Synthesis of Sophorol, Violanone, Lonchocarpan, Claussequinone, Philenopteran, Leiocalycin, and Some Other Natural Isoflavonoids by the Oxidative Rearrangement of Chalcones with Thallium(III) Nitrate [1]

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Isoflavones are conveniently prepared by the oxidative rearrangement of 2'-hydroxy- or 2'-acetoxy-chalcones with thallium(III) nitrate in methanol into 1-(2-hydroxyphenyl)-3,3-dimethoxy-2-phenylpropan-1-ones [*e.g.* (46)] followed by cyclisation, and the following natural isoflavonoids were synthesised in this way: the isoflavanones sophorol (49) and violanone (68), the isoflavans vestitol (57), duartin (58), mucronulatol (59), laxifloran (60), and lonchocarpan (61), the isoflavan quinones mucroquinone (66) and claussequinone (67), the pterocarpans philenopteran (69), leiocalycin (54), and 2-hydroxy-3-methoxy-8,9-methylenedioxy-6a,11a-dihydropterocarpan (56).

Acid catalysed cyclisation of 1-(2-hydroxy-4-methoxyphenyl)-2-(2-hydroxy-4,5-methylenedioxyphenyl)-3,3-dimethoxypropan-1-one (48) gave no isoflavone but the two tetracyclic compounds, (53) (a derivative of 2-methoxypterocarp-6-ene) and (52) (a benzofuro[2,3-*b*][1]benzopyran).

Claussequinone (67) was rapidly formed by autoxidation of its hydroquinone precursor (64), suggesting that oxidation may also have occurred during the isolation of the metabolite.

SYNTHESIS of isoflavones usually involves ring closure of benzyl phenyl ketones,[2] the preparation of which is often unsatisfactory [3] or unsuccessful. The generally more accessible chalcones can be converted into isoflavones *via* chalcone epoxides [4] or by the oxidative rearrangement of chalcones by thallium(III) acetate in methanol,[5,6] *via* 1,2-diaryl-3,3-dimethoxypropan-1-ones. Both routes require the protection of the chalcone 2'-hydroxy-group. Recently it was found [7] that thallium(III) nitrate (TTN) is more efficient for the rearrangement of simple chalcones than the triacetate. With TTN the reaction is complete within a few minutes at room temperature, whereas thallium(III) acetate requires up to 100 h at 65°.[5,6]

We have found that simple unprotected 2'-hydroxychalcones, *e.g.* (1) can be smoothly converted by TTN into 1,2-diaryl-3,3-dimethoxypropan-1-ones [*e.g.* (46)], and that acid catalysed (or thermal) ring closure of the acetals gave the corresponding isoflavones: in this respect thallium(III) nitrate differs from the acetate, since the latter gives a number of transformation products [6] but no isoflavones.

The conditions for successful oxidative rearrangement of 2'-hydroxychalcones into acetals require that the chalcone should not be too insoluble in methanol, nor substituted in the position *para* (5') to the free hydroxy-group. With highly insoluble chalcones yields drop drastically; with 5'-substituted chalcones oxidation to quinonoid compounds takes place.

This new route to isoflavones has advantages over previous methods because instead of phenylacetic acid derivatives the readily available benzaldehydes are used for the construction of ring B of the isoflavones, and strongly acidic media as required by the Hoesch and Friedel–Crafts acylations are avoided.

In this paper we wish to demonstrate the value of the chalcone rearrangement in the synthesis of a number of natural isoflavonoids (isoflavanones, isoflavans, and pterocarpans).

(±)-*Sophorol.*—(3*R*)-Sophorol (49) was isolated in 1959 from *Sophora japonica* by Suginome,[8] who also prepared didehydrosophorol 2',7-dimethyl ether (21).[9]

First the synthesis of didehydrosophorol 7-methyl ether (22) was attempted: however, when the dihydroxyacetal (48) prepared from (2) *via* (47) was treated with acid, only a product of composition $C_{18}H_{14}O_6$, and two isomers of the expected isoflavone [m.p.s 175—178° (traces), and 169—171°] were isolated. The product of m.p. 175—178° was formulated as the aroylbenzofuran (51). It gave a positive iron(III) chloride test, in the n.m.r. spectrum instead of the characteristic peak of H-2 of isoflavones (δ *ca.* 7·9 [10]) there was a singlet at δ 7·37 (α-proton of a benzofuran), and in the i.r., C=C stretching bands appeared at 1515 and 1540 cm^{-1}.[11] Structure (52) for the product of m.p. 169—171° was based on its molecular formula ($C_{17}H_{12}O_6$, M^+ 212), the presence of a hydroxy-peak at 3400 cm^{-1} and lack of a carbonyl absorption in the i.r. spectrum, and on the fact that in the n.m.r. spectrum only one signal could be

[1] Presented in part at the 8th International Symposium on the Chemistry of Natural Products, New Delhi, India, February 1972, and published as a preliminary paper (L. Farkas, Á. Gottsegen, M. Nógrádi, and S. Antus, *J.C.S. Chem. Comm.*, 1972, 825).

[2] W. D. Ollis, in 'The Chemistry of Flavonoid Compounds ed. T. A. Geissman, Pergamon Press, Oxford, 1962, p. 385.

[3] M. Nógrádi, L. Farkas, and W. D. Ollis, *Chem. Ber.*, 1970, **103**, 999.

[4] S. K. Grover, A. C. Jain, and T. R. Seshadri, *Indian J. Chem.*, 1963, **1**, 517; see also R. Bognár and Gy. Litkei, *Acta Chim. Acad. Sci. Hung.*, 1971, **67**, 83.

[5] W. D. Ollis, K. L. Ormand, and I. O. Sutherland, *J. Chem. Soc.* (*C*), 1970, 119.

[6] W. D. Ollis, K. L. Ormand, B. T. Redman, R. J. Roberts, and I. O. Sutherland, *J. Chem. Soc.* (*C*), 1970, 125.

[7] A. McKillop, B. P. Swann, and E. C. Taylor, *Tetrahedron Letters*, 1970, 5281; A. McKillop, B. P. Swann, M. E. Ford, and E. C. Taylor, *J. Amer. Chem. Soc.*, 1973, **95**, 3641.

[8] H. Suginome, *J. Org. Chem.*, 1959, **24**, 1655.

[9] H. Suginome, *Bull. Chem. Soc. Japan*, 1966, **39**, 1525.

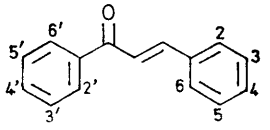
[10] T. J. Mabry, K. R. Markham, and M. B. Thomas, 'The Systematic Identification of Flavonoids,' Springer-Verlag, Berlin, 1970, p. 267.

[11] K. Nakanishi, 'Practical Infrared Spectroscopy,' Holden-Day, San Francisco, 1962, p. 52.

detected (at δ 6·90) which could be assigned to a proton on the hetero-ring. Compound (52) gave a mono-acetate. The only other example of the benzofuro-[2,3-*b*][1]benzopyran ring system of (52) (11-hydroxy-3-methoxy-8,9-methylenedioxy-5a*H*-benzofuro[2,3-*b*][1]-benzopyran) known so far occurs in lisetin.[12] To the compound $C_{18}H_{14}O_6$ (M^+ 326) the mixed acetal structure (53) was assigned, because its n.m.r. spectrum showed besides aromatic and methylenedioxy-protons only two methoxy-signals and a one-proton singlet at δ 6·88. This structure was confirmed by its mass spectrum, in which the base peak corresponded to the loss of CH_3O,

