Tetrahedron. 1967. Vol. 23, pp. 261 to 265. Pergamon Press Ltd. Printed in Northern Ireland

SESQUITERPENES OF *NEOLITSEA ZEYLANICA* MERR.—I*

ISOLATION OF SOME CONSTITUENTS

B. S. Joshi, V. N. Kamat and T. R. Govindachari
CIBA Research Centre, Goregaon, Bombay 63

(*Received* 27 *May* 1966)

Abstract—From the roots of *Neolitsea Zeylanica* six sesquiterpenes, linderalactone, linderane, neolinderane, zeylanine, zeylanicine and zeylanidine, have been isolated. The chemistry of the first two compounds is discussed.

Neolitsea Zeylanica Merr. (Lauraceae) is a tree growing in the Western Ghats of India the roots of which have not previously been investigated. By the extraction of the powdered roots and chromatographic purification, the six compounds listed in Table 1 were isolated. In the present paper, the salient features of the first two compounds in Table 1 are discussed.

Table 1

Substance	Mol. formula	m.p.	$[\alpha]_D^{26}$:	R_f*
1. Linderalactone	$C_{15}H_{16}O_3$	140°	+102°	0·79
2. Linderane	$C_{15}H_{16}O_4$	190°	+179°	0·90
3. Neolinderane	$C_{15}H_{16}O_4$	170°	+31·5°	0·41
4. Zeylanine	$C_{17}H_{18}O_6$	175°	+271°	0·39
5. Zeylanicine	$C_{17}H_{18}O_6$	235°	−153°	0·17
6. Zeylanidine	$C_{17}H_{18}O_7$	220°	−174°	0·34

* TLC on silica gel plates; solvent system—$CHCl_3$:EtOAc (19:1); characteristic coloured spots are observed on spraying with Ehrlich reagent.

Linderalactone. The compound m.p. 140° analysed for $C_{15}H_{16}O_3$ (mol. wt. by mass spectrum, 244). The UV spectrum showed a max at 208 mμ (log ϵ 4·19). The IR spectrum showed bands at 1747 (α, β-unsaturated γ-lactone) and at 3130, 3110, 1640 and 1545 cm^{-1} (furan ring). The NMR spectrum (Fig. 1) showed signals at 1·3 δ (d, J = 1 c/s, 3H), ascribed to methyl groups on double bonds, and at 7·14 δ (d, J = 1 c/s, 1H) ascribed to the α-proton on a furan ring.[1] A positive Ehrlich test confirmed the presence of a furan ring indicated by the IR and NMR spectra.

Reduction of the compound with hydrogen in presence of Pd–C yielded a dihydro derivative, m.p. 140°, $[\alpha]_D$ −38°. In this compound, the original signal at 1·3 is shifted to a more normal position at 1·6 δ for a methyl group on a double bond. The abnormal upfield shift in the original compound should be ascribed to the diamagnetic shielding associated with the π-electrons of the other double bond which is altered on reduction of this double bond in conjugation with the lactone carbonyl

---

* Contribution No. 55 from CIBA Research Centre.

[1] E. J. Corey, G. Slomp, S. Dev, S. Tobinga and E. R. Glazier, *J. Amer. Chem. Soc.* **80**, 1204 (1958).

group.[2] Similar abnormal shielding of the methyl protons in the germacrane sesquiterpenes is seen in the case of costunolide (1·41 δ), germacrone (1·42 δ) and aristolactone (1·48 δ).[3,4]

The data presented above indicated the possibility of the compound being linderalactone (I) for which a specific rotation of +5·2° has been recorded[5] instead of +102° observed by us. However, a direct comparison kindly carried out by Dr. Takeda established its identity with linderalactone.[*]

