Structure and Synthesis of Some Complex Pyranoisoflavonoids from the Bark of *Dalbergia nitidula* Welw. *ex* Bak.

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Exhaustive examination of the flavonoid content of the bark of *Dalbergia nitidula* revealed, amongst other substances a mixture of eight novel and complex (3*S*)-isoflavans [leiocin, leiocinol, nitidulin, nitidulan, heminitidulan] and (6a*S*,11a*S*)-pterocarpans [nitiducarpin, hemileiocarpin, nitiducol]. These insoflavonoids all possess the equivalent of prenyl or geranyl side-chains, which, with one exception, are cyclized to stereochemically related 2*H*-pyran moeities during biogenesis. Structures determined by physical means were substantiated for the isoflavans by a single synthesis.

THE practice of dressing wounds with the bark of the slender tree or shrub *Dalbergia nitidula* Welw. *ex* Bak. (Leguminosae) by our indigenous African population [1] has prompted the present investigation, although the extent of such practice, or whether it parallels the wide distribution of the species which ranges from tropical Africa south to northern and eastern Transvaal and Natal,[1] is at present unknown.

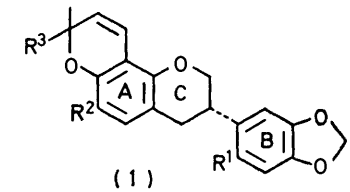
[1] E. Palmer and N. Pittman, ' Trees of Southern Africa,' vol. II, Balkema, Cape Town, 1972, p. 936.

Structural examination of bark metabolites revealed, in addition to a group of glycosides, a novel class of pyrano-isoflavonoids (isoflavans and pterocarpans), and led to the synthesis of a derivative of one of the isoflavans. This group of compounds is of therapeutic interest, considering the reputed pathological activity of isoflavans as phytoalexins,[2,3] and of pterocarpans as antitumour agents.[4]

Compounds derived from the bark of *D. nitidula* comprise five new 2′-hydroxyisoflavans named leiocin (1a), nitidulin (2a), nitidulan (1b), heminitidulan (2b), and leiocinol (1c), as well as four pterocarpans, nitiducarpin (3a), hemileiocarpin (4), nitiducol (5), and leiocarpin [5] (3b), of which only the last was previously recorded. Remarkably, with the exception of nitiducol (5), all possess a 2*H*-pyran moiety attached to ring A; two pterocarpans, nitiducarpin (3a) and leiocarpin (3b), are analogues of the isoflavans nitidulan (1b) and leiocin (1a), respectively.

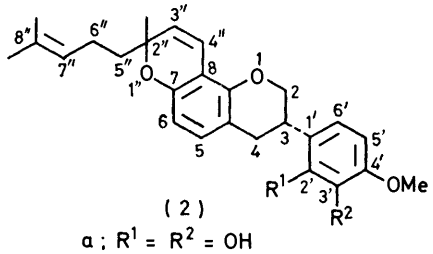
The basic skeletal structure of the isoflavans may be recognized from ^{1}H n.m.r. data. All display the complex ABMXX′ system typical of the five-proton heterocycle ring C.[6,7] The H-3 signal occurs as an undefined multiplet (τ 6.1—6.7) resulting from its coupling with the 2- and 4-protons. The 2- and 4-methylene groups show coupling characteristic of isoflavans, H-2$_{eq}$ and H-2$_{ax}$ resonating as the AM portion (doublet of doublets, and ' triplet ' respectively) of an AMX system, and H-4$_{eq}$ and H-4$_{ax}$ as a doublet of an AA′B system, except for the more complex ABX system in the case of heminitidulan (2b). Accordingly the appearance of the 4-methylene group does not correlate with the suggested [7] steric hindrance offered by the 2′-substituent on ring B in these instances.

The natural isoflavans isolated may be subdivided into two groups based on their ring B substitution pattern, namely 2′,4′,5′ (1) or 2′,3′,4′ (2). Thus for leiocin (1a), with hydroxy- and methylenedioxy-groups allocated to ring B (from mass and ^{1}H n.m.r. spectra [8,9]), the observed *para*-coupled singlets (τ 3.40 and 3.60) could originate from this ring only, and leave no alternative but the indicated 2′,4′,5′-substitution pattern. This conclusion is confirmed by the anticipated paramagnetic shift of the two singlets due to H-6′ and H-3′ respectively (τ 3.30, Δτ −0.1; τ 3.40, Δτ −0.2 p.p.m.), of the monoacetate (1d). With the remaining *ortho*-coupled benzenoid protons and a 2,2-dimethyl-2*H*-pyran moiety [8,9] to be assigned to ring A, four arrangements of substituents are possible. However, the abnormal low-field resonance



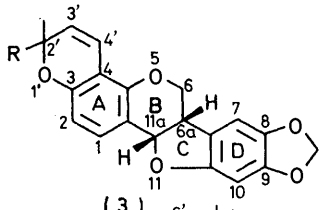
(1)

a; R^1 = OH, R^2 = H, R^3 = Me
b; R^1 = OH, R^2 = H, R^3 = 
c; R^1 = R^2 = OH, R^3 = Me
d; R^1 = O$_2$CMe, R^2 = H, R^3 = Me
e; R^1 = OMe, R^2 = H, R^3 = Me
f; R^1 = R^2 = O$_2$CMe, R^3 = Me

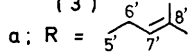


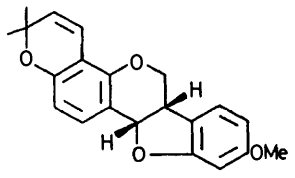
(2)

a; R^1 = R^2 = OH
b; R^1 = OH, R^2 = H
c; R^1 = R^2 = OMe
d; R^1 = R^2 = OEt
e; R^1 = R^2 = O$_2$CMe



(3)

a; R = 
b; R = Me



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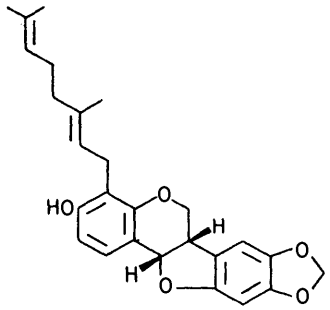
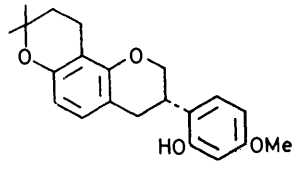


(5)



(6)

of one of the *ortho*-coupled doublets (τ 3.13) suggests its allocation to a proton *meta* to both oxygen functions, and in the 5- as opposed to the 7-position, which would also

[2] E. Wong in ' The Flavonoids,' eds. J. B. Harborne, T. J. Mabry, and H. Mabry, Chapman and Hall, London, 1975, pp. 791—795.
[3] H. D. Van Etten, *Phytochemistry*, 1976, **15**, 655.
[4] R. Kojima, S. Fukushima, A. Neno, and Y. Saiki, *Chem. and Pharm. Bull. (Japan)*, 1970, **18**, 2555.
[5] R. Braz Filho and O. R. Gottlieb, *Phytochemistry*, 1971, **10**, 2433.
[6] K. Kurosawa, W. D. Ollis, B. T. Redman, I. O. Sutherland, O. R. Gottlieb, and H. Magalhães Alves, *Chem. Comm.*, 1968, 1265.
[7] A. Pelter and P. I. Amenechi, *J. Chem. Soc. (C)*, 1969, 887.
[8] A. J. East, W. D. Ollis, and R. E. Wheeler, *J. Chem. Soc. (C)*, 1969, 365.
[9] I. Fleming and D. H. Williams, ' Spectroscopic Methods in Organic Chemistry,' McGraw-Hill, New York, 1966, p. 127.

be in biogenetic contrast to all known isoflavans. This is substantiated by synthesis.

