Tetrahedron Vol. 47, No. 42, pp. 8931-8940, 1991
Printed in Great Britain

0040-4020/91 \$3.00+.00
Pergamon Press plc

ISOLATION, STRUCTURE AND SYNTHESIS OF NEW DIARYLBUTANE LIGNANS FROM PHYLLANTHUS NIRURI[1] : SYNTHESIS OF 5' -DESMETHOXY NIRANTHIN AND AN ANTITUMOUR EXTRACTIVE

PANCHAGNULA SATYANARAYANA* AND SOMEPALLI VENKATESWARLU

Department of Organic Chemistry, School of Chemistry, Andhra University,
Visakhapatnam - 530 003, India.

(*Received in UK* 14 *May* 1991)

Abstract : The structures of three new lignans (1-3) and a phenolic lignan (4) isolated from Phyllanthus niruri have been determined. The structures (1-3) were confirmed by their total synthesis and that of (4) was by its conversion to (3). The synthesis of (±) 5'-desmethoxy niranthin (5) and an antitumour extractive (6) is described.

Previous extraction of the bitter leaves of **Phyllanthus niruri L** (Euphorbiaceae) a well known medicinal plant[2,3] has yielded nine new lignans[4-7] of which four (phyllanthin, niranthin, hydroxyniranthin, seco-isolariciresinoltrimethyl ether) are diarylbutanes, four (hypophyllanthin, nirtetralin, phyltetralin and lintetralin) belong to aryltetralin class and the ninth compound is an unusual seco-lignan. The present paper describes the isolation of four more new compounds of which one is diol (**1**), a diacetate (**2**), a methyl ether (**3**) and a phenolic (**4**). They are new members of the diarylbutane class.

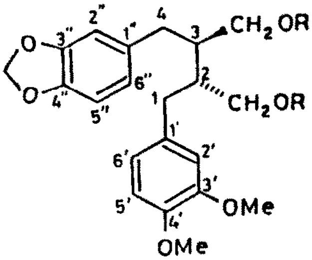
The 2,3-desmethoxy seco-isolintetralin (**1**) $C_{21}H_{26}O_6$ (M^+374), $[\alpha]_D^{28}$ -1.6° exhibited UV maxima at 242, 284.6 nm and showed strong absorption at 3450 cm^{-1} in its IR Spectrum. The ^1H and ^{13}C nmr spectra gave clear evidence for the presence of both 3,4-dimethoxyphenyl and 3,4-methylenedioxyphenyl groups. The four protons multiplet at δ 3.5 in the ^1H nmr spectrum (table 1) was consistant to the presence of two primary CH_2OH groups. This conclusion was further supported by the ^{13}C nmr spectrum (table 2) which contained two low field signals δ 63.1, 62.9 in the noise decoupled spectrum. Further analysis of the ^1H & ^{13}C nmr spectra and comparision with phyllanthin (7), dihydrocubebin (8) led to structure (1) which was also supported by the mass spectrum (m/z 151 and 135). The structure was confirmed by its total synthesis. The veratrylidene piperonylidene succinic acid, m.p. 172-3°C was reduced with Raney Ni-Al alloy to give (±) diacid, m.p.178°C which was esterified and reduced with LAH to give the corresponding (±) diol, oil R_f 0.42 (pet.ether-EtOAc, 4:6) whose spectral data (^1H nmr, mass, IR, UV) was found to be identical with the natural compound (1).

The second new compound, 2,3-desmethoxy seco-isolintetralin diacetate (2), $C_{25}H_{30}O_8$ (M^+ 458), $[\alpha]_D^{28}$ -1.3° exhibited UV maxima at 241, 285 nm and gave a prominent peak at 1730 cm^{-1} in its IR spectrum. The δ 2.08 singlet in its ^1H nmr spectrum (table 1) indicated the presence of two $COCH_3$ groups and the down field multiplet at δ 4.1 for four protons is consistent with the acetylated two primary CH_2OH groups. These observations were supported by the low field signal in its ^{13}C nmr spectrum (table 2). Further analysis of ^1H & ^{13}C nmr spectra including its mass spectra (m/z 151 and 135) gave clear evidences that this new lignan (2) is the acetylated product of (1). The (±) diol (1) was acetylated with Py/Ac_2O to yield the diacetate, oil R_f 0.73 (pet.ether-EtOAc, 8:2). Whose spectral properties (^1H nmr, mass, IR, UV) were identical with the natural product (2) confirming structure (2).

