Tetrahedron. Vol. 29, pp. 1291 to 1298. Pergamon Press 1973. Printed in Great Britain

CRYSTALLINE CONSTITUENTS OF EUPHORBIACEAE—XII†

ISOLATION AND STRUCTURAL ELUCIDATION OF THREE NEW LIGNANS FROM THE LEAVES OF *PHYLLANTHUS NIRURI* LINN.

A. S. R. ANJANEYULU, K. JAGANMOHAN RAO, L. RAMACHANDRA ROW* and C. SUBRAHMANYAM

Department of Chemistry, Andhra University, Waltair, India

(*Received in UK* 12 *December* 1972; *Accepted for publication* 16 *January* 1973)

Abstract—Three more new lignans from the hexane extract of *Phyllanthus niruri* Linn. are now reported besides phyllanthin and hypophyllanthin. The structure of niranthin is now established as 3,3′,4′,9,9′-pentamethoxy-4,5-methylenedioxy-8,8′-butyrolignan (2). Nirtetralin and phyltetralin are shown to be 1-phenyl tetralins. On the basis of NMR and mass spectra, nirtetralin is assigned the structure (7) and phyltetralin (11).

Further examination of the hexane extract of the bitter leaves of *Phyllanthus niruri* Linn. (Euphorbiaceae) revealed the presence of three more new lignans besides phyllanthin (1) and hypophyllanthin (6).[1-3] They have now been isolated in a pure state through extensive chromatography on alumina and also by preparative chromatography on silica gel 'C' followed by careful crystallisation. These new lignans are now named niranthin, nirtetralin and phyltetralin. Table 1 gives them in order of their R_f values together with their yields and colour reactions with $MeOH/H_2SO_4$ (9 : 1).

Like phyllanthin (1), niranthin (2) is intensely bitter and from elemental analysis and other reactions, it belongs to the class of diaryl butanes. It is resistant to permanganate oxidation; only a small quantity of veratric acid being isolated. But unlike phyllanthin (1), it yields a permanent emerald green colour in Labat test indicating the presence of a methylenedioxy group in the molecule. Further, bromine in chloroform furnishes a tribromo derivative readily, unlike phyllanthin (1) which affords a dibromo derivative.

In the NMR spectrum (Table 2) of niranthin (2), three of the five aromatic protons (δ 6·6 to 6·3 m) can be clearly analysed into a veratryl system. The pair of doublets (δ 6·2 and 6·12, J = 2 Hz) are assignable to a pair of meta coupled protons which are obviously in a ring system (A) containing a methylenedioxy and OMe group, for which two alternate structures 2 and 3 may be proposed. The latter structure (3) can be rejected as the two meta protons are non-equivalent and will differ prominantly in their NMR behaviour. The NMR spectrum of niranthin (2) also shows the methylenedioxy group as a singlet at δ 5·85 and significantly, the four benzylic protons at 7 and 7′ appear as a doublet at δ 2·53 (J = 8 Hz) as in phyllanthin (1) indicating their equivalence. On this basis, niranthin is shown to be 3,3′4′9,9′-pentamethoxy-4,5-methylenedioxy-8,8′-(R,R)-butyrolignan (2).

The structure 2 for niranthin is further supported by the NMR spectrum (Table 2) of its tribromo derivative (4). The latter crystallises as colourless needles from hexane and analyses for $C_{24}H_{29}O_7Br_3$, m.p. 121°, $(\alpha)_D^{30°}$ +25° ($CHCl_3$) with no significant

†This paper was presented at the IUPAC Symposium on 'The Chemistry of Natural Products' held at New Delhi, between February 6–12, 1972.

Table 1

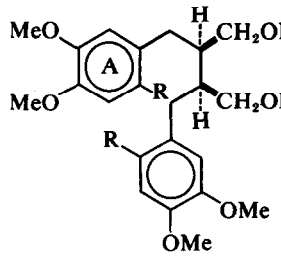
S.No.	Compound	Molecular form	m.p.	$(\alpha)_D^{30°}$	R_f	Yield	Colour
1.	Nirtetralin	$C_{24}H_{30}O_7$	55–7°	+14·39°	0·53	2·00	Violet
2.	Niranthin	$C_{24}H_{32}O_7$	67–9°	+28·00°	0·49	1·20	Dark Blue
3.	Hypophyllanthin	$C_{24}H_{30}O_7$	128–9°	+3·50°	0·43	2·50	Violet
4.	Phyltetralin	$C_{24}H_{32}O_6$	110–1°	+17·50°	0·38	0·03	Deep Bluish Green
5.	Phyllanthin	$C_{24}H_{34}O_6$	98°	+12·40°	0·35	3·00	Bluish Green

$(\alpha)_D$ Values are in $CHCl_3$.

