H*)-one, $\lambda_{max.}$ 276, 299, and 314 nm. Debenzylation over 30 min with aluminium chloride (0·2 g) in acetonitrile (2 cm³) gave a product with the same t.l.c. characteristics as 9-demethylmunduserone.

Hydrogenation of Rotenone.—(i) (6a*S*,12a*S*,5′*R*)-Rotenone (20 g) in pyridine (120 cm³) was hydrogenated over palladium catalyst (on barium sulphate support) (5 g), according to the published method.[30] The alkali-soluble part of the product yielded (6a*S*,12a*S*)-rot-2′-enonic acid (17a) (10·5 g, 52%), m.p. 206—207° (lit.,[30] 206—208°), $[\alpha]_D^{21}$ +32·3° (*c* 2·1, $CHCl_3$). This compound (2 g) in pyridine (15 cm³) with acetic anhydride (10 g) was set aside overnight. The solution was diluted with water and extracted with ethyl acetate. The extracts were washed with aqueous sodium bicarbonate and brine, and dried. Evaporation gave 9,12-*diacetoxy*-2,3-*dimethoxy*-8-(3-*methylbut*-2-*enyl*)-6,6a-*dihydro*[1]*benzopyrano*[3,4-b][1]*benzopyran* (26) (1·4 g), m.p. 132—133° (Found: *M*, 480·1777. $C_{27}H_{28}O_8$ requires *M*, 480·1784), $\lambda_{max.}$ 215 (4·39), 242infl. (4·06), 249 (4·13), 256 (4·09), 298 (3·92), 308infl. (3·84), 343infl. (4·15), 355 (4·35), and 372 nm (4·28), $\nu_{max.}$ 1754, 1615, and 1514 cm⁻¹, τ 7·68 and 7·80 (both 3H, s, 2 × Ac). Acetylation of rot-2′-enonic acid with acetic anhydride and aqueous alkali afforded 9-*acetoxy*-2,3-*dimethoxy*-8-(3-*methylbut*-2-*enyl*)-6a,12a-*dihydro*[1]*benzopyrano*[3,4-b][1]*benzopyran*-12(6H)-*one* (17b), m.p. 176—178° (Found: C, 68·05; H, 5·65. $C_{25}H_{26}O_7$ requires C, 68·6; H, 6·0%), $\lambda_{max.}$ 218 (4·47), 266 (4·02), 291 (3·76), and 319 nm (3·61), $\lambda_{max.}$ (alkali) 262 (3·91), 293 (3·59), and 350 nm (4·08), $\nu_{max.}$ 1764, 1682, 1597, and 1518 cm⁻¹, τ 7·72 (3H, s, Ac).

(ii) The above experiment was repeated but using palladium on carbon as catalyst (1 g). The products were collected in ether and extracted with aqueous alkali (2 × 500 cm³). The alkaline extracts were mixed with acetic anhydride (100 cm³) with stirring. The precipitated solid was removed and crystallised from chloroform–ethanol. The first two fractions afforded the monoacetate (17b) (12 g), m.p. 176—177°, and identical with the specimen described above. The next three fractions gave a solid (3·9 g), which was further purified by p.l.c. (B.E.M.P. as eluant) and crystallisation to give (6aS,12aS)-*rot*-3′-*enonic acid acetate* (27a), m.p. 140—141° (Found: C, 68·65; H, 6·15%; *M*, 438·1675. $C_{25}H_{26}O_7$ requires C, 68·5; H, 6·0%; *M*, 438·1678). The acetate (0·5 g) was refluxed in ethanol (15 cm³) with 2N aqueous sodium hydroxide (5 cm³) for 2 min. The cooled mixture was acidified. The precipitate was collected and recrystallised from aqueous isopropanol, to provide (6aS,12aS)-*rot*-3′-*enonic acid* (27b) (0·19 g, 42%), m.p. 176—178° (Found: C, 69·85; H, 5·85%; *M*, 396·1548. $C_{23}H_{24}O_6$ requires C, 69·7; H, 6·05%; *M*, 396·1573), $\lambda_{max.}$ 217infl. (4·37), 234 (4·22), 283 (4·21), and 291infl. nm (4·20), $\lambda_{max.}$ (alkali) 278 (4·07), 285 (3·96), 322infl. (4·03), and 352 nm (4·30), $\nu_{max.}$ 3592, 3253, 1670, 1603, and 1518 cm⁻¹, τ (100 MHz) 2·30 (1H, d, *J* 9 Hz, 11-H), 3·23 (1H, s, 1-H), 3·49 (1H, d, *J* 9 Hz, 10-H), 3·56 (1H, s, 4-H), 5·12 (1H, t, *J* 3·5 Hz, 6a-H), 5·35 and 5·40 (both 1H, 4′-Hz), 5·40 (1H, dd, *J* 12, 3·5 Hz, 6-H_a), 5·84 (1H, d, *J* 12 Hz, 6-H_b), 6·12 (1H, d, *J* 3·5 Hz, 12a-H), 6·22 and 6·28 (both 3H, s, OMe), 7·22 (2H, 1′-H_2), 7·83 (2H, 2′-H_2), and 8·24 (3H, s, 3′-Me).