TABLE 1

Analytical and physical data of chalcone derivatives

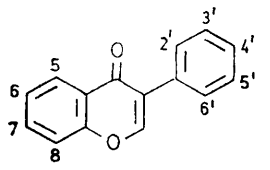


Compd. no.	Substituents 2′	3′	4′	5′	6′	2	3	4	5	6	Method of preparation *	Yield (%)	M.p. (°C)	Recryst. solvent	Analysis Found (%) C	H	Formula	Reqd. (%) C	H
(1)	OH	H	OMe	H	H	H	H	OMe	H	H	A	75	112—113	EtOH	71·8	5·5	$C_{17}H_{16}O_4$	71·8	5·7
(2)	OCH_2Ph	H	OMe	H	H	OCH_2Ph	H	OCH_2O		H	C	84	143—144	$CHCl_3$–MeOH	75·2	5·2	$C_{31}H_{26}O_6$	75·3	5·3
(3)	OAc	H	OCH_2Ph	H	H	OCH_2Ph	H	OCH_2O		H	H	69	133—135	AcOH	73·5	5·1	$C_{32}H_{28}O_7$	73·5	5·0
(4)	OH	H	OMe	OCH_2Ph	OMe	OCH_2Ph	H	OCH_2O		H	D	37	137—139	$CHCl_3$–MeOH	70·4	5·1	$C_{32}H_{28}O_8$	71·1	5·2
(5)	OAc	H	OMe	OCH_2Ph	OMe	OCH_2Ph	H	OCH_2O		H	H	65	121—122	MeOH	70·3	5·2	$C_{34}H_{30}O_9$	70·1	5·2
(6)	OH	H	OMe	OCH_2Ph	H	OCH_2Ph	H	OCH_2O		H	E	53	152—154	AcOH	73·0	5·0	$C_{31}H_{26}O_7$	72·9	5·1
(7)	OAc	H	OMe	OCH_2Ph	H	OCH_2Ph	H	OCH_2O		H	H	74	128—130	MeOH	71·7	5·1	$C_{33}H_{28}O_8$	71·7	5·1
(8)	OH	H	OCH_2Ph	H	H	OCH_2Ph	H	OMe	H	H	A	75	142—144	AcOH	76·9	5·6	$C_{30}H_{26}O_5$	77·2	5·6
(9)	OH	OMe	OCH_2Ph	H	H	OMe	OCH_2Ph	OMe	H	H	F	28	138—140	MeOH	72·6	5·8	$C_{32}H_{30}O_7$	73·0	5·7
(10)	OH	OMe	OCH_2Ph	H	H	H	OCH_2Ph	OMe	H	H	F	58	135—137	MeOH	75·3	6·0	$C_{31}H_{28}O_6$	75·0	5·7
(11)	OAc	OMe	OCH_2Ph	H	H	H	OCH_2Ph	OMe	H	H	H	82	151—153	MeOH	73·2	5·2	$C_{33}H_{30}O_7$	73·6	5·6
(12)	OH	H	OCH_2Ph	H	H	H	OCH_2Ph	OMe	H	H	E	85	166—168	AcOH	77·1	5·6	$C_{30}H_{26}O_5$	77·2	5·6
(13)	OAc	H	OCH_2Ph	H	H	H	OCH_2Ph	OMe	H	H	H	95	125—127	MeOH	75·5	5·6	$C_{32}H_{28}O_6$	75·6	5·6
(14)	OH	H	OCH_2Ph	H	H	OCH_2Ph	H	OMe	OCH_2Ph	H	G	61	168—170	AcOH	77·8	5·7	$C_{37}H_{32}O_6$	77·6	5·6
(15)	OAc	H	OCH_2Ph	H	H	OCH_2Ph	H	OMe	OCH_2Ph	H	H	82	124—126	MeOH	75·9	5·7	$C_{39}H_{34}O_7$	76·2	5·6
(16)	OH	H	OCH_2Ph	H	H	OMe	OCH_2Ph	OMe	H	H	A	39	118—121	MeOH	74·9	5·7	$C_{31}H_{28}O_6$	75·0	5·7
(17)	OH	H	OCH_2Ph	H	H	OMe	OMe	OCH_2Ph	H	OMe	A	54	115—117	MeOH	72·8	5·8	$C_{32}H_{30}O_7$	73·0	5·7
(18)	OH	H	OCH_2Ph	H	H	OCH_2Ph	OMe	OMe	H	H	A	44	136—137	MeOH	74·8	5·4	$C_{31}H_{28}O_6$	75·0	5·7
(19)	OH	H	OCH_2Ph	H	H	OMe	OMe	OCH_2Ph	H	H	A	80 †		MeOH	74·8	5·3	$C_{31}H_{28}O_6$	75·0	5·7
(20)	OH	H	OCH_2Ph	H	H	OCH_2Ph	OMe	OCH_2Ph	H	OMe	A	66	126—128	AcOH	75·9	5·7	$C_{38}H_{34}O_7$	75·7	5·7

* For details, see Experimental section. † Data given for the mixture of (18) and (19).

TABLE 2

Analytical and physical data of isoflavone derivatives

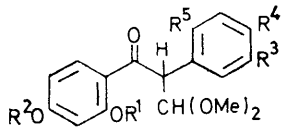


Compd. no.	Substituents 5	6	7	8	2′	3′	4′	5′	6′	Method of preparation ª	Yield (%) ᵇ	M.p. (°C)	Recryst. solvent	Analysis Found (%) C	H	Formula	Reqd. (%) C	H
(21)	H	H	OMe	H	OMe	H	OCH_2O		H	A	47	212—213	EtOH	66·0	4·2	$C_{18}H_{14}O_6$	66·2	4·3
(22)	H	H	OMe	H	OH	H	OCH_2O		H	C	60	203—204	MeOH	65·1	3·8	$C_{17}H_{12}O_6$	65·4	3·9
(23)	H	H	OCH_2Ph	H	OCH_2Ph	H	OCH_2O		H	B	62	152—154	MeOH	74·3	4·6	$C_{29}H_{22}O_6$	74·7	4·8
(24)	H	H	OH	H	OH	H	OCH_2O		H	C	78	246—248	MeOH	64·2	3·6	$C_{16}H_{10}O_6$	64·4	3·4
(25)	H	H	OAc	H	OAc	H	OCH_2O		H	D	75	189—191	MeOH	62·6	3·8	$C_{20}H_{14}O_8$	62·8	3·7
(26)	OMe	OCH_2Ph	OMe	H	OCH_2Ph	H	OCH_2O		H	B	34	159—160	MeOH	71·3	5·0	$C_{32}H_{26}O_8$	71·4	4·9
(27)	OMe	OH	OMe	H	OH	H	OCH_2O		H	C	46	248—249	MeOH	59·9	4·0	$C_{18}H_{14}O_8$	60·3	3·9
(28)	OMe	OAc	OMe	H	OAc	H	OCH_2O		H	D	65	180—182	MeOH	59·6	4·0	$C_{32}H_{28}O_{10}$	59·7	4·1
(29)	H	OCH_2Ph	OMe	H	OCH_2Ph	H	OCH_2O		H	B	57	179—180	Me_2CO	73·3	4·8	$C_{31}H_{24}O_7$	73·2	4·8
(30)	H	OH	OMe	H	OH	H	OCH_2O		H	C	59	259—261	Me_2CO	62·5	4·0	$C_{17}H_{12}O_7$	62·2	3·7
(31)	H	H	OCH_2Ph	H	OCH_2Ph	H	OMe	H	H	A	70	132—134	MeOH	77·7	5·2	$C_{30}H_{24}O_5$	77·6	5·2
(32)	H	H	OH	H	OH	H	OMe	H	H	C	72	220—221	EtOH ᶜ	67·3	4·3	$C_{16}H_{12}O_5$	67·6	4·3
(33)	H	H	OCH_2Ph	OMe	OMe	OCH_2Ph	OMe	H	H	A	14	136—138	EtOH	73·6	5·1	$C_{32}H_{26}O_7$	73·3	5·4
(34)	H	H	OCH_2Ph	OMe	H	OCH_2Ph	OMe	H	H	B	44	150—151	MeOH	75·0	5·0	$C_{31}H_{26}O_6$	75·3	5·3
(35)	H	H	OCH_2Ph	H	H	OCH_2Ph	OMe	H	H	B	61	132—134	MeOH	77·9	4·9	$C_{30}H_{24}O_5$	77·6	5·2
(36)	H	H	OCH_2Ph	H	OCH_2Ph	H	OMe	OCH_2Ph	H	B	56	127—129	MeOH	77·7	5·3	$C_{37}H_{30}O_6$	77·9	5·3
(37)	H	H	OCH_2Ph	H	OMe	OCH_2Ph	OMe	H	H	A	77	145—147	EtOH	75·1	5·3	$C_{31}H_{26}O_6$	75·3	5·3
(38)	H	H	OH	H	OMe	OH	OMe	H	OMe	C	68	251—253	MeOH	64·8	4·5	$C_{17}H_{14}O_6$	65·0	4·5
(39)	H	H	OCH_2Ph	H	OMe	OMe	OCH_2Ph	H	OMe	A	73	172—174	AcOH	73·0	5·5	$C_{32}H_{28}O_7$	73·3	5·4
(40)	H	H	OH	H	OMe	OMe	OH	H	OMe	C	72	267—268	MeOH	62·6	5·1	$C_{18}H_{16}O_7$	62·8	4·7
(41)	H	H	OCH_2Ph	H	OCH_2Ph	OMe	OMe	H	H	A	19	126—128	MeOH	75·4	5·5	$C_{31}H_{26}O_6$	75·3	5·3
(42)	H	H	OCH_2Ph	H	OMe	OMe	OCH_2Ph	H	H	A	42 ᵈ	151—153	MeOH	75·5	5·1	$C_{31}H_{26}O_6$	75·3	5·3
(43)	H	H	OH	H	OMe	OMe	OH	H	H	C	68	277—279	MeOH	64·8	4·4	$C_{17}H_{14}O_6$	65·0	4·5
(44)	H	H	OCH_2Ph	H	OCH_2Ph	OMe	OCH_2Ph	H	OMe	A	68	153—155	EtOH	75·8	5·4	$C_{38}H_{32}O_7$	76·0	5·4
(45)	H	H	OH	H	OH	OMe	OH	H	OMe	C	66	266—268	EtOH	61·6	4·3	$C_{17}H_{12}O_7$	61·8	4·3