Two other isoflavans, leiocinol (1c) and nitidulan (1b), were found to contain ring B systems identical with that in leiocin, differing only with regard to ring A. The first possesses a hydroxy-group in addition to the 2,2-dimethyl-2*H*-pyran ring, the proposed arrangement for these substituents as in (1c) being tentative, pending future synthesis. In the second a single methyl group on the 2,2-dimethyl-2*H*-pyran ring is replaced by a 4-methylpent-3-enyl chain, clearly defined by ^{1}H n.m.r.[10] and confirmed by H-3″(τ 4.49)/H-4″(τ 3.33) as well as H-6″(τ *ca.* 7.95)/H-7″(τ *ca.* 4.90) spin–spin decoupling. The mass spectrum of nitidulan (1b) exhibits a fragmentation very similar to that of leiocin (1a) after initial loss of the pentenyl side-chain ($M - 83$), and chemical shifts of H-5 (d, τ 3.19) and H-6 (d, τ 3.65, $J_{5,6}$ 8.0 Hz) are remarkably similar to those of leiocin (d, τ 3.13, and d, τ 3.60, $J_{5,6}$ 8.0 Hz). The latter suggests an identical 7,8-coupling of the 2-methyl-2-(4-methylpent-3-enyl)-2*H*-pyran system to ring A. This arrangement of ring A substituents is also applicable to the remaining isoflavans, nitidulin (2a) and heminitidulan (2b), although they differ with respect to rings B.

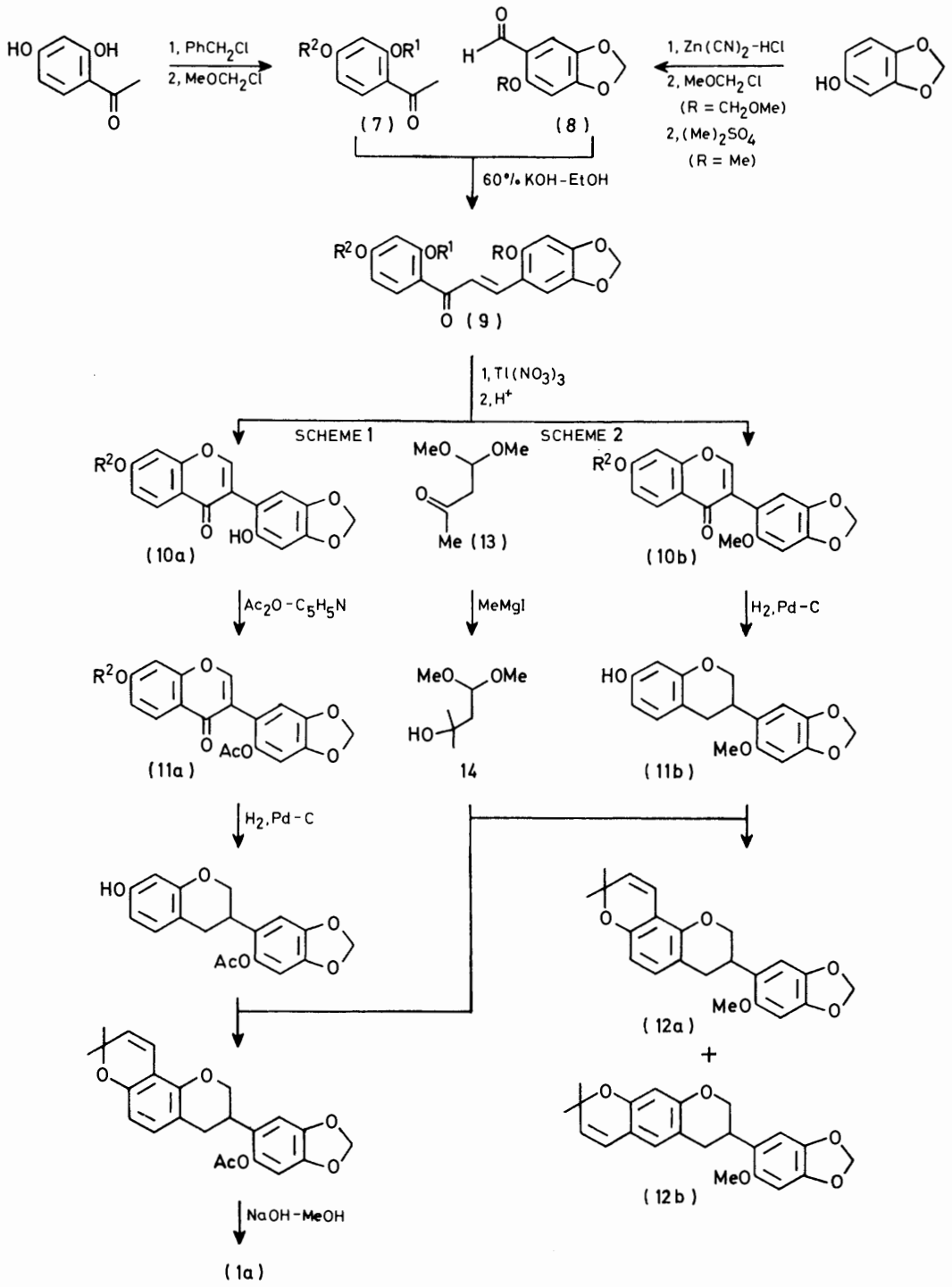
The mass and ^{1}H n.m.r. spectra of nitidulin (2a) leave little doubt as to the placement of two hydroxy-groups and a methoxy-group on ring B, but pose a problem as regards their arrangement in spite of ^{1}H n.m.r. features (dd, τ 3.40 and 3.62, J 8.0 Hz), indicating a vicinal arrangement of substituents adjacent to the point of attachment of ring B. Following methylation to give the dimethyl ether (2c) it was shown by benzene-induced methoxy-shift experiments[11] that only one methoxy-group (Δτ +0.10, +0.10, and +0.30 p.p.m.) was *ortho* to an aromatic proton. Subsequent repetition of the experiment on the diethyl ether (2d) afforded a similar result (Δτ +0.32 p.p.m.) for the methoxy-function, thus substantiating the proposed 4′-methoxy-substitution pattern (2a) for ring B. In the case of heminitidulan (2b), with a single hydroxy- and a methoxy-group allocated to the ring B, the ABX system displayed by the aromatic protons could only be derived from a 2′,4′-arrangement of substituents, with the abnormally low-field resonance of the *ortho*-coupled doublet (τ 2.96) allocated to H-6′. Final assignment of the alternative 2′- or 4′-positions to the hydroxy- or methoxy-groups can only be solved by synthesis, although the 2′-hydroxy-4′-methoxy-arrangement is favoured in view of the coexistence of heminitidulan (2b) and its pterocarpan analogue, hemileiocarpin (4).

Structural elucidation of the pterocarpans was simplified by the coexistence and isolation of the known leiocarpin[5] (3b), identical with the product isolated from *Apuleia leiocarpa*,[5] which served as useful reference for spectrometric comparison. Thus, nitiducarpin (3a) differed from leiocarpin solely with regard to the substitution of the 2,2-dimethyl-2*H*-pyran system by 2-methyl-2-(4-methylpent-3-enyl)-2*H*-pyran, readily recognized from ^{1}H n.m.r. data.[7] In a like manner, ^{1}H n.m.r. and mass spectra of hemileiocarpin (4) compared favourably with those of leiocarpin (3b), proving the former to be devoid of methylenedioxy-function, but possessing a methoxy-group. This methoxy-group could be assigned to ring D on grounds of its mass spectrum, since the 3″,4″-dihydro-2′-hydroxy-2″*H*-pyrano-isoflavan (6) which results from hydrogenation of hemileiocarpin permits retro-Diels–Alder fragmentation. Apart from the appearance of *ortho*-coupled doublets, readily attributed to H-1 and H-2, in the aromatic region of the ^{1}H n.m.r. spectrum, the residual ABX system includes a doublet to low-field (τ 2.73, J 8.5 Hz). By assigning the latter to H-7, *meta* relative to each of the two oxygen functions, the methoxy-group may be placed at C-9.