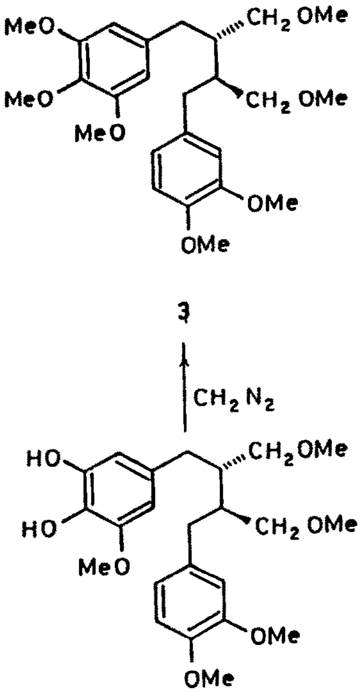
The third new compound, linnanthin (3), $C_{25}H_{36}O_7$ (M^+ 448) $[\alpha]_D^{28}$ + 13.8° exhibited UV maximum at 210, 280 nm. Its ^1H & ^{13}C nmr spectra gave clear evidences for the presence of both 3,4-dimethoxyphenyl, 3,4,5-trimethoxyphenyl groups and two aliphatic methoxyls. Further analysis of ^1H & ^{13}C nmr spectra (table 1&2) and comparision with phyllanthin (7), niranthin (9) led to structure (3) which was also supported by the mass spectrum (m/z 181 and 151). Starting from veratrylidene, 3,4,5-trimethoxybenzylidene succinic acid, m.p. 182°C, carried through the same process as described above to secure the (±) diol, oil, R_f 0.51 (pet.ether-EtOAc, 2:8). Methylation of the diol (CH_3I + Ag_2O in DMF) yielded the dimethyl ether, oil, R_f 0.45 (pet.ether-EtOAc, 6:4) whose spectral data (^1H nmr, mass, IR, UV) were found to be identical with the natural compound (3).

The fourth new compound demethylenedioxyniranthin (4) $C_{23}H_{32}O_7$ (M^+ 420), $[\alpha]_D^{28}$ + 18° exhibited UV maxima at 228, 281 nm (log ε 4.1, 3.28) and showed strong absorption at 3450 cm^{-1} in its IR spectrum. It gave green colouration with alcoholic $FeCl_3$ solution suggesting the presence of phenolic hydroxyls. The ^1H nmr and mass spectra gave clear evidence for the presence of both 3,4-dimethoxyphenyl, 3,4-dihydroxy-5-methoxyphenyl groups and two aliphatic methoxyls. Comparision of ^1H nmr (table 1) with the known lignans led to structure (4) which was also supported by the mass spectrum (m/z 151 and 153). The compound (4) was treated with diazomethane to yield a product, oil, R_f 0.44 (pet.ether-EtOAc, 3:2), $[\alpha]_D^{28}$ + 2 5° (M^+448). Whose spectral properties (^1H nmr, mass, IR, UV) were found to be identical in all respects with linnanthin (3). Compounds (3) and (4) showed positive rotation therefore assumed to have the same absolute configuration as in phyllanthin (7) and niranthin (9). For (1) and (2) it is opposite to that of (3) and (4) because of its negative rotation.

Incidentally the (±) diol (1) was methylated (CH_3I + Ag_2O in DMF) to give 5'-desmethoxy niranthin (5) oil, R_f 0.78 (benzene -EtOAc, 8:2) (M^+402). The same (±) diol was oxidised using silica gel-silver carbonate to secure the antitumour extractive (6) oil, R_f 0.80 (benzene-EtOAc, 8:2) (M^+370) which was previously reported from Bursera schlechtendalii[7].