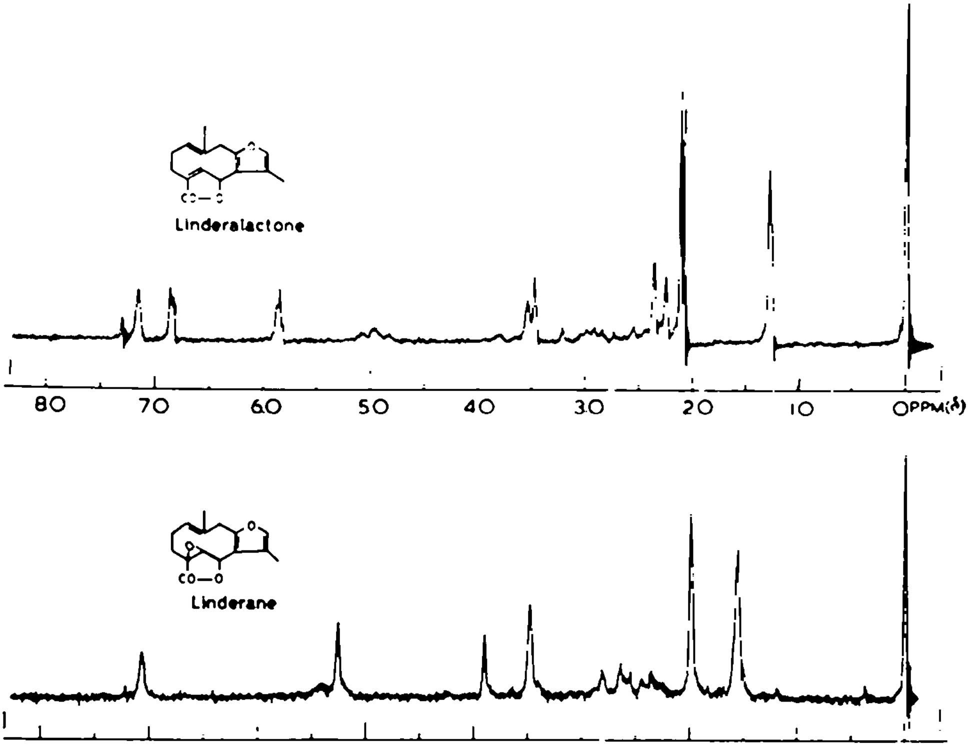


Fig. 1

Linderane. The compound m.p. 190° analysed for $C_{15}H_{16}O_4$ (mol. wt. by mass spectrum 260). The UV spectrum had a max at 212 mμ ($\log \epsilon$ 3·81) and the IR spectrum bands at 3130, 3060, 1616 and 1558 (furan) and at 1770 cm^{-1} (saturated γ-lactone). The NMR spectrum (Fig. 1) had signals at 1·58 and 2·0 (d, J = 1 c/s, 3H each) and at 7·08 δ (d, J = 1 c/s, 1H). The compound gave a positive Ehrlich test. The physical

---

[*] Dr. Takeda kindly informed us that the value recorded in his paper was an error.

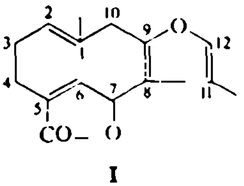
[2] L. M. Jackman, *Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry*, p. 129. Pergamon Press (1959).

[3] R. B. Bates and D. M. Gale, *J. Amer. Chem. Soc.* 82, 5750 (1960).

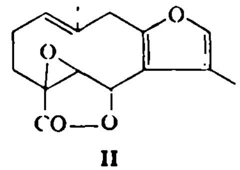
[4] M. Martin-Smith, P. De Mayo, S. J. Smith, J. B. Stenlake and W. D. Williams, *Tetrahedron Letters* 2391 (1964).

[5] K. Takeda, H. Minato and M. Ishikawa, *J. Chem. Soc.* 4578 (1964).

constants and spectral data indicated that the compound was linderane and comparison with an authentic sample* confirmed its identity with linderane (II).[6]



I



II

Since the 1,2-epoxide is conjugated with the carbonyl group of the lactone[7] by the action of chromous chloride, II gave I, in 50% yield. This has an analogy in the conversion of limonin to deoxylimonin[8] and veprisone to deoxyveprisone.[9]

