Phytochemistry, 1974, Vol. 13, pp. 1233 to 1236. Pergamon Press. Printed in England.

TWO LIGNANS FROM *LITSEA GRANDIS* AND *L. GRACILIPES**

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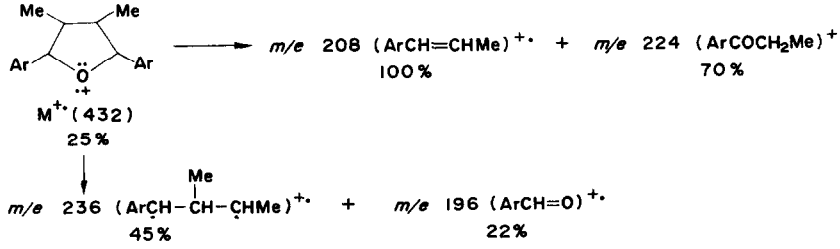
(*Received* 26 *October* 1973)

Key Word Index—*Litsea grandis* (Wall) Hook.f.; *L. gracilipes* Hook.f.; Lauraceae; tetrahydrofuranoid lignans; (+)-eudesmin; grandisin.

Abstract—Two lignans, grandisin and (+)-eudesmin have been isolated from *Litsea grandis* and *L. gracilipes* respectively.

IN A RECENT publication[1] we reported a new natural lignan, dehydrodieugenol, which co-occurs with the aporphine alkaloids boldine and laurolitsine in *Litsea turfosa* (Lauraceae). We now report the isolation of two further lignans from *L. grandis* and *L. gracilipes* to which the furan structures (**1**) and (**7**) have been assigned.

Concentration of the petroleum extract of the ground bark of *Litsea grandis* gave a solid which on recrystallisation from Et_2O gave colourless rhombic crystals, $[\alpha]_D = -57{\cdot}1$, which we have named grandisin. Elemental analysis and high resolution mass spectrometry indicated a molecular formula of $C_{24}H_{32}O_7$. It gave a UV spectrum typical of a pyrogallol system[2] and evidence for its aromatic character was confirmed by its NMR spectrum. This showed signals corresponding to two pyrogallol trimethyl ether moieties with six methoxyl groups (18H), four of which were shown to have vacant *ortho* positions by upfield shifts of methoxyl signals on addition of deuteriobenzene (Table 1). A four proton singlet at $\tau 3{\cdot}4$ indicated four magnetically equivalent aromatic protons. The symmetry of the rest of the spectrum indicated a lignan of the tetrahydrofuran type which was confirmed by the MS fragmentation pattern (Scheme 1).



SCHEME 1. MAJOR FRAGMENTATION PATTERN OF GRANDISIN.

* Part II in the series "Extractives from *Litsea* species". For Part I see ref. 1.

[1] HOLLOWAY, D. M. and SCHEINMANN, F. (1973) *Phytochemistry* **12**, 1503.
[2] SCOTT, A. I. (1964) *Interpretation of the Ultraviolet Spectra of Natural Products*, Pergamon Press, Oxford.

This fragmentation agrees with the reported data[3] for lignans of this class. However it gives no indication of the stereochemistry of the compound but this can be elucidated by comparison of the NMR data with that reported for related tetrahydrofuran lignans[4] galgravin (**2**), which is optically inactive, and the optically active lignans veraguensin (**3**) and galbelgin (**4**), all of which have only four methoxyl groups (Table 2).

TABLE 1. ^{1}H NMR CHEMICAL SHIFTS (τ) AND SOLVENT SHIFTS (Δ) FOR THE METHOXYL GROUPS IN GRANDISIN (**1**) IN C_6D_6 AND $CDCl_3$*

	3′ And 5′-OMe	4′-OMe
τC_6D_6	6·54	6·25
$\tau CDCl_3$	6·20	6·25
$\Delta\tau$	0·34	0

* All values of τ relative to TMS; all spectra run at 100 MHz.