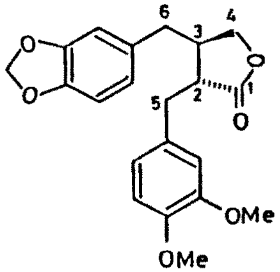


1. R = H
2. R = COMe
5. R = Me

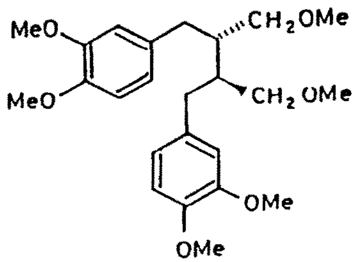


3

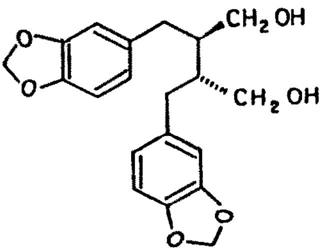
4



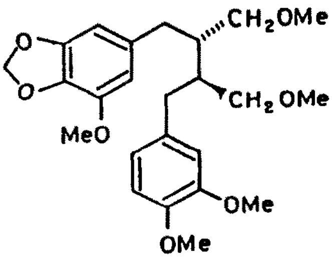
6



7



8



9

Table 1 ^{1}H nmr Spectra[a]

Assignment	1	2	3	4	7	8	9
1 4	2.6m	2.7m	2.7m	2.58m	2.64d	2.64m	2.61dd
2 3	1.9m	2.10m	2.05m	2.05m	2.04m	1.82m	2.02m
CH_2's	3.5m	4.1m	3.32m	3.35m	3.32m	3.73dd(2,11) 3.43dd(4,11)	3.29m
ROMe	-	-	3.3s	3.21s	3.26s	-	3.25s
ArOMe	3.85 s	3.85s	3.79s 3.81s 3.84s	3.80s 3.85s	3.76s 3.80s	-	3.77s 3.79s 3.81s
OCH_2O	5.85s	5.95s	-	-	-	5.82s	5.88s
$OCOCH_3$	-	2.08s	-	-	-	-	-
PhenolicOH	-	-	-	5.9s 6.45s	-	-	-
Ar-H	6.5-6.8m	6.6-6.9m	6.3m 6.6-6.8m	6.5-6.7m	6.5-6.8m	6.4-6.7m	6.25m 6.5-6.8m

Table 2 ^{13}C nmr Spectra[a]

Assignment	1	2	3	7	8	9
1 4	33.5 33.1	34.5	35.1 35.3	35.2	35.74	34.94 35.49
2 3	44.9 44.5	39.5	41.8 41.6	40.77	44.08	40.78 40.93
CH_2's	63.1 62.9	64.5	71.1 71.7	72.7	59.89	72.60 72.71
1',1''	133.0 132.9	133.0 132.0	130.0 132.9	133.70	134.29	133.95 135.70
2',2''	109.0 108.0	109.0 108.0	111.2 106.8	112.36	109.19	112.31 103.21
3',3''	148.0 147.5	147.5 146.0	148.1 137.1	147.21	145.47	147.25 143.37
4',4''	150.0 149.0	149.0 148.0	153.0 148.6	148.83	147.34	148.85 133.26
5',5''	112.5 111.3	112.5 111.0	111.6 153.1	111.17	107.88	111.15 148.69
6',6''	121.8 121.0	122.0 121.0	120.5 106.8	121.25	121.69	121.13 108.29
ROMe	-	-	57.8	58.72	-	58.71
ArOMe	55.7 55.1	55.0	60.2 55.8 56.0	55.75 55.91	-	55.75 55.90 55.50
OCH_2O	100.8	101.0	-	-	100.59	101.14
CO	-	171.5	-	-	-	-
CH_3CO-	-	20.5	-	-	-	-

[a] All Spectra recorded in $CDCl_3$ Solution

Experimental

General Experimental Procedures : IR spectra were recorded on Shimadzu IR 408 and UV spectra on shimadzu UV 260. Mass spectra were recorded on an AE1 MJ 9 spectrometer, simple EI and ^1H & ^{13}C nmr spectra on Jeol JNM Ex 90 Instrument. Optical rotations were determined with Perkin Elmer 241 MC spectropolarimeter. Melting points are uncorrected.