A by-product obtained in this reaction was a compound m.p. 208° with the molecular formula $C_{15}H_{18}O_3$. The compound is assigned structure III on the following evidence: The UV spectrum showed max at 208 and 236 mμ (log ϵ 4·07 and 3·97). The IR spectrum showed bands at 1760, 1740 and 1725(sh) cm^{-1}. The NMR spectrum showed the following signals: 1·3 (d, 3H; J = 1 c/s; Me at C-1), 1·68 and 1·81 (s, 3H each, *gem*-dimethyls on C-11), 6·85 (d, J = 1 c/s, C-6 proton), 5·8 (C-7 proton), 5·0 (broad t, J = 7 c/s; C-2 proton) and 3·5 δ (broad d, J = 4 c/s; C-10 protons). The compound gave acetone on ozonolysis. These observations are consistent with

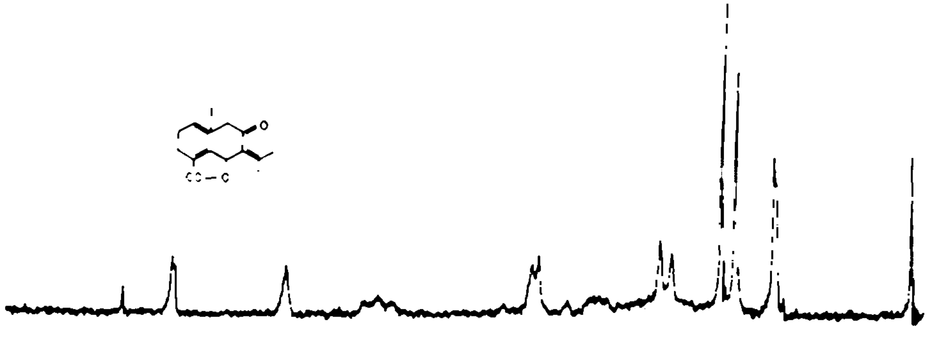
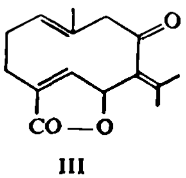
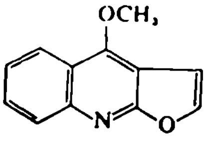


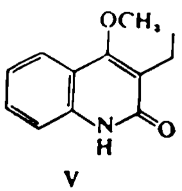
FIG. 2



III



IV



V

---

* Kindly presented by Dr. Takeda.

[6] K. Takeda, H. Minato and I. Hirobe, *Tetrahedron* 19, 2307 (1963).

[7] W. Cole and P. L. Julian, *J. Org. Chem.* 19, 131 (1954).

[8] D. H. R. Barton, S. K. Pradhan, S. Sternhell and J. F. Templeton, *J. Chem. Soc.* 255 (1961).

[9] T. R. Govindachari, B. S. Joshi and V. N. Sundararajan, *Tetrahedron* 20, 2985 (1964).

structure III. Such a rearrangement of a furan ring with chromous chloride has not been reported, although the transformation of the furanoquinoline (IV) to the quinolone (V) on catalytic hydrogenation is known.[10] The anomalous UV and IR spectra observed for the compound should be ascribed to the germacrone unit present in the structure.[11]

EXPERIMENTAL

NMR spectra: $CDCl_3$, Varian A60. All signals are reported in ppm as δ values, TMS as internal standard. UV spectra: Beckmann DB spectrophotometer and IR spectra: Perkin-Elmer Infrared spectrophotometer, Model 421.

Isolation of linderane and linderalactone. The dried powdered roots (10 kg) were soaked with hexane (30 l.) overnight at room temp. The extract was drawn off and the plant material re-extracted with hexane (30 l. × 5). Each extract was worked up separately as detailed. The material was then extracted with ether by cold percolation and the extract processed separately.

The first hexane extract was evaporated under red. press. leaving a dark brown oily residue. Ether (130 ml) was added and the mixture left in the refrigerator overnight, yielding a crude crystalline mass. This was washed with a little cold ether. TLC examination showed it to be a mixture of two closely moving substances, R_f 0·90 and 0·79 with traces of a slower moving compound having R_f 0·41 (chf: EtOAc—19:1). A separation was effected by chromatography.

The crude mass (12 g) dissolved in benzene (50 ml) was chromatographed over silica gel (250 g, 0·2–0·5 mm) using hexane–benzene (1:1) as eluent. 25 ml fractions were collected and the course of this chromatography followed by TLC.