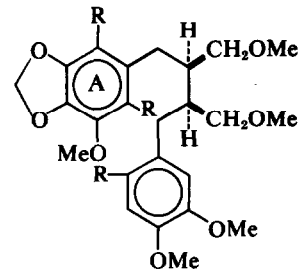
Table 2

Niranthin **2**			Tribromo niranthin **4**			Dibromo phyllanthin **5**		
δ Values	No. of Protons	Assignment	δ Values	No. of Protons	Assignment	δ Values	No. of Protons	Assignment
6·60 to 6·43 m	3 Ar—H	2′,3′,6′	6·81 s	1 Ar—H	2′	6·75 s	2 Ar—H	2,2′
6·20 d J = 2Hz	1 Ar—H	2,6	6·55 s	1 Ar—H	5′	6·50 s	2 Ar—H	5,5′
6·12 d J = 2Hz	1 Ar—H							
5·85 s	2 O—CH_2—O	4,5	5·98 s	2 O—CH_2—O	4,5			
3·80 s	3		3·95 s	3 Ar—OCH_3	3	3·71 s	6 Ar—OCH_3	3,3′
3·76 s	3 Ar—OCH_3	3,4′,5′	3·78 s	3				
3·73 s	3		3·72 s	3 Ar—OCH_3	4′,5′	3·68 s	6 Ar—OCH_3	4,4′
3·26 s	6 CH_2—OCH_3	9,9′	3·30 s	6 CH_2—OCH_3	9,9′	3·22 s	6 CH_2—OCH_3	9,9′
3·26 s	4 CH_2—OCH_3	9,9′	3·30 s	4 CH_2—OCH_3	9,9′	3·21 s	4 CH_2—OCH_3	9,9′
2·53 d J = 8Hz	4 Ar—CH_2	7,7′	2·99 d J = 7·5Hz	2 Ar—CH_2	7			
			2·76 d J = 7·5Hz	2 Ar—CH_2	7′	2·77 d J = 7Hz	4 Ar—CH_2	7,7′
2·10 to 1·76 m	2 C—H	8,8′	2·45 to 1·86 m	2 C—H	8,8′	2·45 to 1·86 m	2 C—H	8,8′

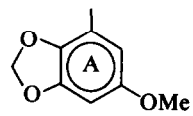
The NMR spectrum of niranthin was taken on Varian Associates S-60T spectrometer in $CDCl_3$.
The NMR spectra of tribromo niranthin and dibromo phyllanthin were taken on Varian Associates A-60 spectrometer.



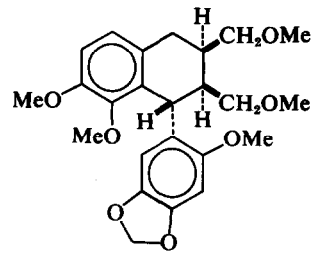
1: R = H
5: R = Br



2: R = H
4: R = Br



3



6

change in optical rotation. It exhibits only two aromatic protons as singlets at δ 6·81(s) and δ 6·55(s) which are now assigned to 3′,6′ in ring B (4). The effect of Br atoms at 2,6 and 2′ positions is clearly visible on the four benzylic protons at 7 and 7′. The former appear as a doublet separately downfield at δ 2·99(d) (J = 7·5 Hz) and the latter at δ 2·76(d) (J = 7·5 Hz) clearly supporting the substitution of Br at 2,6 and 6′. Similarly, the 4,5 methylenedioxyl and 3-methoxyl also moved downfield (δ 5·98 and 3·95) as might be expected. The rest of the spectrum is very similar to the parent niranthin (2).