Nitiducol (5) represents the only metabolite isolated from *D. nitidula* bark not possessing the 2*H*-pyran system, but instead the uncyclicized geranyl side-chain. Its ^{1}H n.m.r. spectrum showed virtually no deviation from that of leiocarpin (3b) in the aromatic region, indicating the same substitution pattern, but with the conventional 2*H*-pyran system replaced by hydroxy and geranyl groups. The *ortho*-relationship of these was confirmed by the i.r. spectrum, which exhibited a hydroxy-group (3 000 cm^{-1}) hydrogen-bonded[12] to the 2,3-vinyl function of the geranyl side-chain. Thus, all the physical data, including the mass spectrum,[13] are in line with the proposed structure.

Stereochemically the isoflavans were found to be identical, all exhibiting a negative c.d. Cotton effect in the region 270—300 nm, indicative of a (3*S*)-configuration.[6] Comparison of the o.r.d. curves of 2′-*O*-methylleiocin (1e) and (3S)-vestitol[6] provided confirmation. Those isoflavans [(1b), (2a) and (2b)] with an additional chiral centre at C-2″ showed a second but positive c.d. Cotton effect (240—290 nm) implying the same configuration at C-2″. This could not be defined on account of lack of suitable reference compounds. The pterocarpans (3a), (3b), (4), and (5) similarly feature Cotton effects corresponding to that of leiocarpin (3b) (positive 240—270 nm; negative 270—320 nm), previously shown to have the (6a*S*,11a*S*)-configuration by comparison with (6a*R*,11a*R*)-pterocarpin.[7] This was substantiated for the new pterocarpans by their large positive optical rotations, characteristic of (6a*S*,11a*S*)-pterocarpans.[14] Nitiducarpin (3a), with an additional C-2′ chiral centre furnished a subsidiary positive Cotton effect (260—290 nm) resembling that of analogous isoflavans, and possibly indicating the same configuration at this point. From the above, the stereochemistry of isoflavan and pterocarpan metabolities from *D. nitidula* is

[10] G. Cardillo, L. Merlini, and R. Mondelli, *Tetrahedron*, 1968, 497.
[11] J. H. Bowie, J. Ronayne, and D. H. Williams, *J. Chem. Soc.* (*B*), 1966, 785.
[12] A. W. Baker and A. T. Shulgin, *J. Amer. Chem. Soc.*, 1959, **81**, 4524.
[13] E. Ritchie and W. C. Taylor, *Tetrahedron Letters*, 1964, **23**, 1437.
[14] L. Verbit and J. W. Clark-Lewis, *Tetrahedron*, 1968, **24**, 5519.



SCHEME 1: R = CH_2OMe, $R^1 = CH_2OMe$, $R^2 = CH_2Ph$

SCHEME 2: R=Me, R^1=CH_2OMe, R^2=CH_2Ph

identical at the corresponding position in their heterocycles. Noteworthy, therefore, is the natural coexistence of isoflavans and pterocarpans bearing strong structural and stereochemical resemblance to each other. This phenomenon is highly reminiscent of the findings of Dewick and Martin [15] linking these two classes of compounds by a common biogenetic precursor, most likely an isoflavan-4-ol.[16]

In order to obtain confirmatory evidence of the structures of the related isoflavans, an attempt was made to synthesise leiocin (1a). Synthesis of conventional isoflavans entails reduction of the corresponding isoflavone obtained from oxidative cyclization and rearrangement of a chalcone with thallium trinitrate (TTN) [17]. A similar route but providing for insertion of the 2,2-dimethyl-2*H*-pyran ring was envisaged for leiocin. This meant deferring insertion to the final step in order to avoid hydrogenation of the 3'',4''-double bond of the pyran ring during reduction of the flavonoid heterocycle. In addition this also required selective blocking of the 2'-hydroxy-group to prevent entry of the 2,2-dimethyl-2*H*-pyran moiety on both 7- and 2'-hydroxy-groups. Such a synthesis was attempted as outlined in Scheme 1. Little difficulty was experienced during synthesis of fragments (7) and (8) by conventional methods.[18-21] These condense with ease to the 4'-benzyloxy-2,2'-di-*O*-methylmethoxy-4,5-methylenedioxychalcone (9) characterized by ^{1}H n.m.r. and the expected α-cleavage during mass spectral fragmentation. Hydrolysis following oxidative rearrangement of this chalcone with TTN did not, however, proceed smoothly, producing several by-products and an unacceptably low yield (*ca.* 20%) of the isoflavone. This was caused most likely by premature hydrolysis of the methoxymethyl groups of the intermediate acetal.[19] Successful application of this step in the synthesis called for stronger protection of the 2'-hydroxy-group.

The synthetic route was accordingly modified to Scheme 2, employing the methyl ether of the aldehyde (8; R = Me), rather than the methoxymethyl ether (8; R = CH_2OMe). This implied retention of the 2'-methoxy-group and unavoidably obtaining 2'-O-methylleiocin (12a) as final product. Thus both chalcone formation (9; R = Me) and subsequent oxidation by TTN to 7-benzyloxy-4',5'-methylenedioxy-2'-methoxyisoflavone (10b) proceeded without difficulty and in good yield, stressing the inhibitory role of the 2'-hydroxy-group in the oxidative rearrangement of the chalcone. Catalytic hydrogenation of the isoflavone produced the isoflavan analogue (11b) in almost quantitative yield.

As final step in the synthesis of 2'-*O*-methyl-leiocin (12a), a 2,2-dimethyl-2*H*-pyran ring was introduced into the isoflavan by the method described by Bandaranayake *et al.*,[22] the reagent, 3-hydroxy-1,1-dimethoxy-3-methylbutane (14), being prepared by the action of a Grignard reagent (MeMgI) on acetoacetaldehyde dimethyl acetal (13). As expected, the pyridine-catalysed condensation of this reagent with the substrate (11b) yielded two products, identified by ^{1}H n.m.r. and mass spectra as 2'-*O*-methyl-leiocin (12a) and its structural isomer (12b). Synthetic 2'-*O*-methyl-leiocin was identical with the methyl ether of the natural compound (1e), apart from the absence of optical activity.

The natural isoflavans and pterocarpans will be examined for therapeutic properties. The glycosides from the bark of *D. nitidula* will be the subject of a future communication.

EXPERIMENTAL

Unless otherwise stated n.m.r. spectra (and Fourier transform analogues) were recorded for solutions in $CDCl_3$ (Me_4Si as internal reference), u.v. spectra for solutions in MeOH, and i.r. spectra for solutions in $CHCl_3$. Mass spectra were obtained with A.E.I. MS-9 and Varian CH-5 instruments. A JASCO J-20 spectropolarimeter was employed for optical rotation and o.r.d. determinations (solvent MeOH).

Systems used for separation of components comprised Whatman No. 3 paper (preparative paper chromatography), Merck silica gel 60 (column chromatography), and Merck silica gel 60 PF_{254} (preparative t.l.c.). T.l.c. bands were located by u.v. illumination and/or spray reagents ($HClO_4$–$FeCl_3$ or HCHO–H_2SO_4).

Difficulties experienced throughout with the retention of organic solvents by the small quantities of oily or non-crystalline natural products available led to unsatisfactory C and H analyses in some instances. Here reliance was placed on accurate mass values, and purity was assessed by n.m.r. spectroscopy.

Isolation of Constituents from D. nitidula *Bark*.—The bark (pulverised and dried; 718 g) was extracted with MeOH (6 × 1 l) at room temperature for 6 consecutive days and produced a brown solid (155 g) on evaporation of the combined extracts. Preparative paper chromatography (2% AcOH; upward migration) of a portion (30 g) of the extract yielded five crude fractions, only one of which (fraction E, 5.2 g; R_F 0.01) was investigated. Fraction E was rechromatographed (column chromatography; cyclohexane–ethyl acetate, 3 : 1) into four subfractions (E_1—E_4).