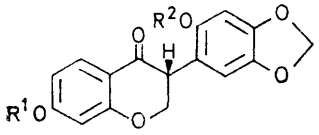
ª For details, see Experimental section. ᵇ Calculated on chalcone. ᶜ M.p. of diacetate 175—177°. ᵈ Isolated from a mixture of (41) and (42).

[12] C. P. Falshaw, W. D. Ollis, J. A. Moore, and K. Magnus, *Tetrahedron Suppl.*, 1966, 333.

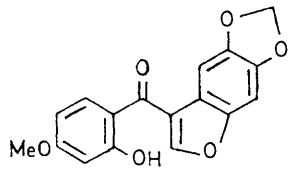
the absence of a carbonyl band in the i.r. and the close similarity of the u.v. spectrum with that of known pterocarpenes.[13]



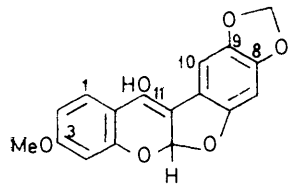
(46) R^1=H, R^2=Me, R^3=R^5=H, R^4=OMe
(47) R^1=CH_2Ph, R^2=Me, R^3,R^4=OCH_2O, R^5=OCH_2PH
(48) R^1=H, R^2=Me, R^3,R^4=OCH_2O, R^5=OH



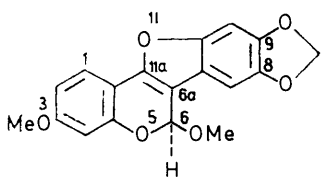
(49) R^1=R^2=H (Sophorol)
(50) R^1=R^2=Ac



(51)



(52)

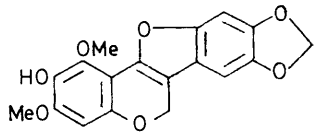


(53)

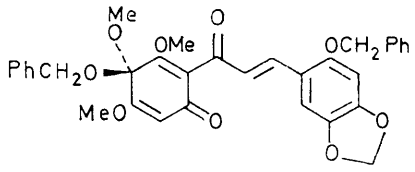
In contrast to acid catalysed ring closure, thermolysis of the dihydroxy-acetal (48) gave a mixture of the expected isoflavone (22) [14] and its furan isomer (51).

In order to avoid the formation of unwanted products sophorol was synthesised from a chalcone in which the 2-hydroxy-group (becoming 2'- in the isoflavone) was blocked. The 2'-hydroxy-chalcone precursor of sophorol was too insoluble and gave only traces of the desired isoflavone (23). Oxidation of the corresponding chalcone acetate (3) was however satisfactory and gave, after successive treatments with sodium methoxide and acid, didehydrosophorol dibenzyl ether (23) in fair yield. This was transformed by hydrogenation of the isoflavone diacetate [15a] [sequence (23) ⟶ (24) ⟶ (25) ⟶ (50) ⟶ (49)] into (±)-sophorol (49).

Leiocalycin.—Leiocalycin (54) [15b] is a pterocarpene of unusual oxygenation pattern. In the course of its synthesis an interesting limitation of the direct oxidation method became apparent. Oxidation of chalcone (4) with TTN in methanol gave a yellow product ($C_{33}H_{30}O_9$, M^+ 570) in which, according to n.m.r., the cinnamoyl part of the chalcone remained unchanged and which contained an additional methoxy-group. The upfield shift of the C-3' proton by 0·70 p.p.m. indicated that the aromaticity of the pertinent ring was disturbed. Formulation of this product as (55) is in accordance with the hypothesis of McKillop *et al.*,[16] who assumed an intermediate of similar type in the oxidation of *p*-substituted phenols to quinones by thallium(III) trifluoroacetate. Details of this and similar reactions will be discussed elsewhere. Oxidative rearrangement of the chalcone acetate (5) proceeded smoothly and gave the isoflavone



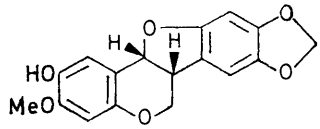
(54) (Leiocalycin)



(55)

(26). This was transformed *via* (27) and (28) into 2',6-diacetoxy-5,7-dimethoxy-4',5'-methylenedioxyisoflavanone and finally by acid catalysed ring closure and saponification into the leiocalycin (54).

2-Hydroxy-3-methoxy-8,9-methylenedioxy-6a,11a-dihydropterocarpan (56).—This pterocarpan was recently isolated from *Neorautanenia edulis*.[17] Its substitution pattern required the use of the acetate (7) of chalcone (6) as starting material. Oxidation of (7) gave the isoflavone (29); debenzylation to (30), reduction by sodium borohydride to a mixture of epimeric isoflavan-4-ols, and finally treatment with acid gave racemic 2-hydroxy-3-methoxy-8,9-methylenedioxy-6a,11a-dihydropterocarpan (56).

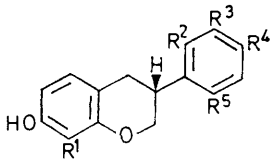


(56)

Natural Isoflavans.—The TTN oxidation of chalcones was utilised to prepare the racemic forms of a series of recently isolated isoflavans, *viz.* vestitol (57), duartin (58), mucronulatol (59),[18,19] laxifloran (60), and lonchocarpan (61),[20] the isoflavan quinones mucroquinone

[13] N. Adityachaudhury and P. K. Gupta, *Chem. and Ind.*, 1970, 1113; *Phytochemistry*, 1973, **12**, 425.
[14] M. Uchiyama, M. Matsui, *Agric. Biol. Chem.* (*Japan*), 1967, **31**, 1490.
[15] (*a*) L. Farkas, Á. Gottsegen, M. Nógrádi, and S. Antus, *J. Chem. Soc.* (*C*), 1971, 1994; (*b*) D. M. X. Donnelly and M. A. Fitzgerald, *Phytochemistry*, 1971, **10**, 3147.
[16] A. McKillop, B. P. Swann, M. J. Zelesko, and E. C. Taylor, *Angew. Chem.*, 1970, **82**, 84.
[17] G. J. H. Rall, J. P. Engelbrecht, and A. J. Brink, *Tetrahedron*, 1970, **26**, 5007.
[18] K. Kurosawa, W. D. Ollis, B. T. Redman, I. O. Sutherland, A. Braga de Oliveira, O. R. Gottlieb, and H. Magelhaes Alves, *Chem. Comm.*, 1968, 1263.
[19] K. Kurosawa, W. D. Ollis, B. T. Redman, I. O. Sutherland, O. R. Gottlieb, and H. Magelhaes Alves, *Chem. Comm.*, 1968, 1265.
[20] A. Pelter and P. I. Amenechi, *J. Chem. Soc.* (*C*), 1969, 887.