The NMR spectrum (Table 2) of dibromophyllanthin (5) ($C_{24}H_{32}O_6Br_2$, m.p. 136°) is now presented for the first time and the proton assignments are in good agreement with those of tribromo niranthin (4) and amply confirm the symmetrical structure of dibromophyllanthin (5).

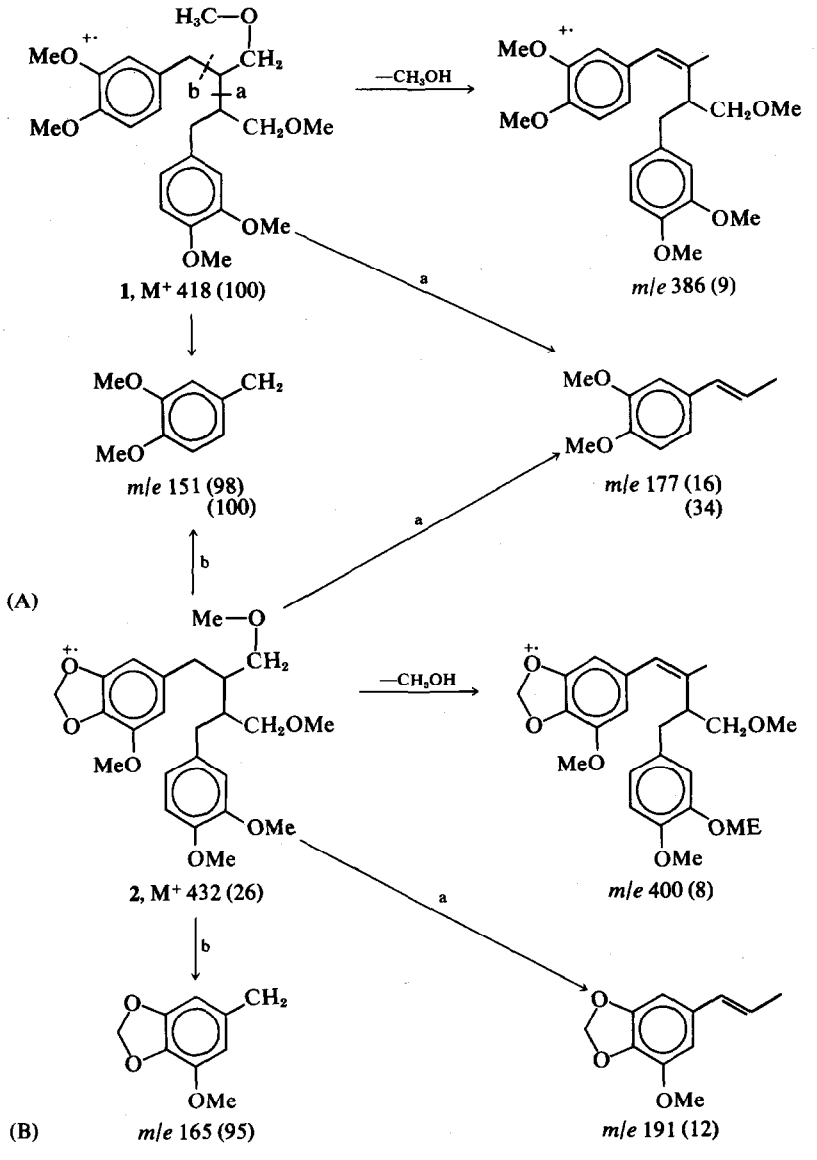
The mass spectral behaviour of phyllanthin (1) and niranthin (2) follows the pattern already observed by Duffield[4] and Burden *et al.*[5] for diaryl butanes. The mass peak (M^+ 418) is also the base peak for phyllanthin (1) while for niranthin (2), (M^+ 432) has a low abundance of 27% in conformity with similar methylenedioxy lignans. Benzylic cations form either a base peak (*m/e* 151, (100) in niranthin) or the next highest peak (*m/e* 151, (98) in phyllanthin). The peak at *m/e* 165 (90), which is absent in phyllanthin (1), confirms ring A in niranthin (2). Other peaks of low abundance refer to the loss of 32 mu (MeOH) or cleavage at 8-8′ bond. Here too, the presence of the peak *m/e* 191 (12) in niranthin (2) and its absence in phyllanthin (1) offers further support to the structure of niranthin (2).