T.l.c. separation (toluene–acetone, 199 : 1, × 3) of fraction E_1 (150 mg) yielded nitiducarpin (3a) (20 mg; R_F 0.60), leiocarpin (3b) (32 mg; R_F 0.55), and hemileiocarpin (4) (30 mg; R_F 0.43). Elucidation of the composition of fraction E_2 (121 mg) proved more complicated and required an initial separation into two fractions (R_F 0.31 and 0.25) by t.l.c. (n-hexane–acetone, 85 : 15, × 3). T.l.c. separation

[15] P. M. Dewick and M. Martin, *J.C.S. Chem. Comm.*, 1976, 637.
[16] P. M. Dewick, *Phytochemistry*, 1975, **14**, 979; *J.C.S. Chem. Comm.*, 1975, 656; P. J. van der Merwe, M.Sc. Thesis, University of the Orange Free State, Bloemfontein, January, 1977.
[17] L. Farkas, A. Gottsegen, M. Nógrádi, and S. Antus, *J.C.S. Perkin I*, 1974, 305.
[18] K. N. Campbell, P. F. Hopper, and B. K. Campbell, *J. Org. Chem.*, 1951, **16**, 1736.
[19] M. E. Oberholzer, G. J. H. Rall, D. Ferreira, and D. G. Roux, *Tetrahedron Letters*, 1976, **13**, 1033.
[20] K. C. Gulati, S. R. Seth, and K. Venkataraman, *J. Chem. Soc.*, 1934, 1765.
[21] A. I. Vogel, 'A Textbook of Practical Organic Chemistry,' Longmans, London, 1967, p. 690.
[22] W. M. Bandaranayake, L. Crombie, and D. A. Whiting, *J. Chem. Soc.* (*C*), 1971, 811.

(chloroform–acetone, 99 : 1, × 3) of the first of these produced nitiducol (5) (15 mg; R_F 0.80), nitidulan (1b) (17 mg; R_F 0.68), and heminitidulan (2b) (18 mg; R_F 0.61); the second fraction yielded leiocin (1a), (50 mg; R_F 0.58) upon purification by t.l.c. (chloroform–acetone, 99 : 1, × 3).

Nitidulin (2a) (300 mg) was obtained from fraction E_3 by crystallization from cyclohexane. Fraction E_4 was similarly found to contain a single compound, leiocinol (1c) (45 mg; R_F 0.25), following purification by t.l.c. (hexane–acetone, 65 : 35).

Constituents from D. nitidula *Bark and their Derivatives.*—*Leiocin* (1a) formed white needles (from EtOH), m.p. 150° (Found: C, 71.4; H, 5.8%; M^+, 352.134. $C_{21}H_{20}O_5$ requires C, 71.6; H, 5.7%; M, 352.131), *m/e* 352(60%, M^+), 337(100), 199(26), 188(32), 187(43), 186(13.2), 173(61), 164(43), 163(38), 151(37), 145(20), 137(2.3), and 135(14.5); $\lambda_{max.}$ (log ε) 292(4.11), 280(4.12), 227(4.55), and 207 nm (4.65); c.d. (*c* 0.048 4) $[\theta]_{350}$ 0, $[\theta]_{290}$ −2.28 × 10^5, $[\theta]_{278}$ 0, $[\theta]_{270}$ 1.20 × 10^4, $[\theta]_{260}$ 0, $[\theta]_{230}$ 3.00 × 10^5; τ 3.13(d, *J* 8.0 Hz, H-5), 3.28(d, *J* 10.0 Hz, H-4″), 3.40(s, H-6′), 3.60(d, *J* 8.0 Hz, H-6), 3.60(s, H-3′), 4.10 (s, OCH_2O), 4.42(s, H-3″), 5.08br (s, OH), 5.63(dd, *J* 10.0 and 4.0 Hz, H-2_{eq}), 6.00(t, *J* 10.0 and 10.0 Hz, H-2_{ax}), 6.33—6.63(m, H-3), 7.12(d, *J* 8.0 Hz, H-4), and 8.57(s, 2″-CH_3).

2′-O-*Acetyl-leiocin* (1d), from acetylation of leiocin (20 mg) with acetic anhydride–pyridine was a white amorphous compound (21 mg), m.p. 114°; *m/e* 394(45%, M^+) and 379(100); τ 3.15(d, *J* 8.0 Hz, H-5), 3.30(s, H-6′), 3.32(d, *J* 10.0 Hz, H-4″), 3.40(s, H-3′), 3.60(d, *J* 8.0 Hz, H-6), 4.00(s, OCH_2O), 4.42(d, *J* 10.0 Hz, H-3″), 5.53—6.33(m, H-2_{eq}, H-2_{ax}, and H-3), 7.15(d, *J* 8.0 Hz, H-4), 7.70(s, $COCH_3$), and 8.57(s, 2″-CH_3).

2′-O-*Methyl-leiocin* (1e), from methylation of leiocin (20 mg) with diazomethane was an oil (19 mg) (Found: C, 72.5; H, 6.9%; M^+, 366.147. $C_{22}H_{22}O_5$ requires C, 72.1; H, 6.1%; M, 366.147), *m/e* 366 (70%, M^+), 351(100), 199(21), 188(13.3), 187(9.7), 186(11.3), 185(29), 179(24), 178(76), 173(82), 166(40), 165(70), 163(20), 149(14.2), 145(21), 137(2.8), 135(40), and 133(65); o.r.d. (*c* 0.0468) $[M]_{350}$ 0, $[M]_{302}$ −312, $[M]_{298}$ 0, $[M]_{297}$ 78, $[M]_{296}$ 0, $[M]_{290}$ −703, $[M]_{285}$ 0, $[M]_{283}$ 312, $[M]_{280}$ 0, $[M]_{275}$ −156, $[M]_{273}$ 0, $[M]_{230}$ 3 597; τ 3.18(d, *J* 8.0 Hz, H-5), 3.35(d, *J* 10.0 Hz, H-4″), 3.36(s, H-6′), 3.44(s, H-3′), 3.64(d, *J* 8.0 Hz, H-6), 4.10(s, OCH_2O), 4.45(d, *J* 10.0 Hz, H-3″), 5.68(dd, *J* 10.0 and 4.0 Hz H-2_{eq}), 6.04(t, *J* 10.0 and 10.0 Hz, H-2_{ax}), 6.22(s, 2′-OCH_3), 6.30—6.60(m, H-3), 7.14(d, *J* 8.0 Hz, H-4), and 8.59(s, 2″-CH_3).

Nitidulin (2a) formed yellow cubes (from cyclohexane), m.p. 128° (Found: C, 73.8; H, 7.1%; M^+, 422.209. $C_{26}H_{30}O_5$ requires C, 73.9; H, 7.2%; M, 422.209), *m/e* 422(70, M^+), 407(31), 339(100), 199(9.8), 187(52), 186(3.0), 173(74), 166(11.3), 165(7.8), 153(49), 145(10.9), 139(8.2), and 137(8.2); $\lambda_{max.}$ (log ε) 283(4.01) and 295 nm (4.02); c.d. (*c* 0.044 0) $[\theta]_{350}$ 0, $[\theta]_{310}$ −8.28 × 10^4, $[\theta]_{301}$ 0, $[\theta]_{276}$ 1.10 × 10^6, $[\theta]_{241}$ 0, $[\theta]_{238}$ −4.14 × 10^5; τ 3.20(d, *J* 8.0 Hz, H-5), 3.30(d, *J* 10.0 Hz, H-4″), 3.40(d, *J* 8.0 Hz, H-6′), 3.62(d, *J* 8.0 Hz, H-5′), 3.67(d, *J* 8.0 Hz, H-6), 4.52(d, *J* 10.0 Hz, H-3″), 4.33—5.10(m, H-7″, 2′-OH, and 3′-OH), 5.60(dd, *J* 10.0 and 4.0 Hz, H-2_{eq}), 5.97(t, *J* 10.0 and 10.0 Hz, H-2_{ax}), 6.20(s, 4′-OCH_3), 6.20—6.67(m, H-3), 7.10(d, *J* 8.0 Hz, H-4), 7.50—8.1(m, H-6″), 8.33—8.50(m, H-5″), 8.33(s, 8″-CH_3), 8.43 (s, 8″-CH_3), and 8.63(s, 2″-CH_3).