The NMR data for the tetrahydrofuran ring of grandisin corresponds very closely to that of galbelgin (**4**) which has all of its substituents in the *trans* configuration.[4] Thus a lignan structure with the stereochemistry of galgravin (**2**) may be eliminated on the basis of the low chemical shift (τ7·6) of the protons on the methyl-bearing carbon atoms and the fact that it is optically inactive.[4] In contrast the NMR spectrum of the optically active veraguensin (**3**) is much more complex,[4] and clearly indicates that grandisin (**1**) has a different stereochemistry. Therefore grandisin can be represented by structure (**1**) or its antipode. It is hoped that ORD/CD analysis and X-ray analysis currently being carried out may enable the absolute configuration of grandisin, and hence that of the other lignans of this class to be determined.

TABLE 2. COMPARISON OF NMR DATA (τ)* OF GRANDISIN WITH THAT OF RELATED LIGNANS

Lignan	Me	Me C–H	Ar C–H	Ar	–Me
Galgravin (**2**)	8·95(d), 6H	7·60(m), 2H	5·47(m), 2H	3·00(m), 6H	6·13 12H
Veraguensin (**3**)	8·95(d), 3H	7·95(m), 2H	5·52, 1H	3·02(m), 6H	6·15 6H
	9·35(d), 3H		4·90, 1H		6·10 6H
Galbelgin (**4**)	8·95(d), 6H	8·25(m), 2H	5·40(m), 2H	3·10(m), 6H	6·11 6H
					6·15 6H
Grandisin (**1**)	8·90(d), 6H	8·20(m), 2H	5·40(d), 2H	3·42(s), 4H	6·25 18H

* All values of τ relative to TMS; spectra of (**2**), (**3**) and (**4**) run at 60 MHz, and spectrum of (**1**) at 100 MHz in $CDCl_3$.

Concentration of the petrol. extract of the ground bark of *L. gracilipes* gave a solid which on recrystallization from ethanol gave colourless plates, $[\alpha]_D = +69·4°$. The UV spectrum showed typical catechol absorptions[2] and the MS[5] and NMR[6] data was consistent with that of a fused bistetrahydrofuran system. Comparison of its NMR data with that of similar lignans,[6] diaeudesmin (**5**), epieudesmin (**6**) and (+)-eudesmin (pinoresinol dimethyl

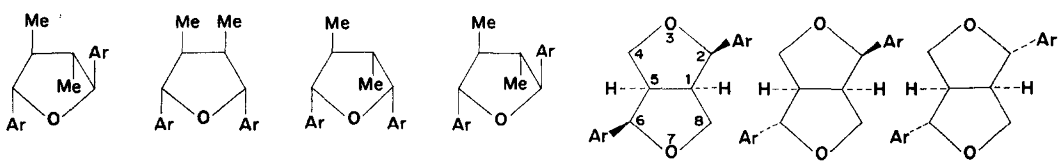
[3] PELTER, A., STAINTON, P. and BARBER, M. (1966) *J. Heterocyclic Chem.* **3**, 191.
[4] CROSSLEY, N. S. and DJERASSI, C. (1962) *J. Chem. Soc.* 1459.
[5] PELTER, A. (1967) *J. Chem. Soc. C*, 1376.
[6] ATAL, C. K., DHAR, K. L. and PELTER, A. (1967) *J. Chem. Soc. C*, 2228.

ether) (7) (Table 3) indicates that this lignan is (+)-eudesmin because both aromatic substituents are *cis* to the bridgehead protons. With (+)-eudesmin (7) the aryl groups deshield two opposite methylene protons at C-4 and C-8 so that the resonance appears in the region of τ5·8 in contrast to diaeudesmin where these protons appear at τ6·5. The melting point and optical rotation are also in good agreement for (+)-eudesmin.

TABLE 3. COMPARISON OF RECORDED NMR DATA (τ)* OF (+) EUDESMIN AND RELATED LIGNANS[6] WITH THAT OF (+) EUDESMIN FROM *Litsea gracilipes*

Lignan	1,5-H	2,6-H	4,8-H
Diaeudesmin (**5**)	6·85	5·10	6·15
			6·55
Epieudesmin (**6**)	7·1	5·15	5·75
	6·7	5·55	6·20
(+)-Eudesmin (7)			6·60
Lit. data[6]	6·85	5·25	5·70
			6·10
Measured data	7·02	5·40	5·90
			6·20

* All values of τ relative to TMS; all spectra run at 100 MHz in $CDCl_3$.