Finally, the positive rotation (+28°) seem to suggest a 8,8′ (R,R) stereochemistry in this new lignan (2), as in phyllanthin (1).

Structure of nirtetralin

Nirtetralin (7) crystallises as colourless needles from hexane and analyses for $C_{24}H_{30}O_7$, m.p. 55°, $(\delta)_D^{30°}$ + 14·4, λ_{max}^{EtOH} 226 and 284 nm. It is an isomer of hypophyllanthin (6) and like the latter, it is resistant to oxidation and yields a dibromo derivative (10). UV and IR spectra support its characterisation as a 1-phenyltetralin, but with no OH nor a lactone ring system. All the seven oxygens are accounted for by a methylenedioxy, three aromatic OMe's and two aliphatic OMe's, as in hypophyllanthin (6). The NMR spectra of nirtetralin and its dibromo derivative are now presented here in support of the structure (7) for nirtetralin.

The aromatic protons in the NMR spectrum of nirtetralin (7) (Table 3) can be clearly analysed into a veratryl system (δ 6·5–6·6 m) assigned to ring C and the remaining single proton (δ 6·33 s) located at C-5 in ring A containing a methylenedioxy (δ 5·98 s) and a OMe. Ring A can therefore have three alternate structures, 7, 8, or 9. A choice between them is made from the following considerations: (1) the methylenedioxy protons appear as a singlet clearly indicating their equivalence, and therefore can be placed at 6,7 only and not at 7,8 as in otobain.[6] (2) Further, the clinching evidence in favour of



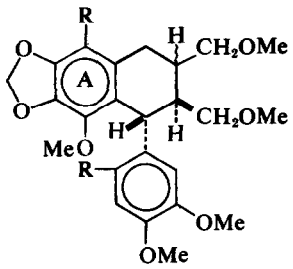
Fragmentation pattern of (A) Phyllanthin and (B) Niranthin

CHART 1

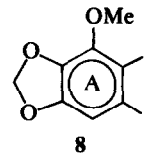
structure (7) is furnished by the OMe which appears as a singlet at δ 3·45. It is now located at C-8 in ring A, where alone it can be definitely shielded by the phenyl ring C as in (±) lyoniresinol or thomasic acid.[7] If the position 8 is thus occupied by a OMe, the methylenedioxyl must be placed at 6,7 as in ring A of structure (7). Obviously, the position 5 for the OMe cannot be supported, where it is unshielded and can absorb at about δ 4·05 as in β-peltatin-A-methyl ether or its 5′-desmethoxy derivative.[8]

Seikal *et al.*[7] remarked that the upfield shift of 8-OMe, noticed in (±) lyoniresinol (δ 3·42), is due to anisotropy of the 1-α-equatorial phenyl ring, which forces the 8-OMe out of plane (Cf. Wallis[9]). Incidentally, the stereochemistry of 1-phenyl and 2-H in these molecules is also fixed, 1-H being β-axial while 2-H will be α-axial in a *trans* position. Thus, structure (7) correctly represents nirtetralin. Other assignments of the NMR spectrum of nirtetralin (7) are shown in Table 3. They do not, however, establish the stereochemical relationship of C-2,3 hydrogens.

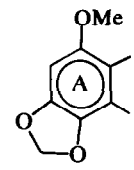
The structure of nirtetralin (7) is further con-



7: R = H
10: R = Br



8



9

firmed by the NMR spectrum of its dibromo derivative (**10**) (Table 3). The aromatic portion consists of two singlets (δ 6·83 and 6·15) each integrating to one proton and assignable to 3′ and 6′ positions. The methylenedioxy protons remain unsplit as also the 8-OMe appearing in the shielded position at δ 3·40. Bromination has not therefore caused any shift in these groups. But very significantly the

Structure of phyltetralin

Phyltetralin (**11**), M^+ 416, $C_{24}H_{32}O_6$, m.p. 110°, $(\alpha)_D^{30°} + 17·5°$ λ_{max}^{EtOH} 228 and 284 nm, is comparatively a simple molecule with four OMe's (aromatic), two aliphatic OMe's and no methylenedioxy group. Like other lignans of *P. niruri*, it is also resistant to oxidation by permanganate. One of the four aromatic OMe's appears as a singlet at