2′,3′-*Di*-O-*acetylnitidulin* (2e) (21 mg) was obtained as a yellow oil by acetylation (acetic anhydride–pyridine) of nitidulin (20 mg); *m/e* 506(7.3%, M^+) and 423(100); τ 7.70(s, 2 × $COCH_3$).

2′-3′-*Di*-O-*methylnitidulin* (2c), from methylation (diazomethane) of nitidulin (30 mg) was a yellow oil (27 mg), *m/e* 450(40%, M^+) and 367(100); τ 3.14(d, *J* 8.0 Hz, H-5), 3.20(d, *J* 10.0 Hz, H-4″), 3.30(d, *J* 8.0 Hz, H-6′), 3.34(d, *J* 8.0 Hz, H-5′), 3.64(d, *J* 8.0 Hz, H-6), 4.50(d, *J* 10.0 Hz, H-3″), 4.70—5.02 (m, H-7″), 5.33—6.00(m, H-2_{eq} and H-2_{ax}), 6.10(s, 3 × OCH_3), 6.30—6.70(m, H-3), 7.13(d, *J* 8.0 Hz, H-4), 7.70—8.10(m, H-6″), 8.20—8.50(m, H-5″), 8.33(s, 8″-CH_3), 8.40(s, 8″-CH_3), and 8.62(s, 2″-CH_3); τ(C_6D_6) 2.97—3.73(m, H-5, H-6, H-5′, H-6′, and H-4″), 4.65(d, *J* 10.0 Hz, H-3″), 4.73—5.10(m, H-7″), 5.50—5.83(m, H-2_{eq}), 6.07(t, *J* 10.0 and 10.0 Hz, H-2_{ax}), 6.27(s, OCH_3), 6.33(s, OCH_3), 6.63(s, OCH_3), 6.50—6.85(m, H-3), 7.23(d, *J* 8.0 Hz, H-4), 7.67—8.00(m, H-6″), 8.00—8.50(m, H-5″), 8.33(s, 8″-CH_3), 8.47(s, 8″-CH_3), and 8.63(s, 2″-CH_3).

2′,3′-*Di*-O-*ethylnitidulin* (2d) was obtained by refluxing nitidulin (50 mg), anhydrous (120 °C) K_2CO_3 (1 g), and EtI (1 g) in dry acetone (10 ml) for 2 h, filtration, and evaporation. The product was dissolved in ether (50 ml) and washed with water (2 × 30 ml). Evaporation of the ether produced the diethyl ether as a yellow oil (45 mg); *m/e* 478(30%, M^+) and 395(100); τ 3.00—3.50(m, H-5, H-5′, H-6′, and H-4″), 3.62(d, *J* 8.0 Hz, H-6), 4.45(d, *J* 10.0 Hz, H-3″), 4.70—5.00(m, H-7″), 5.50—6.10(m, H-2_{ax}, H-2_{eq}, and 2 × OCH_2), 6.25(s, OCH_3), 6.27—6.54 (m, H-3), 7.10(d, *J* 7.0 Hz, H-4), 7.50—8.10(m, H-6″), 8.13—8.66(m, H-5″), 8.33(s, 8″-CH_3), 3.34(s, 8″-CH_3), and 8.60(s, 3 × OCH_2CH_3); τ(C_6D_6) 3.27—4.00(m, H-5, H-6, H-5′, H-6′, and H-4″), 4.90(d, *J* 10.0 Hz, H-3″), 5.00—5.30(m, H-7″), 5.67—6.67(m, H-2_{ax}, H-2_{eq}, and 2 × OCH_2), 6.83(s, OCH_3), 6.83—7.17(m, H-3), 7.47(d, *J* 8.0 Hz, H-4), 7.50—8.33(m, H-6″), 8.33—8.58(m, H-5″), 8.62(s, 8″-CH_3), 8.72(s, 8″-CH_3), and 8.90(s, 3 × OCH_2CH_3).

Nitidulan (1b) was a white amorphous solid, m.p. 55° (Found: C, 73.9; H, 6.7%; M^+, 420.193. $C_{26}H_{28}O_5$ requires C, 74.3; H, 6.7%; M, 420.194), *m/e* 420(13.7%, M^+), 405(5.2), 338(30), 337(100), 187(7.6), 174(3.1), 173(15.2), 169(5.5), 164(4.0), 151(6.1), and 135(2.0); $\lambda_{max.}$ (log ε) 290(4.13), 280(4.13), 227(4.53), and 205 nm (4.54); c.d. (*c* 0.050 0) $[\theta]_{350}$ 0, $[\theta]_{310}$ −1.38 × 10^5, $[\theta]_{299}$ 0, $[\theta]_{275}$ 4.43 × 10^5, $[\theta]_{240}$ 1.10 × 10^5; τ 3.19(d, *J* 8.0 Hz, H-5), 3.33(d, *J* 10.0 Hz, H-4″), 3.39(s, H-6′), 3.60(s, H-3′), 3.65(d, *J* 10.0 Hz, H-6), 4.12(s, OCH_2O), 4.49(d, *J* 10.0 Hz, H-3″), 4.80—5.00(m, H-7″), 5.66(dd, *J* 10.0 and 4.0 Hz, H-2_{eq}), 6.00(t, *J* 10.0 and 10.0 Hz, H-2_{ax}), 6.24—6.70(m, H-3), 7.12(d, *J* 8.0 Hz, H-4), 7.80—8.10(m, H-6″), 8.20—8.55(m, H-5″), 8.35(s, 8″-CH_3), 8.42(s, 8″-CH_3), and 8.62(s, 2″-CH_3).

Heminitidulan (2b) was a white amorphous solid, m.p. 94° (Found: M^+, 406.212. $C_{26}H_{30}O_4$ requires M, 406.214), *m/e* 406(18.0%, M^+), 391(8.2), 337(11.5), 324(42), 323(100), 199(4.0), 187(20), 186(2.1), 173(7.3), 174(60), 150(9.5), 149(8.3), 137(22), 123(2.0), and 121(5.6); $\lambda_{max.}$ (log ε) 280(4.14), 228(4.59), and 205nm (4.58); c.d. (*c* 0.047 2) $[\theta]_{350}$ 0, $[\theta]_{315}$ −7.10 × 10^4, $[\theta]_{299}$ 0, $[\theta]_{275}$ 4.65 × 10^5, $[\theta]_{238}$ 0; τ 2.97(d, *J* 8.0 Hz, H-6′), 3.18(d, *J* 8.0 Hz, H-5), 3.31(d, *J* 10.0 Hz, H-4″), 3.51(dd, *J* 8.0 and 2.0 Hz, H-5′), 3.63(d, *J* 2.0 Hz, H-3′), 3.64(d, *J* 10.0 Hz, H-6), 4.49(d, *J* 10.0 Hz, H-4″), 4.80—5.00(m, H-7″), 5.20br (s, OH), 5.62(dd, *J* 10.0 and 4.0 Hz, H-2_{eq}), 5.96(t, *J* 10.0 and 10.0 Hz, H-2_{ax}), 6.24(s, OCH_3), 6.30—6.70(m, H-3), 7.00—7.18(m, H-4), 7.80—8.05(m, H-6″), 8.20—8.60(m, H-5″), 8.34(s, 8″-CH_3), 8.42(s, 8″-CH_3), and 8.62(s, 2″-CH_3).