(66) [18,19] and claussequinone (67),[21] the closely related isoflavanone violanone (68),[22] and the pterocarpan philenopteran (69).[20]



(57) $R^1 = R^3 = R^5 = H$, $R^2 = OH$, $R^4 = OMe$ (Vestitol)

(58) $R^1 = R^2 = R^4 = OMe$, $R^3 = OH$, $R^5 = H$ (Duartin)

(59) $R^1 = R^5 = H$, $R^2 = R^4 = OMe$, $R^3 = OH$ (Mucronulatol)

(60) $R^1 = R^5 = H$, $R^2 = R^3 = OMe$, $R^4 = OH$ (Laxifloran ?)

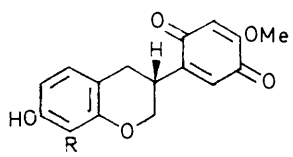
(61) $R^1 = H$, $R^2 = R^3 = R^5 = OMe$, $R^4 = OH$ (Lonchocarpan)

(62) $R^1 = R^4 = OMe$, $R^2 = R^5 = H$, $R^3 = OH$

(63) $R^1 = R^2 = R^5 = H$, $R^3 = OH$, $R^4 = OMe$

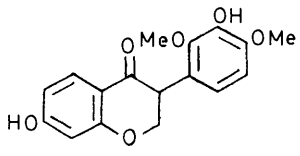
(64) $R^1 = R^2 = H$, $R^3 = R^5 = OH$, $R^4 = OMe$

(65) $R^1 = R^5 = H$, $R^3 = R^4 = OMe$, $R^2 = OH$

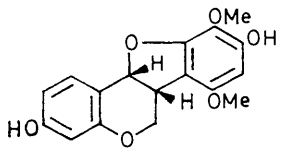


(66) R = OMe (Mucroquinone)

(67) R = H (Claussequinone)



(68) (Violanone)



(69) (Philenopteran)

The synthesis of (±)-vestitol has been carried out both by the classical approach *via* a benzyl phenyl ketone (72) and by the more efficient direct oxidation of a 2′-hydroxychalcone (8) (Scheme). Ring closure of the ketone (72), or oxidation of chalcone (8) followed by ring closure to the dibenzyloxyisoflavone (31) and debenzylation both gave the isoflavone (32), catalytic hydrogenation of which in acetic acid afforded (±)-vestitol (57).

The synthesis of duartin required the condensation of 4′-benzyloxy-2′-hydroxy-3′-methoxyacetophenone [23] with 3-benzyloxy-2,4-dimethoxybenzaldehyde [24] to give the 2′-hydroxychalcone (9), transformation of which into isoflavone (33) and reduction to (±)-duartin (58) was unexceptional.

The chalcone (10) required for the synthesis of mucroquinone (66) was too insoluble in methanol to permit successful oxidation, so it was acetylated to (11) and transformed *via* the isoflavone (34) into the isoflavan (62), which was smoothly oxidised to mucroquinone (66) by Frémy's salt.[25]

A similar sequence [(12) → (13) → (35) → (63) → (67)] led to (±)-claussequinone (67).

We also prepared claussequinone by another route, which has some interesting phytochemical implications. 2′,5′,7-Trisbenzyloxy-4′-methoxyisoflavone (36), prepared from chalcone acetate (15), was reduced to the corresponding trihydroxyisoflavan (64). This could not be isolated pure because of its rapid oxidation by air to claussequinone (67). Reduction of claussequinone by sodium dithionite gave the same unstable hydroquinone. Thus it cannot be excluded that claussequinone and mucroquinone are artefacts formed from the original hydroquinones during isolation.

The isoflavone (37) prepared by TTN oxidation and ring closure of the 2′-hydroxychalcone (16) was first debenzylated to (38) and then catalytically reduced in two steps: first in acetone to (±)-violanone (68) and then in acetic acid to (±)-mucronulatol (59).

4-Benzyloxy-2,3,6-trimethoxybenzaldehyde required for the synthesis of lonchocarpan (61) was prepared by successive monobenzylation and monomethylation of 2,4-dihydroxy-3,6-dimethoxybenzaldehyde.[26] Condensation to chalcone (17), oxidation to the isoflavone (39), debenzylation to (40), and reduction to the isoflavan completed the synthesis of (±)-lonchocarpan (61).

Laxifloran (60) is a minor constituent of *Lonchocarpus laxiflorus*, and could only be isolated as its dimethyl ether.[20] The position of one of the free hydroxy-groups [C(7)–OH) was proved by mass spectroscopy, that of the other [C(4)–OH] was postulated because of the co-occurrence of laxifloran and lonchocarpan (61). Assuming the non-identity of laxifloran and mucronulatol (59), structure (60) and its isomer with a free 2′-hydroxy (65) can be considered for laxifloran. We prepared (65) by an unambiguous sequence starting from the known 2-hydroxy-3,4-dimethoxybenzaldehyde [27] *via* (18) → (41) → (65). Synthesis of the 4′-hydroxy-isomer (60) was less straightforward due to difficulties of preparing pure 4-benzyloxy-2,3-dimethoxybenzaldehyde. Vilsmeier formylation of 1-benzyloxy-2,3-dimethoxybenzene gave an inseparable mixture of 4-benzyloxy-2,3-dimethoxy- and 2-benzyloxy-3,4-dimethoxy-benzaldehyde. This was condensed directly with 2′-hydroxy-4′-benzyloxyacetophenone [28] to give a mixture of chalcones [(18) + (19)], and ultimately the isoflavones [(41) + (42)],

[21] A. Braga de Oliveira, O. R. Gottlieb, T. M. Gonclaves, and W. D. Ollis, *Anais Acad. brasil. Cienc.*, 1971, **43**, 129 (*Chem. Abs.*, 1972, **76**, 110,253).

[22] W. D. Ollis in ' Recent Advances in Phytochemistry,' eds. T. J. Mabry, R. E. Alston, and V. C. Runeckles, Appleton-Century-Crofts, New York, 1968, p. 360.

[23] R. H. Khanna and T. R. Seshadri, *Indian J. Chem.*, 1963, **1**, 385.

[24] D. M. X. Donnelly, P. J. Keenan, J. P. Prendegast, *Phytochemistry*, 1973, **12**, 1157.

[25] L. Hörhammer, H. Wagner, H. Rösler, M. Keckeisen, and L. Farkas, *Tetrahedron*, 1965, **21**, 969.

[26] R. J. Clarke and A. Robertson, *J. Chem. Soc.*, 1949, 302.

[27] W. Baker and H. A. Smith, *J. Chem. Soc.*, 1931, 2542.

[28] K. C. Gulati, S. R. Seth, and K. Venkataraman, *J. Chem. Soc.*, 1934, 1765.

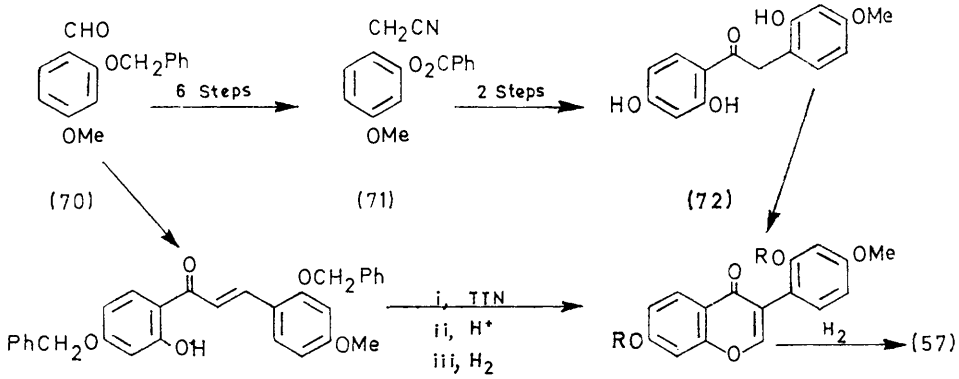
which could be separated. Compound (42) was reduced *via* (43) to (±)-4',7-dihydroxy-2',3'-dimethoxyisoflavan (60).