Isolation of Lignans : The leaves of **P. niruri** were collected from the Simhachalam hills and the identification certificate was deposited in the Botany department of this campus. The dried leaves (10 kg) were powdered and successively extracted with hexane following the procedure already reported[8] and continuing the chromatography, the following compounds were isolated.

Eluent	Fractions	Compounds Isolated
Hexane	1 - 85	oil (110 mg)
Hexane-C_6H_6(75:25)	86 - 125	oil
Hexane-C_6H_6(75:25)	126 - 165	lintetralin (150 mg) + nirtetralin + niranthin + hypophyllanthin (9.5 g)
Hexane-C_6H_6(50:50)	166 - 190	nirtetralin + niranthin + hypophyllanthin (10g) + phyltetralin + dibenzylbutyrolactone (150 mg) + 2,3-desmethoxy seco-isolintetralin diacetate (25 mg)
Hexane-C_6H_6 (25:75)	191 - 215	hypophyllanthin + phyltetralin + phyllanthin (17 g)
C_6H_6	216 - 230	hypophyllanthin + phyltetralin + phyllanthin (15 g)
C_6H_6	231 - 245	phyllanthin (3 g)
C_6H_6-EtOAc (90:10)	246 - 255	phyllanthin
C_6H_6-EtOAc (90:10)	256 - 275	phyllanthin + seco-4-hydroxylintetralin (200 mg) + seco-isolariciresinol trimethyl ether (150 mg) + hydroxyniranthin (40 mg) + linnanthin (20 mg)
C_6H_6-EtOAc (90:20)	276 - 291	phyllanthin + demethylenedioxy niranthin (20 mg) + 2,3-desmethoxy seco-isolintetralin (20 mg)

2,3-desmethoxy seco-isolintetralin (1)

Oil, R_f 0.40 (pet.ether-EtOAc, 4:6), $[\alpha]_D^{28}$ -1.6 (c, 1.3, $CHCl_3$) and gave a positive Labat test for the OCH_2O group. λ max ($CHCl_3$) : 242 and 284.6 nm (log ε 4.06 and 3.96), ν max ($CHCl_3$) : 3600, 3450, 1600, 1520, 1450, 1320, 1030, 920 cm^{-1}; m/z 375 (8%), 374 (28%, M^+), 356 (11%), 212 (9%), 177 (10%), 152 (20%), 151 (100%), 136 (12%), 135 (90%), 84 (25%). Anal.calcd. for $C_{21}H_{26}O_6$ C, 67.36, H, 6.99 found C, 67.12, H, 6.90%; for ^1H & ^{13}C nmr see tables 1 & 2.

2,3-desmethoxy seco-isolintetralin diacetate (2)

Oil, R_f 0.72 (pet.ether-EtOAc, 8:2), $[\alpha]_D^{28}$ -1.3 (c, 1.6, $CHCl_3$) and gave a positive Labat test for OCH_2O group. λmax ($CHCl_3$): 241 and 285 nm (log ε 4.39 and 4.16); ν max ($CHCl_3$) : 3000, 2950, 1730, 1600, 1520, 1490, 1360, 1030, 920 cm^{-1}; m/z 458 (22%, M^+), 203 (20%), 177 (9%), 152 (23%), 151 (100%), 136 (7%), 135 (52%). Anal.calcd. for $C_{25}H_{30}O_8$ C, 65.48, H, 6.59 found C, 65.12, H, 6.4%. For ^1H & ^{13}C nmr see tables 1 & 2.

Linnanthin (3)

Oil, R_f 0.44 (pet.ether-EtOAc, 3:2), $[\alpha]_D^{28}$ + 13.8° (c, 0.3, $CHCl_3$); λ max (MeOH): 210, 280 nm (log ε 4.69 and 3.61); ν max ($CHCl_3$): 3000, 2938, 2838, 1591, 1514, 1510, 1460, 1129, 1028 cm^{-1}; m/z 448 (24%, M^+), 416 (6%), 208 (7%), 205 (20%), 182 (18%), 181 (100%), 152 (10%), 151 (95%), 45 (35%). Anal.calcd. for $C_{25}H_{36}O_7$ C, 66.94, H, 8.09 found C, 66.98, H, 8.06%. For ^1H & ^{13}C nmr see tables 1 and 2.

