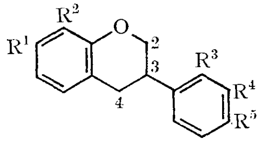
The Natural Occurrence of Isoflavans and an Isoflavanquinone

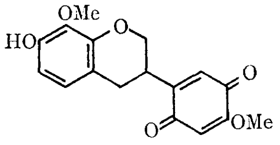
By K. KUROSAWA, W. D. OLLIS,* B. T. REDMAN, and I. O. SUTHERLAND
(*Department of Chemistry, The University, Sheffield* S3 7HF)

and A. BRAGA DE OLIVEIRA, O. R. GOTTLIEB, and H. MAGALHÃES ALVES
(*Instituto de Química, Universidade Federal de Minas Gerais, Belo Horizonte, Brasil*)

ALTHOUGH natural products of the isoflavonoid type are well known,[1] and have been recognised at several different oxidation levels, the natural occurrence of isoflavans in plants has not been reported. The extensively investigated animal metabolite equol[2] (I) has been regarded as the only known natural isoflavan, but we now report the isolation of three optically active isoflavans, (−)-duartin (II), (−)-mucronulatol (III), and (+)-vestitol (IV), from *Dalbergia variabilis* (Vogel) and five *Machaerium* species (Table). One of these compounds, mucronulatol (III), has also been isolated as a racemate from some of these sources.



	R^1	R^2	R^3	R^4	R^5
(I)	OH	H	H	H	OH
(II)	OH	OMe	OMe	OH	OMe
(III)	OH	H	OMe	OH	OMe
(IV)	OH	H	OH	H	OMe
(VI)	OH	OMe	H	OH	OMe



(V)

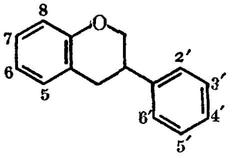
(−)-Duartin,† m.p. 149°, $C_{18}H_{20}O_6$, had an n.m.r. spectrum consistent with a trimethoxydihydroxyisoflavan structure [τ 3·3 (d, 1*H*), τ 3·48 (d, 1*H*) (AB system J_{AB} 8·5 c./sec.); τ 3·37 (s, 2*H*), four aromatic protons; τ 4·29 (s, 1*H*), τ 4·36 (s, 1*H*), two exchangeable hydroxy-protons; τ 6·07 (s, 6*H*), τ 6·11 (s, 3*H*), three methoxy-groups; τ 5·65 (q, 1*H*), *J* 10 and 3·5 c./sec., τ 6·03 (t, 1*H*), *J* 10 c./sec., τ 6·3—6·8 (m, 1*H*), τ 7·11 (d, 2*H*), *J* 7·5 c./sec., ABMXX′ system assignable to five protons at positions C(2), C(3), and C(4) respectively]. The four aromatic protons were observed as two AB systems (J_{AB} 8·5 c./sec.) in the spectra of duartin dimethyl ether and duartin diacetate. The constitution of (−)-duartin was shown to be (II) by synthesis of (±)-duartin by catalytic reduction[3] (10% palladium–carbon catalyst in acetic acid) of 7,3′-dihydroxy-8,2′,4′-trimethoxyisoflavone. The general features of the structures of (−)-mucronulatol (III), m.p. 145°, (±)-mucronulatol (III), m.p. 227°, and (+)-vestitol (IV), m.p. 156°, were similarly deduced from their mass and n.m.r. spectra. The relative positions of the hydroxy- and methoxy-substituents which were favoured on biogenetic grounds and which were indicated by the n.m.r. spectral comparison of the acetates and methyl ethers of (−)-mucronulatol and (+)-vestitol were settled by the synthesis of (±)-mucronulatol (III) and (±)-vestitol (IV) by the catalytic reduction of 7,3′-dihydroxy-2′,4′-dimethoxyisoflavone and 7,2′-dihydroxy-4′-methoxyisoflavone respectively. Details for the syntheses of 7,3′-dihydroxy-8,2′,4′-trimethoxyisoflavone, 7,3′-dihydroxy-2′,4′-dimethoxyisoflavone, and 7,2′-dihydroxy-4-methoxyisoflavone, which were the precursors of (±)-duartin (II), (±)-mucronulatol (III), and (±)-vestitol (IV) respectively, and 7,3′-dihydroxy-8,4′-dimethoxyisoflavone (see below) will be given in our full publication.

A related optically active compound, (−)-mucroquinone, $C_{17}H_{16}O_6$, was isolated from *M. mucronulatum* as orange needles, m.p. 192°, and its n.m.r. spectrum showed signals [τ 3·54 (d, 1*H*), *J* 1 c./sec. and τ 4·02 (s, 1*H*)] more characteristic of methoxy-*p*-benzoquinone ring protons (*cf.* the dalbergiones[4]) than benzenoid protons. This quinonoid structural assignment was supported by the visible, u.v., and i.r. spectral characteristics of mucroquinone. The n.m.r. spectrum of mucroquinone also included signals [τ 3·34 (d, 1*H*), τ 3·50 (d, 1*H*), AB system, J_{AB} 8·5 c./sec.)] assignable to a pair of *ortho*-related aromatic protons, two methoxyl groups [τ 6·22 (s, 3*H*); τ 6·27 (s, 3*H*)],

---

† All new compounds have been fully characterised by analytical, spectroscopic (u.v., i.r., and n.m.r.), and mass spectrometric data.