Since the mass spectra of (59), (60), and (65) differed only in minor details and a comparison with the mass spectrum of natural laxifloran was inconclusive, the position of the free hydroxy-groups in ring B of laxifloran has remained undecided.

Philenopteran.—The pterocarpan philenopteran (69) has the same oxygenation pattern as lonchocarpan (61). Preparation of chalcone (20) and its transformation into mucronulatol, lonchocarpan, mucroquinone, philenopteran, and 2-hydroxy-3-methoxy-8,9-methylenedioxy-6a,11a-dihydropterocarpan in chloroform solutions were identical with those of the natural products.

Aldehydes.—2-Benzyloxy-4-methoxybenzaldehyde,[15] 2-methoxy-4,5-methylenedioxybenzaldehyde,[9] 3-benzyloxy-4-methoxybenzaldehyde,[29] 2,5-dibenzyloxy-4-methoxybenzaldehyde,[30] and 3-benzyloxy-2,4-dimethoxy-benzaldehyde [24] were prepared by known methods.

2-Benzyloxy-4,5-methylenedioxybenzaldehyde. 2-Hydroxy-4,5-methylenedioxybenzaldehyde [9] (1·66 g) in dimethylformamide (10 ml) was boiled with benzyl chloride (1·25 ml)



SCHEME

the trisbenzyloxyisoflavone (44) and finally into the trihydroxyisoflavone (45) proceeded without difficulties. Presumably owing to steric hindrance caused by *ortho*-substituents of ring B, reduction of (45) both by $LiAlH_4$ or $NaBH_4$ was very slow and gave, after ring closure by acid, racemic philenopteran (69) only in very low yield.

In the paper describing their isolation,[18] reference was made to unpublished syntheses of (±)-vestitol, (±)-duartin, (±)-mucronulatol, and (±)-mucroquinone. The syntheses of laxifloran, lonchocarpan, violanone, claussequinone, and philenopteran have not previously been reported.

EXPERIMENTAL

The purity of all compounds was checked by t.l.c. and their structure confirmed by i.r. and n.m.r. spectra, but only relevant data are quoted.

^1H N.m.r. spectra were recorded on a Perkin-Elmer R 12 (60 MHz) spectrometer in $CDCl_3$; i.r. spectra were determined, unless otherwise stated, for KBr discs with a Spectromom 2000 spectrometer. Mass spectra were recorded on an A.E.I. MS9 instrument. U.v. spectra were determined for ethanolic solutions with a Unicam SP 700 spectrometer. M.p.s were determined with a Kofler hot-stage apparatus.

Acetylations were carried out by heating the hydroxy-compounds with acetic anhydride in pyridine on a steam-bath for 2 h.

I.r. spectra of synthetic racemic vestitol, duartin, and potassium carbonate (2 g). Dilution with water and recrystallisation from MeOH gave the *aldehyde* (1·5 g), m.p. 98—99° (Found: C, 70·5; H, 4·7. $C_{15}H_{12}O_4$ requires C, 70·3; H, 4·7%).

4-Benzyloxy-2-hydroxy-3,6-dimethoxybenzaldehyde. 2,4-Dihydroxy-3,6-dimethoxybenzaldehyde [26] (2 g) in dimethylformamide (50 ml) was stirred at 65° for 35 min with benzyl chloride (1·37 ml, 1·2 equiv.) and potassium carbonate (3 g) in the presence of sodium iodide. Steam distillation and recrystallisation from MeOH gave the *monobenzylated aldehyde*, m.p. 122—123° (Found: C, 67·2; H, 6·2. $C_{16}H_{16}O_5$ requires C, 66·6; H, 5·6%).

4-Benzyloxy-2,3,6-trimethoxybenzaldehyde. 4-Benzyloxy-2-hydroxy-3,6-dimethoxybenzaldehyde (800 mg) in dry acetone (15 ml) was stirred at 56° for 4 h with dimethyl sulphate (0·37 ml) and potassium carbonate (1·12 g). Steam distillation and recrystallisation from methanol gave the *trimethoxy-aldehyde*, m.p. 77—79° (Found: C, 67·1; H, 5·8. $C_{17}H_{18}O_5$ requires C, 67·5; H, 6·0%).

Formylation of 1,2-dimethylpyrogallol. 1-Benzyloxy-2,3-dimethoxybenzene was obtained as an oil by benzylation of 2,3-dimethoxyphenol (3·1 g) in dimethylformamide. This was added in portions to a complex of phosphoryl chloride (2·7 ml) and *N*-methylformanilide (4 ml). Stirring for 5 h at room temperature, dilution with ice-cold water, and extraction with chloroform and chromatography on silica gel (chloroform) resulted in a mixture of 4-benzyloxy-2,3-dimethoxybenzaldehyde and 2-benzyloxy-3,4-dimethoxybenzaldehyde.

2,4-Bisbenzyloxy-3,6-dimethoxybenzaldehyde. 1,3-Bisbenzyloxy-2,5-dimethoxybenzene (2·1 g) in chlorobenzene

[29] A. Lovecy, R. Robinson, and S. Sugasawa, *J. Chem. Soc.*, 1930, 817.

[30] J. Daly, L. Horner, and B. Witkop, *J. Amer. Chem. Soc.*, 1961, **83**, 4787.

(7 ml) was added in portions to a complex of phosphoryl chloride (0·93 ml) and *N*-methylformanilide (1·37 ml). This was stirred at room temperature for 4 h, diluted with ice-cold water, and neutralised with sodium acetate. Steam distillation and crystallisation of the residue gave the *aldehyde*, m.p. 100—102° (from methanol) (Found: C, 73·3; H, 5·9. $C_{23}H_{22}O_5$ requires C, 73·0; H, 5·9%).

Acetophenones.— 4′-Benzyloxy-2′-hydroxy-3′-methoxyacetophenone,[23] 4′-benzyloxy-2′-hydroxyacetophenone,[28] 2′-hydroxy-4′,6′-dimethoxyacetophenone,[31] 2′-benzyloxy-4′-methoxyacetophenone,[32] 3′-benzyloxy-6′-hydroxy-2′,4′-dimethoxyacetophenone,[33] and 5′-benzyloxy-2′-hydroxy-4′-methoxyacetophenone [34] were prepared by known methods.

Chalcones.—2′-Hydroxy-4,4′-dimethoxychalcone (1) [35] is a known compound. The new chalcones were prepared by one of the general methods (A—H) given below, and their physical and analytical data were summarised in Table 1. Equimolecular amounts (0·01 mol) of aldehyde and acetophenone were treated with alkali as specified under A—G, acidified with 10% aqueous HCl, and separated and recrystallised from the solvent given in Table 1. General methods: A, heating on a steam-bath for 1 h with a mixture of EtOH (30 ml) and 50% (w/w) aqueous NaOH (5 ml); B, refluxing for 8 h with a mixture of EtOH (35 ml) and piperidine (3·5 ml); C, stirring at room temperature for 12 h with a mixture of MeOH (100 ml) and 50% (w/w) aqueous KOH (40 ml); D, refluxing for 5 h with a mixture of MeOH (4·5 ml) and 16% (w/w) aqueous NaOH (8·5 ml); E, heating on a steam-bath for 8 h with a mixture of MeOH (11 ml) and 24% (w/w) NaOH (22 ml); F, heating at 65° for 16 h with a mixture of n-butanol (50 ml) and 25% (w/w) aqueous NaOH (100 ml) followed by steam distillation; G, refluxing for 10 h with a mixture of n-butanol (50 ml) and 25% (w/w) aqueous NaOH (100 ml) followed by steam distillation; and H, acetylation of the corresponding 2′-hydroxychalcone.