Table 3

Nirtetralin (7)			Bromonirtetralin (10)		
δ values	No. of Protons	Assignment	δ Values	No. of Protons	Assignment
6·60, 6·50 m	3 Ar—H	2′,5′,6′	6·83 s	1 Ar—H	3′
6·33 s	1 Ar—H	5	6·15 s	1 Ar—H	6′
5·98 s	2 O—CH_2—O	6,7	5·85 s	2 O—CH_2—O	6,7
4·19 m	1 Ar—CH—Ar	1	4·53, 4·38 m	1 Ar—CH—Ar	1
3·73 s	6 Ar—OCH_3	3′,4′	3·78 s	3 Ar—OCH_3	4′ or 5′
3·45 s	3 Ar—OCH_3	8	3·63 s	3 Ar—OCH_3	4′ or 5′
			3·40 s	3 Ar—OCH_3	8
3·30 s	4 CH_2—OCH_3	2,3	3·40 s	6 CH_2—OCH_3	2,3
3·21 s	6 CH_2—OCH_3	2,3	3·30 s	4 CH_2—OCH_3	2,3
2·65, 2·50 d	2 Ar—CH_2—	4	3·10, 2·88 m	2Ar—CH_2	4
1·85 m	2 —CH—	2,3	1·80 m	2 —CH—	2,3

benzyl protons at C-4 experienced a deshielding effect from 2·65–2·50(d) to 3·10–2·88(m) evidently due to the Br atom at the peri position 5. Similar deshielding effect was also noticed in hypophyllanthin.

Finally, the mass spectrum of nirtetralin (**7**) exhibits the fragmentation pattern characteristic of the phenyl tetralins.[4] Unlike in hypophyllanthin (**6**), M^+ 430(22), the mass peak, is the base peak for nirtetralin (**7**). The reverse Diels-Alder fragment *m/e* 313(5) appears as a minor peak as also the cyclic ion *m/e* 283(9). Another important fragment *m/e* 203(3) is derived from rings A and B only. The benzylic cations from rings A and C make their appearance at *m/e* 165(22) and 151(30).

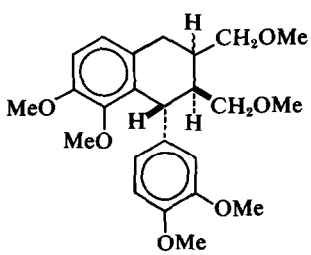
δ 3·58, shielded obviously by the 1-phenyl ring as in nirtetralin (**7**) and it is for this reason, this OMe is placed at C-8. The second OMe can be obviously placed at C-7. The aromatic proton signals at δ 6·23(d) J = 8 Hz, suggests two ortho coupled protons, which therefore confirm the assignment for ring A. The multiplet between δ 6·77–6·61 further analyses for a veratryl ring system in ring C. The remaining signals appear at their usual positions as noticed in nirtetralin (**7**) or hypophyllanthin (**6**) (Table 4). As in nirtetralin (**7**), the stereochemistry at 1,2 in phyltetralin may be regarded as *trans* with ring C in α-equatorial conformation which alone permits the shielding effect experienced by 8-OMe. On the above basis, phyl-

Table 4

Phyltetralin (11)

δ values	No. of protons	Assignment
6·77, 6·61 m	4 Ar—H	2′,5′,6′,6
6·23 d J = 8Hz	1 Ar—H	5
4·05 m	1 Ar—CH—Ar	1
3·88 s, 3·84 s, 3·80 s	3, 3, 3 Ar—OCH_3	7,3′,4′
3·58 s	3 Ar—OCH_3	8
3·35 s	4 CH_2—OCH_3	2,3
3·26 s	6 CH_2—OCH_3	2,3
2·88, 2·80 d	2 Ar—CH_2—	4
1·55, 2·00 m	2 —CH—	2,3

tetralin is now tentatively assigned structure **11**. However, the stereochemistry at C-3 is not definitely established.