Demethylenedioxy niranthin (4)

Oil, R_f 0.47 (pet.ether-EtOAc, 1:1), $[\alpha]_D^{28}$ + 18° (c, 3.4, $CHCl_3$) gave a green colouration with $FeCl_3$ solution. λ max (MeOH): 228, 281 nm (log ε 4.1 and 3.28); ν max ($CHCl_3$): 3450, 2975, 2925, 2850, 1650, 1600, 1580, 1400, 1200, 1135, 1020 cm^{-1}; m/z 420 (10%, M^+), 339 (10%), 248 (17%), 235 (10%), 203 (23%), 189 (34%), 177 (12%), 153 (25%), 151 (100%), 45 (32%). Anal.calcd. for $C_{23}H_{32}O_7$ C, 65.70 H, 7.62 found C, 65.65 H, 7.53%. For ^1H nmr see table 1.

Preparation of (±) 1-(3,4-dimethoxyphenyl)-4(3,4-methylenedioxyphenyl)-butane 2,3-dicarboxylic acid

The veratrylidene piperonylidene succinic acid m.p. 172-3°C (lit, 170-3°) (anhydride, m.p. 180°C) was prepared by a two stage stobbe condensation between veratraldehyde, piperonal and diethyl succinate. The above diacid (10 g) was dissolved in 10% NaOH solution (300 ml), then reduced with Raney Ni-Al alloy (15g) following the schwenk[9] procedure to give the acid, m.p. 178-80°C (6.5 gm, 65%); R_f 0.50 (benzene-methanol, 7:3); λ max (MeOH) : 230, 282 nm (log ε 4.2 and 3.61) ; ν max(KBr) : 3450, 3100, 2960, 2840, 1700, 1635, 1590, 1450, 1140, 1030, 925, 820 cm^{-1}. Anal.calcd. for $C_{21}H_{22}O_8$ C, 62.65, H, 5.48 found C, 62.80, H, 5.12%.

(±) 1-(3,4-dimethoxyphenyl)-4-(3,4-methylenedioxyphenyl) butane 2,3-dicarboxylic acid dimethyl ester

The (±) acid (1 g) was dissolved in methanol (15 ml) and diazomethane in ether was added. After 24 hours, gave the ester as white granules (900 mg, 84%), m.p.113-4°C, R_f 0.76 (benzene-EtOAc, 8:2); λmax (MeOH) : 230, 283 nm;ν max (KBr): 2985, 1728, 1590, 1515, 1475, 1450, 1240, 1160, 1040, 920, 820 cm^{-1}; ^1H nmr ($CDCl_3$, δ) : 2.65-2.76 (m, 2H, H-2, H-3), 2.78-2.8 (m, 4H, H-1, H-4), 3.45 (s, 6H, 2 x $-COOCH_3$), 3.70 (s, 6H, 2 x $ArOCH_3$), 5.85 (s, 2H, OCH_2O), 6.35-6.60 (m, 6H, Ar-H); m/z 430 (M^+). Anal.calcd. for $C_{23}H_{26}O_8$ C, 64.18, H, 6.05 found C, 63.88, H, 5.97%.

(±) 1-(3,4-dimethoxyphenyl)-4-(3,4-methylenedioxyphenyl)-2,3-dihydroxymethyl butane(1)

The (±) above ester (500 mg) in dry THF (20 ml) was added dropwise to a suspension of LAH (1.5 gm) in THF (20 ml) during 30 min. The mixture was refluxed on a water bath for 3 hours (change in R_f 0.76→ 0.21 (benzene-EtOAc, 8:2). After usual workup the (±) diol (1) (300 mg, 70%) was obtained as colourless oil, R_f 0.42 (pet.ether-EtOAc, 4:6); λmax (MeOH): 230, 282 nm (log ε 4.3 and 3.92); ν max ($CHCl_3$): 3660, 3600, 3450, 2980, 2960, 2930, 1600, 1480, 1450, 1320, 1220, 1160, 1030, 920, 830, 815 cm^{-1}; ^1H nmr ($CDCl_3$, δ): 1.8-2.12 (m, 2H, H-2, H-3), 2.5-2.7 (m, 4H, H-1, H-4), 3.4-3.6 (m, 4H, CH_2's), 3.8 (s, 6H, $ArOCH_3$), 5.85 (s, 2H, OCH_2O), 6.5-6.7 (m, 6H, Ar-H); M^+ (374). Anal.calcd. for $C_{21}H_{26}O_6$ C, 67.36, H, 6.95 found C, 67.12, H, 6.94%.