Leiocinol (1c) was an amorphous solid, m.p. 70° (Found: M^+, 368.127. Calc. for $C_{21}H_{20}O_6$: M, 368.126), *m/e* 368 (96%, M^+), 353(88), 339(65), 218(23), 217(40), 215(14.6), 206(62), 205(73), 204(46), 203(78), 202(15.1), 201(53), 191(64), 190(35), 189(86), 187(59), 177(30), 176(70), 175(27), 173(45), 165(33), 164(100), 163(86), 162(29), 161(17.1), 153(29), 152(60), 151(84), 147(43), 137(14.9), 135(40), 133(76), and 121(38); $\lambda_{max.}$ (log ε) 297(3.85), 287(3.86), and 208 nm (4.41); c.d. (*c* 0.044 0) $[\theta]_{370}$ -1.35×10^3, $[\theta]_{320}$ -6.21×10^3, $[\theta]_{290}$ 0, $[\theta]_{275}$ 6.48×10^3, $[\theta]_{235}$ 1.30×10^4; τ 3.35(d, *J* 10.0 Hz, H-4″), 3.39, 3.47, and 3.60 (3 × s, H-6′, H-5, and H-3′), 4.10(s, OCH_2O), 4.43(d, *J* 10.0 Hz, H-3″), 4.90br (s, 2 × OH), 5.50—6.30(m, H-2_{eq} and H-2_{ax}), 6.30—6.76(m, H-3), 7.15(d, *J* 8.0 Hz, H-4), and 8.38(s, 2 × 2″-CH_3).

2′,6-Di-*O*-acetyl-leiocinol (1f) (21 mg) was obtained by acetylation of leiocinol (20 mg) with acetic anhydride–pyridine as an amorphous solid, m.p. 135°; *m/e* 452(87%, M^+); τ 3.35(d, *J* 10.0 Hz, H-4″), 3.35 and 3.40(2 × s, H-5, H-3′, and H-6′), 4.02(s, OCH_2O), 4.42(d, *J* 10.0 Hz, H-3″), 5.60—6.40(m, H-2 and H-3), 7.20(d, *J* 8.0 Hz, H-4), 7.70(s, 2 × $COCH_3$), and 8.60(s, 2 × 2″-CH_3).

Leiocarpin (3b) afforded white needles (from EtOH), m.p. 96° (lit.,[5] 98°) (Found: M^+, 350.133. Calc. for $C_{21}H_{18}O_5$: M, 350.115), *m/e* 350(69%, M^+) and 335(100); $\lambda_{max.}$ (log ε) 305(4.06), 290(4.00), 227(4.78), and 205 nm (4.69); c.d. (*c* 0.048 0) $[\theta]_{350}$ 0, $[\theta]_{315}$ -6.98×10^5, $[\theta]_{292}$ 0, $[\theta]_{245}$ 1.10×10^6; o.r.d. (*c* 0.048 8) $[M]_{345}$ 0, $[M]_{320}$ −100 4, $[M]_{309}$ 0, $[M]_{290}$ 1 721, $[M]_{280}$ 1 434, $[M]_{270}$ 1 721, $[M]_{230}$ 6 166, $[M]_{210}$ 0; $[\alpha]_D^{24}$ +215 (*c* 0.1300 in $CHCl_3$); τ 2.74(d, *J* 8.0 Hz, H-1), 3.27(s, H-7), 3.34(d, *J* 10.0 Hz, H-4′), 3.47(d, *J* 8.0 Hz, H-2), 3.55(s, H-10), 4.08(s, OCH_2O), 4.42(d, *J* 10.0 Hz, H-3′), 4.55(d, *J* 6.0 Hz, H-11a), 5.60—5.90(m, H-6_{eq}), 6.10—6.63(m, H-6_{ax} and H-6a), and 8.58(s, 2 × 2′-CH_3).

Nitiducarpin (3a) was a white amorphous solid, m.p. 84° (Found: M^+, 418.177. $C_{26}H_{26}O_5$ requires M, 418.178), *m/e* 418(69%, M^+), 403(6.1), 375(5.0), 350(6.4), 337(7.8), 338(30), 335(100), 322(6.4), 321(28), 198(2.7), 185(27), 175(6.2), 173(25), 168(7.4), 167(36), 162(3.8), 160(6.0), 149(14.4), 113(7.4), 111(6.7), and 109(5.7); $\lambda_{max.}$ (log ε) 307(3.81), 292(3.80), 230(4.38), and 205 nm (4.20); c.d. (*c* 0.452 0) $[\theta]_{350}$ 0, $[\theta]_{311}$ -3.50×10^5, $[\theta]_{293}$ 0, $[\theta]_{238}$ 7.22×10^5; τ[$(CD_3)_2CO$] 2.73(d, *J* 8.0 Hz, H-1), 3.07(s, H-7), 3.32(d, *J* 10.0 Hz, H-4′), 3.52(d, *J* 8.0 Hz, H-2), 3.60(s, H-10), 4.07(s, OCH_2O), 4.34(d, *J* 10.0 Hz, H-3′), 4.49(d, *J* 6.0 Hz, H-11a), 4.60—5.03(m, H-7′), 5.47—5.80(m, H-6_{eq}), 6.20—6.50(m, H-6_{ax}, H-6a), 7.80—8.10(m, H-6′), 8.35(s, 8′-CH_3), 8.40(s, 8′-CH_3), 8.26—8.53(m, H-5′), and 8.64(s, 2′-CH_3).

Hemileiocarpin (4) was an oil (Found: M^+, 336.138. $C_{21}H_{20}O_4$ requires M,336.136), *m/e* 336(78%, M^+), 335(7.9), 322(38), 321(100), 306(7.6), 293(7.4), 279(10.5), 213(1.6), 200(1.4), 198(2.0), 185(23), 173(20), 167(27), 161(12.7), 160(30), 153(26), 150(9.3), 149(76), 148(1.4), 139(12.8), 113(14.1), and 111(7.7); $\lambda_{max.}$ (log ε) 287(2.97) and 245 nm (4.09); c.d. (*c* 0.047 6 in $CHCl_3$) $[\theta]_{350}$ 0, $[\theta]_{290}$ -3.14×10^5, $[\theta]_{256}$ 0, $[\theta]_{243}$ 6.40×10^5; τ[$(CD_3)_2CO$] 2.73(2 × d, *J* 10.0 Hz, H-1 and H-7), 3.37(d, *J* 10.0 Hz, H-4′), 3.52(d, *J* 8.0 Hz, H-2), 3.53(dd, *J* 8.0 and 2.0 Hz, H-8), 3.58(d, *J* 2.0 Hz, H-10), 4.33(d, *J* 10.0 Hz, H-3′), 4.48(d, *J* 6.0 Hz, H-11a), 5.50—6.00(m, H-6_{eq}), 6.23(s, OCH_3), 6.17—6.50(m, H-6_{ax} and H-6a), 8.60(s, 2 × 2′-CH_3).

2′-Hydroxy-4′-methoxy-3″,4″-dihydro-2″,2″-dimethylpyrano[6″,5″ : 7,8]*isoflavan* [15] (6). Hemileiocarpin (5 mg), dissolved in EtOH (4 ml) and acetic acid (1 ml), was hydrogenated for 8 h at room temperature (3 atm) over 10% Pd–C. Subsequent filtration and evaporation yielded the isoflavan analogue (4 mg); *m/e* 340(39%, M^+), 279(14.5), 216(28), 203(10.4), 192(17.2), 191(72), 190(2.5), 167(31), 161(14.3), 160(23), 151(12.2), 150(62), 149(100), 147(14.5), 137(41), 136(11.2), 135(37), 123(24), 121(20), 113(17.8), and 112(10.5).