The natural occurrence of isoflavans



Compound	Name	Substituents	M.p.	$[\alpha]_D$[a]	Source[b]
(II)	(−)-Duartin	7,3′-(OH)$_2$-8,2′,4′-(OMe)$_3$	149°	−25°	B, C, D, F
(III)	(−)-Mucronulatol	7,3′-(OH)$_2$-2′,4′-(OMe)$_2$	145	−18·5	B, C, D, E, F
(III)	(±)-Mucronulatol	7,3′-(OH)$_2$-2′,4′-(OMe)$_2$	227	—	A, C
(IV)	(+)-Vestitol	7,2′-(OH)$_2$-4′-OMe	156	+21·6	A, E
(V)	(−)-Mucroquinone	7-(OH)-8,4′-(OMe)$_2$-2′,5′-quinone	192	−15·4	C

[a] In acetone solution, except for (+)-vestitol (IV), which was measured in methanol.

[b] A, *Dalbergia variabilis* Vogel (total wood); B, *Machaerium acutifolium* Vogel (heartwood); C, *Machaerium mucronulatum* Mart. (total wood); D, *Machaerium opacum* Vogel (heartwood); E, *Machaerium vestitum* Vogel (total wood); F, *Machaerium villosum* Vogel (heartwood).

one exchangeable hydroxyl proton [τ *ca.* 4·2 (broad s, 1*H*)], and the protons at C(2), C(3), and C(4) of an isoflavan structure [τ 5·68 (q, 1*H*), *J* 2·5 and 10·5 c./sec; τ 5·91 (q, 1*H*), *J* 6·5 and 10·5 c./sec.; τ 6·54 (m, 1*H*); τ 6·98 (q, 1*H*) *J* 6 and 16 c./sec.; τ 7·28 (q, 1*H*), *J* 6·5 and 16 c./sec., ABMXY system‡]. The structure (V) (or its isomer with 7-OH and 8-OMe interchanged) was accordingly assigned to mucroquinone. The synthesis of racemic mucroquinone by the oxidation of the synthetic isoflavan (VI) with Fremy's salt[5] proved that mucroquinone had the structure (V).

The assignment of absolute configurations to the natural isoflavans (II), (III), and (IV) and the quinone (V) are discussed in the following Communication.

(*Received, July 26th, 1968; Com.* 1011.)

---

‡ This analysis is based upon the spectrum recorded at 220 Mc./sec. We thank the S.R.C. and Imperial Chemical Industries Limited, Petrochemical and Polymer Laboratory, for providing facilities for recording this spectrum.

[1] W. D. Ollis, "The Chemistry of Flavonoid Compounds", ed. T. A. Geissman, Pergamon, Oxford, 1962, p. 353; F. M. Dean, "Naturally Occurring Oxygen Ring Compounds", Butterworths, London, 1963, p. 366; W. D. Ollis, "Recent Advances in Phytochemistry", ed. T. J. Mabry, R. E. Alston, and V. C. Runeckles, Appleton–Century–Crofts, New York, 1968, p. 329.

[2] G. F. Marrian and D. Beall, *Biochem. J.*, 1935, **29**, 1586; F. Wessely, H. Hirschel, G. Schögl-Petziwal, and F. Prillinger, *Monatsh.*, 1938, **71**, 215; E. L. Anderson and G. F. Marrian, *J. Biol. Chem.*, 1939, **127**, 649; F. Wessely and F. Prillinger, *Ber.*, 1939 **72B**, 629; W. Dirscherl and K. Schodder, *Z. physiol. Chem.*, 1940, **264**, 57; R. Suemitsu, M. Hiura, and N. Makajima, *J. Agric. Chem. Soc. Japan*, 1955, **29**, 591 (*Chem. Abs.*, 1958, **52**, 20511); W. Klyne and A. A. Wright, *Biochem. J.*, 1957, **66**, 92; *J. Endocrinol.*, 1959, **18**, 32; H. F. MacRae, D. G. Dale, and R. H. Common, *Canad. J. Biochem. Physiol.*, 1960, **38**, 523; F. Hertelendy and R. H. Common, *J. Chromatog.*, 1964, **13**, 570; A. L. Carter and R. H. Common, *Biochim. Biophys. Acta*, 1964, **86**, 56.

[3] A. Robertson, C. W. Suckling, and W. B. Whalley, *J. Chem. Soc.*, 1949, 1571.

[4] W. B. Eyton, W. D. Ollis, I. O. Sutherland, O. R. Gottlieb, M. Taveira Magalhães, and L. M. Jackman, *Tetrahedron*, 1965, **21**, 2683.

[5] H. J. Teuber and G. Jellinek, *Chem. Ber.*, 1952, **85**, 95; H. J. Teuber and W. Rau, *ibid.*, 1953, **86**, 1036.