(±) 1-(3,4-dimethoxyphenyl)-4-(3,4-methylenedioxyphenyl)-2,3-diacetoxy methyl butane(2)

The (±) diol (1) (50 mg) was taken in dry Ac_2O (5 ml) and two drops of pyridine was added. The diacetate was obtained as colourless oil (2) (46 mg, 76%), R_f 0.73 (pet.ether-EtOAc, 8:2); λmax (MeOH): 231, 284, nm (log ε 4.29 and 3.91): νmax ($CHCl_3$): 3000, 2960, 2940, 2860, 1730, 1600, 1490, 1470, 1370, 1160, 1145, 1030, 920 cm^{-1}; ^1H nmr ($CDCl_3$, δ): 1.94 (s, 6H, 2 x $OCOCH_3$), 1.94-2.2 (m, 2H, H-2, H-3), 2.5-2.6 (m, 4H, H-1, H-4), 3.80 (s, 6H, $ArOCH_3$), 4.10 (m, 4H, CH_2's), 6.4-6.6 (m, 6H, Ar-H), M^+ (458). Anal.calcd. for $C_{25}H_{30}O_8$ C, 65.50, H, 6.50 found C, 65.38, H, 6.42%.

(±) 1-(3,4-dimethoxyphenyl)-4-(3,4-methylenedioxyphenyl)-2,3-dimethoxymethyl butane: 5'-desmethoxy niranthin (5)

The (±) diol (1) (100 mg) was dissolved in dry DMF (5 ml) methyliodide (1.5 ml) and freshly prepared dry silver oxide (1.4 g) were added druing 1 hour in small portions to the solution. The reaction mixture was stirred for 24 hours at room temperature [change in R_f 0.28→ 0.78(benzene-EtOAc, 8:2)]. After workup and chromatography of the residue dimethyl ether obtained as an oil (5) (60 mg, 56%), R_f 0.78 (benzene-EtOAc, 8:2); λ max (MeOH) : 227, 280 nm (log ε 4.29 and 3.65); ν max ($CHCl_3$): 3000, 2975, 2900, 1600, 1590, 1450, 1220, 1100, 1040, 930, 850 cm^{-1}; ^1H nmr ($CDCl_3$,δ): 1.95-2.05 (m, 2H, H-2, H-3), 2.50-2.65 (m, 4H, H-1, H-4), 3.3 (s, 6H, $ROCH_3$), 3.32 (s, 4H, CH_2's), 3.71 (s, 6H, $ArOCH_3$), 5.81 (s, 2H, OCH_2O), 6.5-6.7 (m, 6H, Ar-H); m/z 403 (10%), 402 (41%, M^+), 387 (81%), 356 (21%), 203 (75%), 189 (35%), 187 (20%), 178 (22%), 177 (57.5%), 173 (48.7%), 165 (20.5%), 164 (38.5%), 152 (45%), 151 (100%), 135 (45%), 121 (42%). Anal.calcd. for $C_{23}H_{30}O_6$ C, 68.65, H, 7.46 found C, 68.54 H, 7.30%.

(±) 2-(3,4-dimethoxybenzyl)-4-(3,4-methylenedioxybenzyl) butyrolactone (6) : Antitumour extractive