Fraction	Eluent	Weight	R_f TLC on Si gel in chf_3:EtOAc—19:1	
1–56	Hexane:Benzene 1:1	—		
57–78		0·8 g	0·9	
79–118		2·6 g	0·9	0·79
119–133		3·0 g		0·79
134–153	$CHCl_3$	4·3 g		0·79
154–160	MeOH	0·6 g (resinous mass)		

Fractions 57–78 were combined and the solvent distilled off. The residue on crystallization from CH_2Cl_2–ether gave II, 0·7 g, m.p. 190°, $[\alpha]_D^{24°}$ +179° (*c*, 1·45, dioxan); UV (EtOH) 212 mμ (log ϵ 3·81). IR (nujol): 3130, 3060, 1770, 1616, 1558, 1325, 1145, 1131, 1113, 1084, 1055, 1025, 1004, 948, 926, 893, 835, 818, 785, 765 cm^{-1}. (Found: C, 69·2; H, 6·3. Mol. wt. by mass spectrum 260. Calc. for $C_{15}H_{16}O_4$; C, 69·2; H, 6·2%. Mol. wt. 260.)

Fractions 119–153 were combined, the solvent removed and the residue crystallized from CH_2Cl_2–ether (6 g), m.p. 140°. This was identified as I, $[\alpha]_D^{24°}$ +102° (*c*, 0·98, dioxane); UV (EtOH): 208 mμ (log ϵ 4·19). IR (nujol): 3130, 3110, 1747, 1739, 1640, 1545, 1290, 1267, 1219, 1199, 1137, 1104, 1087, 1059, 1024, 944, 899, 880, 864, 810, 788, 779 cm^{-1}. (Found: C, 73·7; H, 6·9. Mol. wt. by mass spectrum 244. Calc. for $C_{15}H_{16}O_3$; C, 73·7; H, 6·6%. Mol. wt. 244.)

Isolation of neolinderane. The TLC examination of the crude crystalline mass obtained from the second hexane extract, showed it to contain mainly a single compound with R_f 0·41. This was recrystallized from CH_2Cl_2–ether (6 g), m.p. 170°, $[\alpha]_D^{24°}$ +31·5° (*c*, 2·5; dioxan); UV (EtOH): 210 mμ (log ϵ 4·09). IR (nujol): 3120, 3040, 1750, 1740, 1640, 1605, 1540, 1310, 1298, 1282, 1262, 1210, 1185, 1140, 1100, 1060, 1035, 965, 930, 922, 890, 875, 835, 798, 785, 758, 748 cm^{-1}. (Found: C, 69·0; H, 6·0. Mol. wt. by mass spectrum 260. $C_{15}H_{16}O_4$ requires C, 69·2; H, 6·2%. Mol. wt. 260.)

---

[10] T. Ohta, *J. Pharm. Soc. Japan* 73, 63 (1953); T. Ohta and Y. Mori, *Pharm. Bull.* 3, 396 (1955).

[11] F. Šorm, *Progress in the Chemistry of Natural Products* (Edited by L. Zechmeister) Vol. 19, p. 25.

Isolation of zeylanine. TLC examination of the crystalline mass obtained from the 5th and 6th hexane extracts showed it to contain mainly a single compound. This was recrystallized from CH_2Cl_2–ester (4·0 g), m.p. 175°, $[\alpha]_D^{24°}$ +271° (*c*, 2·5; dioxan); UV (EtOH): 204, 252 mμ (log ε 4·06, 3·76). IR (nujol): 3130, 1755, 1745, 1640, 1530, 1244, 1205, 1126, 1071, 1052, 1022, 955, 940, 880, 775, 724 cm^{-1}. (Found: C, 67·5; H, 6·0; mol. wt. by mass spectrum 302. $C_{17}H_{18}O_5$ requires: C, 67·5; H, 6·0%. Mol. wt. 302.)

Isolation of zeylanicine and zeylanidine. After 6 extractions with hexane, the material was extracted with ether. The crystalline mass obtained from the ether extract was shown to contain by TLC examination two main compounds. The crude mass (2 g) dissolved in benzene (30 ml) was chromatographed over silica gel (25 g, 0·2–0·5 mm) with benzene as eluent. 25 ml fractions were collected and the progress of the chromatography followed by TLC.