(iii) The experiment was repeated using mutarotenone [3e] (10 g), pyridine (100 cm³), and palladium–barium sulphate catalyst (3 g). Isolation and crystallisation of the phenolic product in the previous manner afforded (±)-*rot*-2′-*enonic acid*, m.p. 179—180°, $[\alpha]_D^{26}$ 0° ($CHCl_3$), with u.v., i.r., and n.m.r. spectra identical with those of the optically active compound.

Reaction of (6aS,12aS)-*Rot*-3′-*enonic Acid Acetate with Osmium Tetroxide.*—A mixture of rot-3′-enonic acid acetate (2 g), osmium tetroxide (25 mg), and sodium periodate (5·2 g) in dioxan (75 cm³) and water (25 cm³) was stirred at ambient temperature for 2 h, when more solvent [dioxan–water (3 : 1)] (50 cm³) was added, and the reaction continued for 1 h. The mixture was filtered and the solids were washed with ether. The combined filtrate and washings were diluted with ether (500 cm³) and the solution was washed with water, dried, and evaporated. Crystallisation of the residue gave 9-*acetoxy*-2,3-*dimethoxy*-8-(3-*oxobutyl*)-6a,12a-*dihydro*[1]*benzopyrano*[3,4-b][1]*benzopyran*-12(6H)-*one* (27c), (0·76 g, 38%), m.p. 159—161° (from chloroform–ethanol) (Found: C, 65·35; H, 5·7%; *M*, 440·1452. $C_{24}H_{24}O_8$ requires C, 65·45; H, 5·5%; *M*, 440·1471), $\lambda_{max.}$ 217infl. (4·35), 263 (3·86), 294 (3·33), and 320 nm (3·18), $\nu_{max.}$ 1766, 1716, 1686, 1616, 1598, and 1521 cm⁻¹, τ 7·30 (4H, m, 1′- and 2′-H_2), 7·70 (3H, s, Ac), and 7·90 (3H, s, 3′-Me).

(±)-*Rot*-2′-*enonic Acid from* (±)-9-*Demethylmunduserone.*—(±)-9-Demethylmunduserone (3·90 mg, 0·0119 mmol), methylene chloride–1% boron trifluoride–ether (1 cm³), and [1-³H]-3-methylbut-2-en-1-ol (1·085 mg, 0·0126 mmol; spec. activity 13·708 mCi mmol⁻¹), was kept in a sealed vessel at 5° for 4 h. The solvent was evaporated under nitrogen and the residue dissolved in isopropanol with unlabelled (±)-rot-2′-enonic acid (500 mg). The product was crystallised, and recrystallised sixteen times more from isopropanol–water. Further dilution (1 : 1) was necessary after the tenth crystallisation. Constant activity (3·2 mCi mmol⁻¹) was attained after twelve recrystallisations, corresponding to a yield of 23 ± 2% of (±)-rot-2′-enonic acid.

Reaction of (6aS,12aS)-*Rot*-2′-*enonic Acid with* m-*Chloroperbenzoic Acid.*—(i) *m*-Chloroperbenzoic acid (0·65 g, 85%, 3·2 mmol) in chloroform (20 cm³) was added to (6a*S*,12a*S*)-rot-2′-enonic acid (1 g, 2·5 mmol) in chloroform (20 cm³) at 0°. Sodium carbonate (5·1 g) in water (40 cm³) was added, and the mixture was shaken at 0° for 40 min. The chloroform layer was separated and passed down a short alumina column, with chloroform elution. The eluate was evaporated to a white solid which was recrystallised thrice from benzene to give (−)-dalpanol (156 mg, 13%) as the benzene solvate, m.p. 132—135° (with loss of benzene and subsequent crystallisation); the benzene-free crystals melted at

192—194°, undepressed by mixing with natural (—)-dalpanol (Found: C, 71·1; H, 6·35. Calc. for $C_{23}H_{24}O_7,C_6H_6$: C, 71·0; H, 6·18%), $[\alpha]_D^{24}$ −132° (*c* 2·2, $CHCl_3$). Mass, i.r., u.v., and n.m.r. spectra were identical with those of the natural compound, which had $[\alpha]_D^{24}$ −136° ($CHCl_3$).[33]

(ii) A similar reaction, carried out in dry ether, without the addition of aqueous sodium carbonate, also gave (—)-dalpanol (9%), identical with the above specimen.

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