The (±) diol (1) (200 mg) in dry benzene (26 ml) was refluxed with silica gel-silver carbonate (3 g) in an oil bath. After 3 hours the reaction was completed (change in R_f 0.28→ 0.80, benzene-EtOAc, 8:2). The reaction mixture was worked up yielding an oil (150 mg, 76%), R_f 0.80 (benzene-EtOAc, 8:2); (This showed single R_f value in different solvent systems but it is a mixture of antitumour extractive and Kusnokinin (m/z 192, 208). The oil was dissolved in hexane and kept in refrigerator. After several days,the oil separated was collected (6) (50 mg, 25%); λ max (MeOH) : 232, 283 nm (log ε 4.15, 3.98); ν max ($CHCl_3$): 2960, 2930, 1760, 1600, 1590, 1475, 1340, 1230, 1100, 1040, 920, 850 cm^{-1}; ^1H nmr ($CDCl_3$, δ): 2.5 (m, 4H, H-5, H-6), 2.9 (m, 2H, H-2, H-3), 3.9-4.1 (m, 2H, H-4), 3.80 (s, 3H, $ArOCH_3$), 3.81 (s, 3H, $ArOCH_3$), 5.85 (s, 2H, OCH_2O), 6.4-6.7 (m, 6H, Ar-H); m/z 371 (14%), 370 (46%, M^+), 208 (6%), 235 (3.5%), 162 (3.5%), 151 (100%), 135 (21.7%). Anal.calcd. for $C_{21}H_{22}O_6$ C, 68.10, H, 5.94 found C, 68.15, H, 6.07%.

The decanted solvent evaporated and the residual oil (100 mg) was a mixture of lactones.

(±) 1-(3,4-dimethoxyphenyl)-4-(3,4,5-trimethoxyphenyl) butane 2,3-dicarboxylic acid dimethyl ester

The veratrylidene, (3,4,5 - trimethoxy)benzylidene succinic acid, m.p. 182-3°C, [anhydride, m.p. 148°C, ν max ($CHCl_3$): 1815 and 1760 cm^{-1}; ^1H nmr ($CDCl_3$, δ): 3.6 (s, 9H), 3.8 (s, 3H), 3.9 (s, 3H), 6.2 (s, Ar-H), 6.4-6.6 (m, Ar-H), 7.8 (s, 2H, olefinic); M^+ 426] was prepared by a two step stobbe condensation between veratraldehyde, (3,4,5-trimethoxy)benzaldehyde and diethyl succinate. The above diacid (10 g) was reduced with Raney Ni-Al alloy as described earlier. The (±) diacid was esterified directly with diazomethane. The ester crystalized from chloroform-hexane as white needles (5.5 g, 51%), m.p. 125°C, R_f 0.59 (pet.ether EtOAc, 5:5); λ max (MeOH): 225 281 nm (log ε 4.15, 3.81); ν max ($CHCl_3$): 2980, 1725, 1595, 1550, 1450, 1345, 1150, 1040, 820 cm^{-1}; ^{1}H nmr ($CDCl_3$, δ): 2.65-3.0 (m, 2H, H-2, H-3), 2.8-2.9 (m, 4H, H-1, H-4), 3.5 (s, 6H, $COOCH_3$), 3.75 (s, 9H, $ArOCH_3$), 3.80 (s, 6H, $ArOCH_3$), 6.3 (s, 2H, Ar-H), 6.6-6.8 (m, 3H, Ar-H); M^+ (476). Anal.calcd. for $C_{25}H_{32}O_9$ C, 63.02, H, 6.72 found C, 63.05, H, 6.80%.

(±) 1-(3,4-dimethoxyphenyl)-4-(3,4,5-trimethoxyphenyl) 2,3-dihydroxymethyl butane

The above ester (500 mg) in dry THF (20 ml) was added dropwise to a suspension of LAH (1.5 g) in THF (20 ml) during 30 min. The reaction mixture was refluxed for 3 hrs (change in R_f 0.50→ 0.04, benzene-EtOAc, 8:2). The (±) diol (340 mg, 77%) was obtained as colourless oil, R_f 0.51 (pet.ether-EtOAc, 2:8); ν max ($CHCl_3$): 3650, 3600, 3400, 2950, 1600, 1480, 1390, 1140, 990, 855 cm^{-1}; ^{1}H nmr ($CDCl_3$, δ) : 1.8-2.1 (m, 2H, H-2, H-3), 2.4-2.6 (m, 4H, H-1, H-4), 3.3-3.5 (m, 4H, CH_2's), 3.8 (s, 15H, $ArOCH_3$), 6.25 (s, 2H, Ar-H), 6.5-6.6 (m, 3H, Ar-H); M^+ (420). Anal.calcd. for $C_{23}H_{32}O_7$ C, 65.71, H, 7.62 found C, 65.92, H, 7.51%.