Nitiducol (5) was a white amorphous solid, m.p. 71° (Found: C, 73.7; H, 6.9%; M^+, 420.193. $C_{26}H_{28}O_5$ requires C, 74.3; H, 6.7%; M 420.194), *m/e* 420(96%, M^+), 351(5.8), 335(9.4), 298(12.8), 297(38), 296(100), 295(16.5), 189(14.3), 175(11.5), 163(8.8), 162(16.8), 159(5.1), 151(10.0), 149(17.5), 147(11.7), 146(2.3), 135(25), 123(15.1), 121(7.4), 113(6.5), 111(11.1), and 109(9.6); $\lambda_{max.}$ (log ε) 307(4.91), 283(3.64), and 207 nm (4.76); c.d. (*c* 0.043 6) $[\theta]_{350}$ 0, $[\theta]_{300}$ -3.49×10^5, $[\theta]_{273}$ 0, $[\theta]_{237}$ 1.05×10^6; $\nu_{max.}$ 3 000 cm^{-1}; τ 2.74(d, *J* 8.0 Hz, H-1), 3.28(s, H-7), 3.43(d, *J* 8.0 Hz, H-2), 3.57(s, H-10), 4.10(d, *J* 1.0 Hz, OCH_2O), 4.51(d, *J* 6.0 Hz, H-11a), 4.60—5.98(m, H-2′ amd H-6′), 5.66—5.82(m, H-6_{eq}), 6.26—6.68(m, H-6_{ax}, H-6a, and H-1′), 7.96br(s, H-4′ and H-5′), 8.22(s, 3′-CH_3), 8.34(s, 7′-CH_3), and 8.42(s, 7′-CH_3).

Attempted Synthesis of Leiocin (1a).—4′-Benzyloxy-2′-hydroxyacetophenone was prepared from 2′,4′-dihydroxyacetophenone (5 g) according to the method of Gulati *et al.*,[20] the compound crystallizing from MeOH as platelets (3.08 g), m.p. 104° (lit.,[20] 110°); M^+ 242; τ −2.77(s, OH), 2.40(d, *J* 10.0 Hz, H-6′), 2.64(s, *Ph*CH_2O), 3.52(dd, *J* 10.0 and 2.0 Hz, H-5′), 3.52(d, *J* 2.0 Hz, H-3′), 4.92(s, PhCH_2O), and 7.47(s, $COCH_3$).

4′-Benzyloxy-2′-O-methoxymethylacetophenone (7; R^1 = CH_2OMe, R^2 = CH_2Ph). 4′-Benzyloxy-2′-hydroxyacetophenone (2.42 g), KOH (0.6 g), water (1.5 ml), and MeOH (10 ml) were heated to 96 °C for 2 h. The potassium salt obtained by evaporation was dried at 120 °C for 2 h and redissolved in a solution of 18-crown-6 (2.0 g) in dry acetonitrile (20 mg).[19] The solution was stirred for 30 min at room temperature, $MeOCH_2Cl$ (1.2 ml) was slowly added, and a further 30 min was allowed for completion of the reaction. KCl produced was filtered off and washed with ether, and the combined filtrates were evaporated. The product was dissolved in ether and washed with 10% (w/v) KOH (3 × 30 ml) followed by water (5 × 50 ml), producing the pure compound as a brown oil (1.87 g) on evaporation (Found: M^+, 286.120. $C_{17}H_8O_4$ requires M, 286.121); τ 2.17(d, *J* 8.0 Hz, H-6′), 2.62(s, *Ph*CH_2O), 3.20(d, *J* 2.0 Hz, H-3′), 3.36(dd, *J* 2.0 and 8.0 Hz, H-5′), 4.76(s, OCH_2OCH_3), 4.92(s, PhCH_2O), 6.50(s, OCH_2OCH_3), and 7.40(s, $COCH_3$).

2-Hydroxy-4,5-methylenedioxybenzaldehyde. Dry HCl gas was led through a mixture of 3,4-methylenedioxyphenol (5 g), HCN (7 ml solution), and $Zn(CN)_2$ (5 g) in ether (100 ml; Na-dried) at 0 °C until the mixture was saturated (*ca.* 5 h), after which it was kept at 0 °C for 15 h.[22] The ether was decanted and the iminium chloride hydrolysed with water (100 ml) at 96 °C for 30 min. During this process white crystals of the product were obtained. These were supplemented by steam-distillation of the filtrate, and the product was recrystallized from EtOH to give white needles (5.9 g), m.p. 125° (lit.,[18] 125—126°); M^+ 166; τ[$(CD_3)_2CO$] −1.87(s, OH), 0.17(s, CHO), 2.87(s, H-6), 3.50(s, H-3), and 3.88(s, OCH_2O).

2-O-Methoxy-methyl-4,5-methylenedioxybenzaldehyde (8; R = CH_2OMe). 2-Hydroxy-4,5-methylenedioxybenzaldehyde was methoxymethylated as described.[19] Crystallization

from EtOH yielded white *needles* (2.4 g), m.p. 79° (Found: C, 57.2; H, 4.8. $C_{10}H_{10}O_5$ requires C, 57.1; H, 4.8%); M^+ 210; τ −0.33(s, CHO), 2.73(s, H-6), 3.20(s, H-3), 3.96(s, OCH_2O), 4.75(s, OCH_2OCH_3), and 6.45(s, OCH_2OCH_3).

4′-Benzyloxy-2,2′-bis-O-methoxymethyl-4,5-methylenedioxychalcone (9; R = R^1 = CH_2OMe, R^2 = CH_2Ph). A solution of the acetophenone (7; R^2 = CH_2Ph, R^1 = CH_2OMe) (1.24 g) in EtOH (30 ml) and 60% (w/v) KOH (10 ml) was stirred for 30 min at room temperature, and the aldehyde (8; R = CH_2OMe) (1.14 g) was added. When all the aldehyde had been consumed (t.l.c.), water (30 ml) was added, and the mixture acidified (3N-HCl) and extracted with ether (3 × 50 ml). The extract was washed with water (4 × 50 ml) and taken to dryness. T.l.c. (benzene–hexane–ethyl acetate, 5 : 4 : 2) produced the chalcone (R_F 0.32) as a yellow oil (1.0 g), which crystallized from EtOH as yellow *needles*, m.p. 90° (Found: C, 69.4; H, 5.5. $C_{27}H_{26}O_8$ requires C, 69.6; H, 5.4%), *m/e* 478(4.2%, M^+); τ 1.92(d, *J* 16.0 Hz, H-β), 2.28(d, *J* 8.0 Hz, H-6′), 2.60(s, $PhCH_2O$), 2.70(d, *J* 16.0 Hz, H-α), 2.92(s, H-6), 3.16(d, *J* 2.0 Hz, H-3′), 3.23(d, H-3), 3.32(dd, *J* 8.0 and 2.0 Hz, H-5′), 4.07(s, OCH_2O), 4.77(s, OCH_2OCH_3), 4.85(s, OCH_2OCH_3), 4.90(s, OCH_2Ph), and 6.51(s, 2 × OCH_3).

7-Benzyloxy-2′-hydroxy-4′,5′-methylenedioxyisoflavone (10a; R^2 = CH_2Ph). $Tl(NO_3)_3$ (385 mg), the chalcone (9; R = R^1 = CH_2OMe, R^2 = CH_2Ph); (430 mg) and MeOH (100 ml) were stirred for 30 min, 3N-HCl (10 ml) was added, and the mixture was refluxed for 5 h.[17] After removal of the $TlNO_3$ precipitate, the filtrate was extracted with $CHCl_3$ (3 × 50 ml) and the extract washed with 10% (w/v) $NaHCO_3$ (2 × 30 ml) followed by water (2 × 30 ml). Evaporation yielded the isoflavone as a white *solid* (70 mg), which was purified by t.l.c. (benzene–hexane–ethyl acetate, 5 : 4 : 2; R_F 0.42); *m/e* 388(19.2%, M^+), 269(11.0), 227(6.2), 226(1.0), 162(5.3), 119(5.3), 92(10.2), 91(100) (owing to exceptionally low solubility of the pure isoflavone in a variety of solvents, full characterization was performed on the acetate).