(**1**) (**2**) (**3**) (**4**) (**5**) (**6**) (**7**)

(**1**) Ar = 3,4,5-trimethoxyphenyl
(**2**) (**3**) (**4**) Ar = 3,4-dimethoxyphenyl

Ar = 3,4-dimethoxyphenyl

TABLE 4. CD DATA FOR (+)-EUDESMIN

Δε	λ (nm)
+0·73 m	280
−0·91 m	236
+2·42 sh	216
+13·3 !	205

$\Delta\epsilon = \epsilon_L - \epsilon_R$ where ϵ_L and ϵ_R are molecular extinction coefficients for the left and right circularly polarized light. m = Maximum, sh = shoulder, ! = lowest wavelength measured.

(+)-Eudesmin has been previously reported to occur in *Humbertia madagascariensis*[7] and *Araucaria angustifolia*[8] whereas (−)-eudesmin has been noted to occur in eucalypts which characteristically contain aromadendrin and catechol tannins.[9] The absolute configuration of (+)-eudesmin (pinoresinol dimethyl ether) has been determined by X-ray

[7] COMBES, G., BILLET, D. and MENTZER, C. (1959) *Bull. Soc. Chim. France*, 2014.
[8] DRYSELIUS, E. and LINDBERG, B. (1956) *Acta. Chem. Scand.* **10**, 445.
[9] DEAN, F. M. (1963) *Naturally Occurring Oxygen Ring Compounds*, pp. 46–47, Butterworths, London.

analysis[10] and now we report the CD data (Table 4) which shows a positive Cotton effect. It is hoped that this information may facilitate the determination of absolute stereochemistry of the other lignans in this class.

EXPERIMENTAL

All UV spectra were determined in MeOH, IR spectra as Nujol mulls. NMR spectra were measured in $CDCl_3$ on a Varian HA 100 instrument and MS with an A.E.I. MS12 and MS9 spectrometers. CD analysis was carried out in methanol soln.

Extraction of *L. grandis*. The powdered bark was extracted continuously for 24 hr with petrol. (b.p. 60–80°). Conc. of the yellow soln gave a white amorphous solid. Recrystallization from Et_2O yielded rhombic crystals of grandisin, m.p. 118–120° $[\alpha]_D = -57{\cdot}1°$ (C = 0·35 in $CHCl_3$) (Found: C, 66·51; H, 7·60%. $C_{24}H_{32}O_7$ requires, C, 66·7; H = 7·47%). λ_{max} (log ϵ) 219 (4·21), 226 (4·20) (sh), 233 (4·17) sh and 269 nm (3·21); ν_{max} 1600, 1510, 1330, 1245, 1015, 865, 825, 715, 670 cm^{-1}.

Extraction of *L. gracilipes*. The powdered bark was extracted continuously for 24 hr with petrol. (b.p. 60–80°). Concn. of the yellow soln gave a white amorphous solid. Recrystallization from EtOH yielded colourless plates of (+)-eudesmin, m.p. 103–104°, (lit,[9] 107°) $[\alpha]_D = +69{\cdot}4$ (C = 0·23 in $CHCl_3$) (Lit[6] $[\alpha]_D = +64$). Found: C, 68·09; H, 6·66%. Calc. for $C_{22}H_{26}O_6$ c. 68·39; H, 6·73%. λ_{max} (log ϵ) 233 (4·24) and 279 nm (3·86) ν_{max} 1600, 1522, 1245, 1155, 1035, 825, 755 cm^{-1}.

Acknowledgements—We thank the Tropical Products Institute for a research grant (to D.M.H.) and Dr. P. M. Scopes for C.D. measurements.

[10] LUND, E. W. (1960) *Acta. Chem. Scand.* **14,** 496; VILLARD, A.-M. and WYART, J. (1968) *C. R. Acad. Sci. Paris (C)* **266,** 1284.