11

The mass spectrum of (**11**) is surprisingly full with the characteristic peaks of considerable abundance as in galcatin or galbulin.[10] The molecular ion forms the base peak (M^+ 416 (100)). Fragmentation due to reverse Diels-Alder reaction appears at a low abundance *m/e* 300 (22) which gives place to the cyclic ion *m/e* 269 (35) by the loss of 31 mu. Other fragments *m/e* 384 (20), 370 (16), 325 (16), 339 (65), 340 (41) and 360 (12) are also noticed. This fragmentation pattern is similar to that of lyoniresinol dimethyl ether.[10] These fragments represent successive loss of methanol and methyls from 9,9′-CH_2OMe groups, and are, therefore, taken to support structure **11** proposed for phyltetralin.

The five lignans of *Phyllanthus niruri* Linn. phyllanthin (**1**), niranthin (**2**), hypophyllanthin (**6**), nirtetralin (**7**) and phyltetralin (**11**) form a closely related group of new lignans with 9,9′ carbons each carrying a OMe unlike any of the well known types. Obviously, the lactone ring system is reduced to the 9,9′ alcohols followed by O-methylation.

The distribution of these lignans in the leaves of *P. niruri* has been found to vary considerably with geographic location of the plant. It may be due to ecological factors. The plants growing on the hills of Simhachalam and around Waltair are very rich in all these lignans. Specimens collected from Trivandrum (South India) contained phyllanthin and hypophyllanthin, the rest only in traces. A specimen from Tallahasse (USA) showed traces of hypophyllanthin only.

EXPERIMENTAL

Extraction and separation of lignans from Phyllanthus niruri. The dry leaves (1·5 kg) were extracted with hexane following the procedure described earlier.[1] After removing the waxes from the yellow concentrate, phyllanthin and hypophyllanthin were separated by fractional crystallisation from hexane. The mother liquor, a bitter yellow oil, (25 g) showed eleven prominent spots on TLC plate, coated with silica gel 'C', when developed with hexane: EtOAc mixture (H:E Ac 2:1) (spray reagent: 10% methanolic H_2SO_4) with R_f values 0·97, 0·93, 0·84, 0·79, 0·68(G), 0·61(F), 0·53(E), 0·49(D), 0·42(C), 0·38(B) and 0·35(A). The letters A to G indicate the compounds identified in the sequel.

The crude extract (25 g) was adsorbed on neutral alumina (70 g) and placed in column (30″ × 2·5″) of neutral alumina (700 g) and eluted with hexane. Fractions of 1000 ml were collected and divided into 6 groups by monitoring with TLC as given in Table 5.

Group I. The reddish brown concentrate was a mixture under TLC and not examined further.

Group II. The residue (1·5 g) crystallised from MeOH as colourless shining plates of compound G (m.p. 135°, R_f: 0·68, yield: 300 mg). The mother liquor was transferred to an alumina column (1·5″ × 10″) and eluted with hexane. The eluate (1·5 l.) was worked up as usual and more of compound G was secured (300 mg). A further quantity of

Table 5

Solvent	Fraction No.	Group	State	Compounds
Hexane	1–25	I	Reddish brown liquid	Impurities + G
Hexane	26–40	II	Brown liquid	Impurities + G + F + E
Hexane	41–60	III	Yellow liquid	Impurities + G + F + E + D
Hexane	61–80	IV	Yellow liquid	Impurities + F + E + D + C + A
Hexane + Benzene	81–101	V	Yellow semisolid	E + D + C + B + A
Benzene	101–120	VI	Colourless solid	D + C + B + A

hexane eluate (2 l.) was collected and distilled. The residue was separated on preparative TLC over silica gel 'C'. The plates were developed with H:E Ac mixture (5:2) and dry plates were sprayed with water, when two opaque bands were exposed. The bands were marked, dried, and extracted with acetone. Band I yielded an uncrystallisable yellow oil (R_f: 0·61, yield: 50 mg). Band II afforded a light yellow oil, which crystallised from hexane as colourless needles of compound E (m.p. 55°, R_f: 0·53, yield: 100 mg).

Group III. The residue was separated on preparative TLC as described in group II. There were three bands. Band I afforded compound G (500 mg). Band II was a mixture of compounds F and E (800 mg) and were separated as described in group II. Band III was transferred to a long column (6′ × 1″) of alumina and eluted with hexane. A careful monitoring of the 200 fractions (250 ml each) afforded compound E (m.p. 55°, R_f: 0·53, yield: 500 mg) and compound D (m.p. 67–69°, R_f: 0·49, yield: 640 mg).