Acetylation (acetic anhydride–pyridine) of the isoflavone (50 mg) yielded the *acetate* (45 mg), crystallising from EtOH as white needles, m.p. 165° (Found: C, 69.7; H, 4.3%; M^+, 430.105. $C_{25}H_{18}O_7$ requires C, 69.8; H, 4.2%; *M*, 430.105); τ 1.76(d, *J* 9.0 Hz, H-5), 2.17(s, H-2), 2.53(s, OCH_2Ph), 2.90(dd, *J* 9.0 and 2.0 Hz, H-6), 3.05(d, *J* 2.0 Hz, H-8), 3.18(s, H-3′), 3.27(s, H-6), 3.97(s, OCH_2O), 4.80(s, OCH_2Ph), and 7.90(s, $COCH_3$).

Synthesis of 2′-O-Methyl-leiocin (12a).—*Methoxy-4,5-methylenedioxybenzaldehyde* (8; R = Me). Methylation of 2-hydroxy-4,5-methylenedioxybenzaldehyde (2.5 g) with dimethyl sulphate, and crystallisation from EtOH produced white needles (1.65 g), m.p. 114° (lit.,[18] 112°); M^+ 180; τ −0.32(s, CHO), 2.73(s, H-6), 3.42(s, H-3), 3.97(s, OCH_2O), and 6.12(s, OCH_3).

4′-Benzyloxy-2-methoxy-2′-O-methoxymethyl-4,5-methylenedioxychalcone (9; R = Me, R^1 = CH_2OMe, R^2 = CH_2Ph). The acetophenone (7; R^1 = CH_2OMe, R^2 = CH_2Ph) (1.5 g) and the benzaldehyde (8; R = Me) (1.44 g) were condensed as described [23] to yield the chalcone, which was purified by t.l.c. (hexane–ethyl acetate, 3 : 1; R_F 0.15) and crystallized from EtOH as yellow *needles* (1.15 g), m.p. 125° (Found: C, 69.5; H, 5.3. $C_{25}H_{24}O_7$ requires C, 69.6; H, 5.4%), *m/e* 448(40%, M^+); τ 1.95(d, *J* 16.0 Hz, H-β), 2.30(d, *J* 9.0 Hz, H-6′), 2.57(s, OCH_2Ph), 2.70(d, *J* 16.0 Hz, H-α), 2.92(s, H-6), 3.15(d, *J* 2.0 Hz, H-3′), 3.30(s, H-3), 3.47(dd, *J* 2.0 and 9.0 Hz, H-5′), 4.03(s, OCH_2O), 4.77(s, OCH_2OCH_3), 4.88(s, OCH_2Ph), 6.20(s, OCH_3), and 6.50(s, OCH_2OCH_3).

7-Benzyloxy-2-methoxy-4′,5′-methylenedioxyisoflavone (10b; R^2 = CH_2Ph). Oxidation of the chalcone (9; R = Me, R^1 = CH_2OMe, R^2 = CH_2Ph) (0.9 g) by $Tl(NO_3)_3$ [17] produced the isoflavone, which readily crystallized from EtOH as yellow *cubes* (0.719 g), m.p. 150° (Found: C, 71.4; H, 4.6. $C_{24}H_{18}O_6$ requires C, 71.6; H, 4.5%); *m/e* 402(50%, M^+); τ 1.78(d, *J* 9.0 Hz, H-5), 2.12(s, H-2), 2.56(s, OCH_2Ph), 2.95(dd, *J* 9.0 and 2.0 Hz, H-6), 3.07(d, *J* 2.0 Hz, H-8), 3.17(s, H-6′), 3.37(s, H-3′), 4.05(s, OCH_2O), 4.83(s, OCH_2Ph), and 6.30(s, OCH_3).

(±)-7-Hydroxy-2′-methoxy-4′,5′-methylenedioxyisoflavan (11b). The isoflavone (10b; R^2 = CH_2Ph) (250 mg) in EtOH (45 ml) and acetic acid (5 ml) was hydrogenated (room temperature, 3 atm, 6 h) over 10% Pd–C (250 mg).[7] After filtration, water (10 ml) was added, the EtOH evaporated off, and the residue extracted with $CHCl_3$ (3 × 50 ml). The extract was washed consecutively with 10% (w/v) $NaHCO_3$ (2 × 30 ml) and water (2 × 50 ml), yielding the isoflavan on evaporation. Crystallization from EtOH yielded white *needles* (170 mg), m.p. 168° (Found: C, 67.7; H, 5.5. $C_{17}H_{16}O_5$ requires C, 68.0; H, 5.4%), *m/e* 300(55%, M^+); τ[$(CD_3)_2CO$] 193(s, OH), 3.08(d, *J* 8.0 Hz, H-5), 3.25(s, H-6′), 3.30(s, H-3′), 3.62(dd, *J* 8.0 and 2.0 Hz, H-6), 3.68(d, *J* 2.0 Hz, H-8), 4.07(s, OCH_2O), 5.78(dd, *J* 10.0 and 4.0 Hz, H-2_{eq}), 6.03(t, *J* 10.0 and 10.0 Hz, H-2_{ax}), 6.18(s, OMe), 6.33—6.73(m, H-3), and 7.15(d, *J* 8.0 Hz, H-4).

3-Hydroxy-3-methyl-1,1-dimethoxybutane (14).[22] This was prepared from acetoacetaldehyde dimethyl acetal (13) (13.2 g) by the method of Bandaranyake *et al.*,[22] as a liquid, b.p. 74—78° at 80 mmHg (lit.,[22] 70—80° at 14 mmHg); τ 5.33(t, *J* 6.0 Hz, H-1), 6.53(s, OH), 6.63(s, 2 × OCH_3), 8.20(d, *J* 6.0 Hz, H-2), and 8.75(s, 2 × CH_3).

(±)-2′-O-methyl-leiocin (12a). To a vigorously stirred solution of the isoflavan (11b) (120 mg) in pyridine (40 mg) at 190 °C, 3-hydroxy-3-methyl-1,1-dimethoxybutane (14) (50 mg) was added dropwise, a similar addition being made 4 h later.[20] The mixture was then heated for a further 10 h, the pyridine was evaporated off, and the two products were isolated by t.l.c. (benzene–ethyl acetate, 99 : 1). One compound (R_F 0.65) was obtained as an *oil* (20 mg), identical with the 2′-methyl ether of natural leiocin (1e) (Found: C, 71.8; H, 6.5. $C_{22}H_{22}O_5$ requires C, 72.1; H, 6.1%). The mass and n.m.r. spectra were identical with those of the methyl ether of the natural product.

2′-O-Methylisoleiocin (12b). During the synthesis of 2′-*O*-methyl-leiocin from the isoflavan (11b) a second compound was produced, which was isolated by t.l.c. (R_F 0.53). 2′-O-*Methylisoleiocin* (12b) readily crystallized from EtOH as white needles (20 mg), m.p. 130° (Found: C, 71.7; H, 6.3%; M^+, 366.150. $C_{22}H_{22}O_5$ requires C, 72.1; H, 6.1%; *M*, 366.147), *m/e* 366(60%, M^+), 351(100), 199(48), 188(3.1), 187(5.8), 186(8.6), 185(39), 179(18.1), 178(61), 177(6.4), 176(63), 175(61), 174(53), 173(57), 166(29), 165(61), 163(34), 153(23), 151(26), 149(10.5), 145(15.7), 135(30), and 133(52); τ 3.33(s, H-5), 3.36(s, H-6′), 3.44(s, H-3′), 3.70(s, H-8), 3.74(d, *J* 10.0 Hz, H-4″), 4.10(s, OCH_2O), 4.54(d, *J* 10.0 Hz, H-3″), 5.74(dd, *J* 10.0 and 4.0 Hz, H-2_{eq}), 6.04(t, *J* 10.0 and 10.0 Hz, H-2_{ax}), 6.23(s, OCH_3), 6.30—6.60(m, H-3), 7.16(d, *J* 8.0 Hz, H-4), and 8.59(s, 2 × 2″-CH_3).

[23] F. E. King and T. J. King, *J. Chem. Soc.*, 1951, 569.

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