(±) 1-(3,4-dimethoxyphenyl)-4-(3,4,5-trimethoxyphenyl) 2,3-dimethoxymethyl butane (3)

The above (±) diol (100 mg) was dissolved in dry DMF (5 ml) methyl iodide (1.5 ml) and freshly prepared silver oxide (1.4 g) was added during one hour in small portions. · The reaction mixture was stirred at room temp. for 24 hrs. (change in R_f 0.087→ 0.45, pet.ether-EtOAc, 6:4). After workup obtained dimethyl ether as light yellow oil (3) (69 mg, 65%), R_f 0.45 (pet.ether-EtOAc, 6:4); λmax (MeOH): 212, 281 nm (log ε 4.09, 3.69); ν max ($CHCl_3$) : 3000, 2938, 2828, 1591, 1515, 1510, 1460, 1129, 1028 cm^{-1}; ^{1}H nmr ($CDCl_3$, δ): 2.05 (m, 2H, H-2, H-3), 2.7 (m, 4H, H-1, H-4), 3.3 (s, 6H, $ROCH_3$), 3.32 (m, 4H, CH_2's), 3.8 (s, 15H, $ArOCH_3$), 6.3 (m, 2H, Ar-H), 6.6-6.8 (m, 3H, Ar-H); M^+ (448). Anal.calcd. for $C_{25}H_{36}O_7$ C, 66.96, H, 8.03 found C, 66.82, H, 8.14%.

Conversion of demethylenedioxy niranthin (4) to linnanthin (3)

The compound (4) (10 mg) was dissolved in MeOH (2 ml) and diazomethane in ether was added to a deep yellow colour. After 24 hrs. at room temp. It was wroked up and obtained a compound as an oil (9.5 mg, 89%), R_f 0.44 (pet.ether-EtOAc, 6:4), $[\alpha]_D^{28}$ + 25° (c, 1.6, $CHCl_3$); λ max (MeOH): 215, 281 nm (log ε 4.21, 3.82); ν max ($CHCl_3$): 3000, 2940, 1600, 1505, 1460, 1129 cm^{-1}; ^{1}H nmr ($CDCl_3$, δ): 2.05 (m, 2H, H-2, H-3), 2.7 (m, 4H, H-1, H-4), 3.3 (s, 6H, $ROCH_3$), 3.32 (m, 4H, CH_2's), 3.8 (s, 15H, $ArOCH_3$), 6.35 (m, 2H, Ar-H), 6.65-6.8 (m, 3H, Ar-H); M^+ (448). Anal.calcd. for $C_{25}H_{36}O_7$ C, 66.96, H, 8.03 found C, 67.03, H, 8.15%.

Acknowledgement

We are grateful to CSIR, New Delhi for financial assistance.

References

1. The name of this is now redesignated as **Phylalnthus amarus.**
2. Perry, L.M. "Medicinal plants of East and South East Asia", MIT Press, Cambridge, MAC, 1986, pp.83, 150, 281 and 292.
3. Kirtikar, K.R. and Basu, B.D, Indian Medicinal Plants, 1933, 3,2225.
4. Row, L.R.; Srinivasulu, C.; Smith, M.; Subba Rao, G.S.R. *Tetrahedron,* 1966, 22, 2899.
5. Row, L.R.; Anjaneyulu A.S.R.; Rao, K.J.; Subrahmanyam, C. *Tetrahedron,* 1973, 29, 1291.
6. Satyanarayana, P.; Row, L.R.; Ward R.S.; Gopal Rao, B.V. *Tetrahedron Lett.,* 1979, 3043.
7. Mcdoniel, P.B.; Cole, J.R. *J. Pharm. Sci.,* 1972, 61, 1992.
8. Satyanarayana, P.; Subrahmanyam, P.; Viswanatham, K.N.; Ward, R.S. *J.Nat.Prod.,* 1988, 51, 44-49.
9. Schwenk, E.; Papa, D.; Whitman, B.; Ginsberg, H.F. *J.Org.Chem.,* 1944, 9, 175.