Group IV. Fractional crystallisation from hexane of the residual oil furnished compound C (m.p. 128°) and compound A (m.p. 98°). The mother liquor on further preparative TLC and column chromatography was separated into compounds D, E and F.

Groups V and VI. The yellow semi solid upon fractional crystallisation followed by preparative and column chromatography was separated into compounds A, B, C, D and E as before.

Compound A. It crystallises from hexane as colourless long needles, m.p. 98°, $(\alpha)_D^{30°}+24°$ and identified as phyllanthin (mmp and IR), total yield: 3·0 g.

Compound B, phyltetralin. It is a new lignan which crystallised from hexane as colourless shining needles, m.p. 110–11°, $(\alpha)_D^{30°}+17·5°$, (*c.* 0·16 $CHCl_3$). (Found: C, 68·99; H, 7·74; MeO, 42·2; $C_{24}H_{32}O_6$ requires: C, 69·21; H, 7·75 and 6 MeO, 44·5%), UV λ_{max}^{EtOH} 228 and 284 nm; IR $\nu_{max}^{CHCl_3}$ 1710(sh), 1605(s), and 860(w) cm^{-1}; Mass peaks: 416(100), 384(20), 370(15), 340(41), 339(65), 326(12), 325(26), 300(2), 269(35) and 151(14).

It exhibited a pale pink colour in cold conc H_2SO_4 and bright red on warming. With gallic acid and conc H_2SO_4 it gave a colour fading after 4 hr, total yield: 30 mg.

Compound C, hypophyllanthin. This crystallised from hexane as colourless needles, m.p. 128°, $(\alpha)_D^{30°}+3·9°$ and identified as hypophyllanthin (mmp and IR), yield: 2·5 g.

Compound D, niranthin. This crystallised from hexane as colourless needles, m.p. 67–69°, $(\alpha)_D^{30°}+28°$, (*c.* 1·29, $CHCl_3$). It had bitter taste like phyllanthin. (Found: C, 66·65; H, 7·46; MeO, 33·5; $C_{24}H_{32}O_7$ requires: C, 66·65; H, 7·46 and 5 MeO 36·04%); UV λ_{max}^{EtOH} 230 nm (log ϵ 4·30) and 280 nm (log ϵ 1·59); IR $\nu_{max}^{CHCl_3}$ 1725(sh), 1640(s) and 950(b) cm^{-1}; Mass peaks: 432(22), 400(8), 386(7), 248(8), 227(17), 205(6), 204(16), 203(34), 192 (15), 191(12), 190(10), 189(20), 187(12), 179(18), 178(18), 177(34), 167(40), 166(90), 165(95), 152(80), 151(100), 137(20) and 121(30).

It gave a pale pink colour in cold conc H_2SO_4 turning to green on warming and finally to blue. With gallic acid and conc H_2SO_4 it gave an emerald green colour, yield: 1·2 g.

Compound E, nirtetralin. Compound E is a new lignan and crystallised from hexane as colourless needles, m.p. 55°, $(\alpha)_{max}^{30°}+14·39°$ (*c.* 1·3 in $CHCl_3$). (Found: C, 66·86; H, 7·43; MeO, 34·0; $C_{24}H_{30}O_7$ requires: C, 66·96; H, 7·02 and 5 MeO, 36·04%); UV λ_{max}^{EtOH} 226 and 284 nm (log ϵ 4·40, 2·15); IR ν 2850(s), 1730(b), 1635(s), 1605(b) and 860(w) cm^{-1}. Mass peaks: 430(100), 400(3), 398(6), 383(4), 368(8), 367(4), 354(9), 353(34), 335(6), 326(12), 313(5), 293(6), 283(9), 278(15), 265(12), 247(6), 222(21), 208(37), 203(5), 183(9), 181(11), 165(22), 152(6), 151(30) and 150(15).

With conc H_2SO_4 it gave a light pink to bright red colour on warming. With gallic acid and conc H_2SO_4 it gave an emerald green colour on warming, yield: 2·0 g.