1,2-*Diaryl*-3,3-*dimethoxypropan*-1-*ones.*—*General method.* To a stirred solution or suspension of chalcone (2·0 mmol) in analytical grade methanol (100—300 ml), thallium(III) nitrate trihydrate [36] (2·2 mmol) was added. Reaction was almost instantaneous with soluble chalcones, while suspensions required 1—5 h stirring at room temperature. The solution of the acetal obtained in this way could be directly processed to isoflavones. Acetals were isolated in pure crystalline state in the following cases.

1-(2-*Benzyloxy*-4-*methoxyphenyl*)-3,3-*dimethoxy*-2-(4-*methoxyphenyl*)*propan*-1-*one*.[6] This had m.p. 112° (lit.,[6] 113°) and was obtained from 2′-benzyloxy-4,4′-dimethoxychalcone [6] in 80% yield. With thallium(III) acetate the yield was 36%.[6]

1-(2-*Benzyloxy*-4-*methoxyphenyl*)-2-(2-*benzyloxy*-4,5-*methylenedioxyphenyl*)-3,3-*dimethoxypropan*-1-*one* (47). To a suspension of chalcone (2) in methanol (200 ml), TTN (2·16 g) was added in portions. After 90 min the solution was neutralised with 10% aqueous NaOH, evaporated, the residue extracted with $CHCl_3$, and the extract evaporated. Crystallisation from methanol gave the *propanone* (47) (1·15 g, 50%), m.p. 95—96° (Found: C, 70·9; H, 5·9. $C_{33}H_{32}O_8$ requires C, 71·2; H, 5·8%), δ 3·13 and 3·37 [s, 3,3-$(OMe)_2$], 3·71 (s, ArO*Me*), 4·85 and 4·92 (s, 2- and 2′-OCH_2Ph), 5·12 (d) and 5·83 (d) [AB system, *J* 7 Hz, $CH(OMe)_2CHCO$], 5·83 (s, OCH_2O), 6·23—6·40 (2H, m, 3′,5′-H_2), 6·50 and 6·98 (s, 3′-H and 6′-H), 7·27 (10H, s, 2 × Ph), and 7·55 (d, *J* 7 Hz, 6′-H).

1-(2-*Hydroxy*-4-*methoxyphenyl*)-2-(2-*hydroxy*-4,5-*methylenedioxyphenyl*)-3,3-*dimethoxypropan*-1-*one* (48). Catalytic hydrogenation of (47) in acetone gave the *dihydroxy-acetal* (48), m.p. 139—140° (from MeOH) (Found: C, 60·4; H, 5·3. $C_{19}H_{20}O_8$ requires C, 60·6; H, 5·4%), $\nu_{max.}$ ($CHCl_3$) 3600 (OH), 3300br (chelated OH), and 1625 (CO).

Isoflavones.—4′,7-Dimethoxyisoflavone [37] and 2′,7-dimethoxy-4′,5′-methylenedioxyisoflavone (21) [9] are known compounds; yields calculated on chalcone were 52 and 47%. New isoflavones were prepared by one of the general methods (A—D) given below; their physical and analytical data were summarised in Table 2. General methods: A, to a solution of the corresponding 1,2-diaryl-3,3-dimethoxypropan-1-one in MeOH (either obtained directly from the oxidation of a chalcone or prepared by dissolving the pure acetal), 10% hydrochloric acid (1/20 of the volume of MeOH) was added and the mixture heated on a steam-bath for 3—5 h. Evaporation and crystallisation (eventually column chromatography) gave the isoflavone; B, if the oxidation was carried out with a 2′-acetoxychalcone, treatment A was preceded by saponification with sodium methoxide and subsequent neutralisation; C, hydrogenolysis of the corresponding benzyloxyisoflavones in acetone solution in the presence of 10% palladium on charcoal catalyst; D, acetylation of the corresponding hydroxyisoflavone.

2,4-*Dihydroxyphenyl* 2-*Hydroxy*-4-*methoxybenzyl Ketone* (72).—Resorcinol (3·35 g) and 2-benzoyloxy-4-methoxyphenylacetonitrile [15] (4·05 g) were dissolved in dry ether (80 ml), anhydrous zinc chloride (8 g) was added and the solution was saturated at 0° with dry hydrogen chloride. Next day the solvent was decanted and the residual oil was boiled with water for 1 h; the resulting oil crystallised from methanol to give 2-*benzoyloxy*-4-*methoxybenzyl* 2,4-*dihydroxyphenyl ketone*, m.p. 164—166° (Found: C, 69·6; H, 4·6. $C_{22}H_{18}O_6$ requires C, 69·8; H, 4·8%).

To a solution of the benzoyloxy-ketone (0·5 g) in methanol (15 ml) aqueous sodium hydroxide (180 mg in 6 ml water) was added and the mixture was kept at 50° for 10 min. On acidification and subsequent dilution the hydroxy-ketone (72) (m.p. 137—141°) precipitated. This was sufficiently pure for further ring closure.

2′,7-*Dihydroxy*-4′-*methoxyisoflavone* (32).—The isoflavone (32) was also prepared by boiling ketone (72) (1·5 g) with triethyl orthoformate (1·5 ml) in dimethylformamide (15 ml) in the presence of piperidine (0·3 ml) for 1 h. Dilution with water gave crude material (1·1 g), which was purified by crystallisation from acetic acid to give the *isoflavone* (32), m.p. 220—221° (Found: C, 67·2; H, 4·3. $C_{16}H_{12}O_5$ requires C, 67·6; H, 4·3%).

Acid Catalysed Ring Closure of the Dihydroxy-acetal (48).—When a solution of the dihydroxy-acetal (48) (1·3 g) in methanol (30 ml) containing conc. hydrochloric acid (0·2 ml) was left for 6 h at room temperature and overnight at 0° crystals of 3,6-*dimethoxy*-8,9-*methylenedioxy*-6H-*benzofuro*-[3,2-c][1]*benzopyran* (53) (120 mg) separated, m.p. 141—

[31] V. D. N. Sastri and T. R. Seshadri, *Proc. Indian Acad. Sci.*, 1946, **23A**, 262.
[32] T. H. Simpson and R. S. Wright, *J. Org. Chem.*, 1961, **26**, 4686.
[33] M. G. Stout, H. Reich, and M. H. Huffman, *J. Pharm. Sci.*, 1964, **53**, 192.
[34] F. M. Dean, D. R. Randell, and G. Winfield, *J. Chem. Soc.*, 1959, 1071.
[35] S. V. Kostanecki and F. W. Osices, *Ber.*, 1899, **32**, 321.
[36] A. McKillop, J. D. Hunt, E. C. Taylor, and F. Kienzle, *Tetrahedron Letters*, 1970, 5275.
[37] L. Farkas, *Chem. Ber.*, 1957, **90**, 2940.

142° (from MeOH) (Found: C, 66·5; H, 4·1%; M^+, 326. $C_{18}H_{14}O_6$ requires C, 66·3; H, 4·3%; M, 326), $\nu_{max.}$ 1650, 1610, and 1585 cm^{-1}, $\lambda_{max.}$ 230 (log ε 4·23), 244sh (4·02), 283 (4·03), 331 (4·52), and 350 nm (4·60), δ 3·02 (s, 6-OMe), 3·81 (s, 3-OMe), 5·96 (s, OCH_2O), 6·55 (s, 10-H), 6·65—6·75 (2H, m, 2,4-H_2), 6·88 (s, 6-H), 7·04 (s, 7-H), and 7·50 (d, 1-H), *m/e* 326 (34%), 310 (1·5), 295 (100), 280 (3·4), 267 (1·7), 252 (6·4), 152 (1·9), and 147 (14).