Fraction	Eluent	Weight	*R*$_f$	
1–11	Benzene	—		
12–42	Benzene + $CHCl_3$ (2%)	0·53 g	0·34	
43–63		0·40 g	0·34	0·17
64–100		1·00 g	—	0·17

(a) Fractions 12–42 were combined and the solvent removed. The residue on crystallization from CH_2Cl_2–ether gave zeylanidine (0·5 g), m.p. 220°, $[\alpha]_D^{24°}$ −174° (*c*, 3·19, dioxan); UV (EtOH): 214 and 224 mμ (log ε 3·75, 3·74). IR (nujol): 3130, 3060, 1650, 1779, 1744, 1539, 1332, 1224, 1196, 1164, 1149, 1119, 1087, 1042, 1032, 947, 919, 890, 819, 799, 744 cm^{-1}. (Found: C, 60·9; H, 5·3. Mol. wt. by mass spectrum 334. $C_{17}H_{18}O_7$ requires C, 61·1; H, 5·4%. Mol. wt. 334.)

(b) Fractions 64–100 were combined and the residue obtained therefrom recrystallized from CH_2Cl_2–ether to give zeylanicine, (0·9 g), m.p. 235°, $[\alpha]_D^{24°}$ −153° (*c*, 3·13, dioxan); UV (EtOH): 210 mμ (log ε 4·08). IR (nujol): at 3130, 1758, 1743, 1640, 1553, 1580, 1298, 1230, 1220, 1193, 1166, 1146, 1111, 1098, 1976, 1053, 1030, 978, 960, 943, 920, 886, 800, 763 cm^{-1}. (Found: C, 64·1; H, 5·6. Mol. wt. by mass spectrum 318. $C_{17}H_{18}O_6$ requires C, 64·1; H, 5·7%. Mol. wt. 318.)

Action of $CrCl_2$ *on Linderane.*[18] $CrCl_2$ was prepared as follows: A mixture of $CrCl_3$ (12 g) dissolved in H_2O (20 ml) and Zn-dust (20 g) was stirred and flushed with N for 20 min. Conc. HCl (28 ml) was added dropwise with stirring and the reaction continued for a further 2 hr under N. The clear blue $CrCl_2$ sol was decanted and used for the reaction.

A sol of II (900 mg) in acetone (60 ml) and AcOH (20 ml) was treated with $CrCl_2$ (40 ml), dropwise under stirring in N. The reaction was continued for a further 3½ hr under N. It was then diluted with water and extracted with CH_2Cl_2. The extract was washed with $NaHCO_3$ aq and then dried (Na_2SO_4). Removal of solvent gave a gummy residue (700 mg) which was chromatographed on silica gel column. Elution with benzene (200 ml) yielded I (435 mg), m.p. 140° undepressed on admixture with an authentic specimen. Further elution with chf (100 ml) yielded a gum which after crystallization from CH_2Cl_2–ether gave crystals (200 mg), m.p. 208°, UV (EtOH): 208, 236 mμ (log ε 4·07, 3·97). IR (nujol): 1760, 1740, 1725 (sh), 1224, 1213, 1060, 953, 898, 878 cm^{-1}. (Found: C, 73·3; H, 7·3. $C_{15}H_{18}O_3$ requires C, 73·1; H, 7·4%.)

Ozonolysis of III. Compd III (300 mg) was dissolved in chf (15 ml) and ozonized at −10° for 6 hr. The solvent was removed *in vacuo* and the residual gum steam distilled after addition of water. The distillate was collected in 2,4-dinitrophenylhydrazine sol. A crystalline product identical with acetone 2,4-dinitrophenylhydrazone was obtained (mixed m.p.; IR spectra).

Acknowledgements—We are grateful to Drs. R. Zürcher and H. Hürzeler of CIBA Limited, Basle, for the NMR and mass spectra and Dr. S. Selvavinayakam for the microanalyses.

---

[18] *Inorganic Syntheses* 1, 124 (1939).