Compound F. This did not crystallise from acetone, benzene or methanol, yield: 80 mg. Further work is in progress.

Compound G, β-sitosterol. This crystallised from MeOH as colourless shining plates, m.p. 136–37° and identified as β-sitosterol (mmp and IR with authentic sample).

Bromination of niranthin. A soln of Br in chloroform (4%) was added to niranthin (100 mg) in chloroform (5 ml) dropwise with shaking until the yellow colour persisted. There was copious evolution of HBr. After 1 hr, chloroform was removed. The brown residue was washed with $NaHSO_3$ and the gummy substance crystallised from MeOH to yield colourless needles, m.p. 121°, $(\alpha)_D^{30°}+25°$, (*c.* 1·35 $CHCl_3$), yield: 80 mg. (Found: C, 41·69; H, 4·14; $C_{24}H_{29}O_7Br_3$ requires: C, 41·74; H, 4·93%).

Oxidation of niranthin. Niranthin (110 mg) in acetone was refluxed with $KMNO_4$ for 3 hr. Excess permanganate was decolourised by $NaHSO_3$ and then extracted with ether. After the usual working, a small quantity of colourless needles was isolated and identified as veratric acid (m.p. and mmp 178–80°, yield: 5 mg). The neutral fraction from the residue crystallised from hexane as short needles, m.p. 67–69°, identical with niranthin, yield: 80 mg.

Bromination of nirtetralin. A soln of Br in dry chloroform (4 ml) was added to a soln of nirtetralin (150 mg) in chloroform (5 ml). The mixture was allowed to stand at room temp overnight, then washed with $NaHSO_3$ aq, and water and dried over $MgSO_4$. On evaporation, it gave a pale yellow gum, which showed two spots on TLC plate (H:E Ac 3:5). The gum (120 mg) was dissolved in ether and applied on preparative TLC plate coated with silica gel 'C' and developed with hexane:EtOAc (5:3). The plate was dried and sprayed with water, which brought out two opaque bands. The bands were marked, dried and extracted with acetone. Band I gave a coloured solid, which on crystallisation from hexane yielded a colourless shining prisms, m.p. 205–206°. (Found: C, 48·82; H, 4·55; $C_{24}H_{28}O_7Br_2$ requires: C, 49·00; H, 4·76%) yield: 8 mg. Band II on extraction with acetone gave a solid, which on crystallisation from hexane afforded colourless shining needles, m.p. 139–40°, $(\alpha)_D^{30°}-137·2°$, (*c.* 1·26 $CHCl_3$). (Found: C, 48·92; H, 4·62; $C_{24}H_{28}O_7Br_2$ requires: C, 49·00; H, 4·76%) yield: 75 mg.

Acknowledgements—Our grateful thanks are due to Dr. C. W. Koch, Berkeley University, California, U.S.A., for the mass spectra of niranthin, nirtetralin and hypophyllanthin; Dr. G. S. Sidhu, Director, Regional Research Laboratory, Hyderabad, for NMR spectra.

REFERENCES

[1]L. R. Row, C. Srinivasulu, M. Smith and G. S. R. Subba Rao, *Tetrahedron Letters* No. 24, 1557 (1964)
[2]L. R. Row, C. Srinivasulu, M. Smith and G. S. R. Subba Rao, *Tetrahedron* **22**, 2899 (1966)

[3]L. R. Row, P. Satyanarayana and C. Srinivasulu, *Ibid.* **26**, 3051 (1970)
[4]A. M. Duffield, *J. Heterocyclic Chem.* **4**, 16 (1967)
[5]R. S. Burden, Cromilie, Leslie and D. A. Whitting, *J. Chem. Soc.* (C), **5**, 693–701 (1969)
[6]N. S. Bhacca and R. Stevenson, *J. Org. Chem.* **28**, 1638 (1963)
[7]F. D. Hostettler and M. K. Seikel, *Tetrahedron* **25**, 2325 (1969)
[8]E. Bianchi, K. Sheth and J. R. Cole, *Tetrahedron Letters* No. 32, 2759 (1969)
[9]A. F. A. Wallis, *Ibid.* No. 51, 5287 (1968)
[10]A. Pelter, *J. Chem. Soc.* (C), 1376 (1967)