Concentration of the mother liquor and chromatography on silica gel gave 11-*hydroxy*-3-*methoxy*-8,9-*methylenedioxy*-5a*H*-*benzofuro*[2,3-b][1]*benzopyran* (52) as prisms (225 mg), m.p. 174—176° (from MeOH) (Found: C, 65·2; H, 3·7%; M^+, 312. $C_{17}H_{12}O_6$ requires C, 65·4; H, 3·9%; M, 312); $\nu_{max.}$ 3450 (OH), 1625, 1600, and 1520 cm^{-1} (C=C), $\lambda_{max.}$ 229 (log ε 4·27), 281 (4·30), 331 (4·50), and 347 nm (4·53), δ [$CDCl_3$ + $(CD_3)_2CO$] 3·79 (s, OMe), 5·92 (s, OCH_2O), 6·49—6·67 (2H, m, 2,4-H_2), 6·90 (s, 6-H), 6·98 and 7·10 (each s, 7,10-H_2), and 7·72 (d, J 9 Hz, 1-H), *m/e* 312 (14%), 295 (40), 284 (100), 269 (46), 255 (3·5), 180 (3·1), 162 (8·4), and 142 (17). Compound (52) gave an *acetate* as needles, m.p. 181—182° (Found: C, 64·4; H, 4·0%; M^+, 354. $C_{19}H_{14}O_7$ requires C, 64·4; H, 4·0%; M, 354), $\lambda_{max.}$ 231sh (log ε 4·42), 282 (4·47), 3·29 (4·75), and 345 nm (4·70), δ 2·39 (s, OAc), 3·82 (s, OMe), 5·98 (s, OCH_2O), 6·70—6·90 (2H, m, 2,4-H_2), 6·95 (s, 6-H), 7·00 (each s, 7,10-H_2), and 7·92 (d, J 8 Hz, 1-H).

On rechromatography of the mother liquor a small amount of the benzofuran (51) was isolated.

Thermolysis of the Dihydroxy-acetal (48).—Compound (48) (200 mg) was kept at 175° until bubbling ceased (about 10 min). Chromatography of the product on silica gel with benzene gave some of the isoflavone (22) (for data see Table 2), but mainly 3-(2-*hydroxy*-4-*methoxybenzoyl*)-5,6-*methylenedioxybenzofuran* (51), m.p. 147—148° (Found: C, 65·8; H, 4·2. $C_{17}H_{12}O_6$ requires C, 65·4; H, 3·9%), $\nu_{max.}$ 3100 (C–H), 1635 (CO), 1580 (C=C aromatic), 1540, and 1515 cm^{-1} (C=C furan), $\lambda_{max.}$ 302 (log ε 4·25), 244 nm (4·44), δ (CF_3CO_2H) 3·53 (s, OMe), 5·57 (s, OCH_2O), 6·1—6·4 (2H, m, 3′,5′-H_2), 6·62 and 6·77 (s, 4,7-H_2), 7·46 (d, J 8·5 Hz, 6′-H), and 7·65 (s, 2-H).

(±)-2′,7-*Diacetoxy*-4′,5′-*methylenedioxyisoflavanone*.—Catalytic hydrogenation of 2′,7-diacetoxy-4′,5′-methylenedioxyisoflavone (25) in acetone gave after usual work-up and purification on a silica gel column (benzene–acetone 10 : 1) the *isoflavanone*, m.p. 154—156° (from methanol) (Found: C, 62·6; H, 4·2. $C_{20}H_{16}O_8$ requires C, 62·5; H, 4·2%).

(±)-2′,7-*Dihydroxy*-4′,5′-*methylenedioxyisoflavanone* [(±)-*Sophorol*] (49).—A solution of the diacetoxyisoflavanone in methanol was deacetylated by boiling for 5 min with sodium ethoxide. Acidification with carbon dioxide and subsequent evaporation yielded racemic sophorol (49), m.p. 193—195° (from benzene–methanol) [lit.,[8] for (3*R*)-sophorol 215°] (Found: C, 62·5; H, 4·4. Calc. for $C_{16}H_{12}O_6$,0·5H_2O: C, 62·7; H, 4·3%).

4-*Benzyloxy*-2-(2-*benzyloxy*-4,5-*methylenedioxycinnamoyl*)-3,4,5-*trimethoxycyclohexa*-2,5-*dienone* (55).—To a solution of the chalcone (4) (0·52 g) in methanol (150 ml), TTN (0·54 g) was added at 65°. After refluxing for 30 min the solution was neutralised by passing through a column of basic alumina. Evaporation and column chromatography on silica with $CHCl_3$ as eluant gave the *semiquinone* (55) (0·20 g) as yellow prisms, m.p. 136—138° (from aq. MeOH) (Found: C, 69·2; H, 5·2%; M^+, 570. $C_{33}H_{30}O_9$ requires C, 69·5; H, 5·3%; M, 570), $\nu_{max.}$ 1655 (CO, semiquinone) and 1610 cm^{-1} (CO), δ 3·20 (s, 4-OMe), 3·74 (s, 5-OMe), 3·93 (s, 3-OMe), 4·50 and 4·53 (inner lines of ABq, 4-CH_2Ph), 4·97 (s, 2′-CH_2Ph), 5·64 (s, 6-H), 6·00 (s, OCH_2O), 6·58 (s, 3′-H), 7·12 (s, 6′-H), 6·78 and 7·93 (AB-system, J_{AB} 18 Hz, CO–CH_B=CH_A), and 7·34 (10H, s, Ph).

2-*Hydroxy*-1,3-*dimethoxy*-8,9-*methylenedioxy*-6H-*benzofuro*[3,2-c][1]*benzopyran* (*Leiocalycin*) (54).—Catalytic hydrogenation of the diacetoxyisoflavone (28) in acetone gave 2′,6-*diacetoxy*-5,7-*dimethoxy*-4′,5′-*methylenedioxyisoflavanone*, m.p. 169—170° (from methanol) (Found: C, 59·9; H, 4·6. $C_{22}H_{20}O_{10}$ requires C, 59·5; H, 4·5%), $\nu_{max.}$ 1765 (ester CO) and 1685 cm^{-1} (CO), δ 2·25 and 2·33 [each s, 2′,6-$(OAc)_2$], 3·85 and 3·87 [each s, 5,7-$(OMe)_2$], 3·80—4·10 (1H, m, 3-H), 3·40—3·60 (2H, m, 2-H_2), 5·98 (s, OCH_2O), 6·37 (s, 1H), and 6·68 (2H, s, aromatic protons).

When a solution of this isoflavanone was boiled in methanol with a few drops of conc. hydrochloric acid, precipitation of the product soon began. After 45 min the product was separated and recrystallised from methanol to give leiocalycin (54), m.p. 198—200° (lit.,[15b] 194—196°), $\nu_{max.}$ 3440 (OH) and 1615 cm^{-1} (C=C), $\lambda_{max.}$ 254 (log ε 4·03), 259 (4·02), 292 (3·49), and 361 nm (4·37) (lit.,[15b] $\lambda_{max.}$ 251, 259, 294, 347, and 359 nm).

(±)-2-*Hydroxy*-3-*methoxy*-8,9-*methylenedioxy*-6a,11a-*dihydro*-6H-*benzofuro*[3,2′-c][1]*benzopyran* (56).—To the stirred solution of 2′,6-dihydroxy-7-methoxy-4′,5′-methylenedioxyisoflavone (300 mg) in a mixture of tetrahydrofuran–ethanol (1 : 1) (16 ml), sodium borohydride (700 mg) was added in small portions during 3 h. An hour later acetone (15 ml) was added, the solvent distilled off *in vacuo*, and the residue was acidified with 10% hydrochloric acid. The product gave needles (from acetone), m.p. 223—224° [lit.,[17] for (−)-(56), 238—239°] (Found: C, 64·7; H, 4·2. Calc. for $C_{17}H_{14}O_6$: C, 65·0; H, 4·5%); the n.m.r. spectrum of the synthetic product was identical with that for the natural one.[17] The acetate had m.p. 170—172° (from benzene) [lit.,[17] for the acetate of (−)-(56) 147—148°] (Found: C, 67·3; H, 4·9. Calc. for $C_{18}H_{16}O_7$: C, 67·1; H, 4·8%).

(±)-2′,4-*Dihydroxy*-4′-*methoxyisoflavan* [(±)-*Vestitol*] (57).—Catalytic hydrogenation of the dihydroxyisoflavone (32) gave racemic vestitol (57), m.p. 173—175° (from ethyl acetate) [lit.,[18] m.p. for (+)-vestitol 156°] (Found: C, 70·1; H, 6·1. Calc. for $C_{16}H_{16}O_4$: C, 70·6; H, 5·9%).

(±)-3′,7-*Dihydroxy*-2′,4′,8-*trimethoxyisoflavan* [(±)-*Duartin*] (58).—Catalytic hydrogenation of the dibenzyloxyisoflavone (33) gave racemic duartin, m.p. 199—201° (from MeOH) [lit.,[18] for (−)-duartin 149°] (Found: C, 64·8; H, 6·3%; M^+, 332. Calc. for $C_{18}H_{20}O_6$: C, 65·1; H, 6·1%; M, 332).

(±)-3′,7-*Dihydroxy*-2′,4′-*dimethoxyisoflavan* [(±)-*Mucronulatol*] (59).—Catalytic hydrogenation of the dihydroxyisoflavone (38) gave (±)-mucronulatol, m.p. 227—229° (from MeOH) (lit.,[18] 227°) (Found: C, 67·1; H, 6·0%; M^+, 302. Calc. for $C_{17}H_{18}O_5$: C, 67·5; H, 6·0%; M, 302).

(±)-4′,7-*Dihydroxy*-2′,3′,6′-*trimethoxyisoflavan* [(±)-*Lonchocarpan*] (61).—Catalytic hydrogenation of the dihydroxyisoflavone (40) gave after purification on a silica gel column, and crystallisation from MeOH (±)-lonchocarpan, m.p. 99—101° [lit.,[20] for (+)-(61) 155—157°] (Found: C, 64·8; H, 5·9%; M^+, 332. Calc. for $C_{18}H_{20}O_6$: C, 65·1; H, 6·1%; M, 332).

(±)-4′,7-*Dihydroxy*-2′,3′-*dimethoxyisoflavan* [(±)-*Laxifloran* (?)] (60).—Catalytic hydrogenation of the dihydroxyisoflavone (43) gave the (±)-*isoflavan* (60), m.p. 170—171° (from MeOH) (Found: C, 67·2; H, 5·6%; M^+, 302.

$C_{17}H_{18}O_5$ requires C, 67·5; H, 6·0%; *M*, 302), $\nu_{max.}$ 3370, 3280, 2900, 1620, 1600, 1515, 1495, 1425, 1390, 1330, 1280, 1210, 1180, 1150, 1105, 1070, 1055, 1020, 1005, 960, 875, 830, and 810 cm^{-1}.

(±)-2′,7-*Dihydroxy*-3′,4′-*dimethoxyisoflavan* (65).—Catalytic hydrogenation of the dibenzyloxyisoflavone (41) gave the (±)-*isoflavan* (65), m.p. 190—192° (from MeOH) (Found: C, 67·0; H, 6·0%; M^+, 302. $C_{17}H_{18}O_5$ requires C, 67·5; H, 6·0%; *M*, 302), $\nu_{max.}$ 3300, 2900, 2820, 1620, 1520, 1470, 1440, 1320, 1300, 1270, 1200, 1160, 1100, 1020, 965, 915, 880, 855, and 825 cm^{-1}.

(±)-3′,7-*Dihydroxy*-4′,8-*dimethoxyisoflavan* (62).—Catalytic hydrogenation of the dibenzyloxyisoflavone (34) resulted in the (±)-*isoflavan* (62), m.p. 162—164° (from MeOH) (Found: C, 67·3; H, 6·1. $C_{17}H_{18}O_5$ requires C, 67·5; H, 6·1%).

(±)-3′,7-*Dihydroxy*-4′-*methoxyisoflavan* (63).—Catalytic hydrogenation of the dibenzyloxyisoflavone (35) gave the (±)-*isoflavan* (63), m.p. 189—191° (from MeOH) (Found: C, 70·5; H, 6·1. $C_{16}H_{16}O_4$ requires C, 70·6; H, 5·9%).

(±)-3′,7-*Dihydroxy*-2′,4′-*dimethoxyisoflavan*-4-*one* [(±)-*Violanone*] (68).—Hydrogenation of a solution of the dihydroxyisoflavone (38) in acetone on palladium–charcoal catalyst yielded the (±)-*isoflavanone* (68), m.p. 204—206° (from benzene) (Found: C, 64·2; H, 5·1. $C_{17}H_{16}O_6$ requires C, 64·6; H, 5·1%), $\nu_{max.}$ 3300 (OH), 1665 (CO), and 1590 cm^{-1} (C=C).

(±)-2-(7-*Hydroxy*-8-*methoxy*-3-*chromanyl*)-5-*methoxy*-1,4-*benzoquinone* [(±)-*Mucroquinone*] (66).—To a solution of the isoflavan (62) (170 mg) in acetone–methanol (22 ml; 4 : 1), buffered with M/6-potassium dihydrogen phosphate, Fremy's salt (1·7 g in 27 ml water) was added. Next day the solvent was removed *in vacuo*, and the residue was extracted with chloroform to give the crude quinone. Crystallisation from methanol gave (±)-mucroquinone (66), m.p. 161—164° [lit.,[18] for (−)-mucroquinone 192°] (Found: C, 64·0; H, 4·7%; M^+, 316. $C_{17}H_{16}O_6$ requires C, 64·5; H, 5·1%; *M*, 316).

(±)-2′,5′,7-*Trihydroxy*-4′-*methoxyisoflavan* (64).—Hydrogenation of the tribenzyloxyisoflavone (36) gave the (±)-isoflavan (64), which suffered autoxidation during purification, resulting in claussequinone (67). Reduction of the latter with sodium dithionite in dimethylformamide gave the hydrochinone (64), m.p. 196—199° [mixed m.p. with (65) (m.p. 196—198°) 181—184°], $\lambda_{max.}$ 292 nm (log ε 3·52).

(±)-2-(7-*Hydroxychromanyl*)-5-*methoxy*-1,4-*benzoquinone* [(±)-*Claussequinone*] (67).—The isoflavan (63) (290 mg) was oxidised as described for (66) and chromatographed on silica gel (benzene–ethyl acetate 2 : 1) to yield *claussequinone* (67), m.p. 196—198° (Found: C, 66·5; H, 5·2%; M^+, 286. $C_{16}H_{14}O_5$ requires C, 67·1; H, 4·9%; *M*, 286), $\nu_{max.}$ 3450 (OH), 1675 (CO), and 1645 cm^{-1} (CO), $\lambda_{max.}$ 264 (log ε 3·96), 325 (3·05), and 248 nm (3·01), δ [$(CD_3)_2SO$] 2·7—3·0 (2H, m, 4′-H_2), 3·1—3·5 (1H, m, 3′-H), 3·9—4·4 (2H, m, 2′-H_2), 3·83 (s, OMe), 6·20 (s, 4-H), 6·58 (s, 2-H), and 6·3—7·1 (3H, m, aromatic protons).

(±)-3,9-*Dihyhroxy*-7,10-*dimethoxy*-6a,11a-*dihydro*-6H-*benzofuro*[3,2-c][1]*benzopyran* [(±)-*Philenopteran*] (69).—Reduction of the trihydroxyisoflavon (45) with $LiAlH_4$ in THF under mild conditions (4 h, room temperature) gave only the corresponding isoflavanone (m.p. 189—192°; *M*, 332); more vigorous conditions (10 h, stirring at 65°) resulted in a mixture, which after acidification was separated on a silica gel column (benzene–ethyl acetate 2 : 1) to yield (±)-philenopteran (69), m.p. 180—183° [lit.,[20] for (−)-philenopteran 186—187°] (Found: C, 64·2; H, 5·3%; M^+, 316. Calc. for $C_{17}H_{16}O_6$: C, 64·5; H, 5·1%; *M*, 316).

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