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LIGNANS OF *PIPER TRICHOSTACHYON*

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Key Word Index—*Piper trichostachyon*; Piperaceae; dehydrotrichostin; (−) hinokinin, (−)-cubebin, trichostin, (−)-dihydrocubebin, dihydrotrichostin, ^{13}C NMR, CD

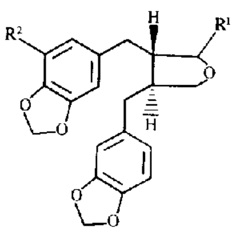
Abstract—From the petrol extract of *Piper trichostachyon*, six lignans have been isolated Three of them were identified as the known compounds (−)-hinokinin, (−)-cubebin and (−)-dihydrocubebin The other three were new compounds and were assigned the structures 2*S*,3*S*,3-(6-methoxy 1,3-benzodioxol 5-yl) methyl 4-(1,3-benzodioxol 5-yl)methyl tetrahydrofuran-2-one, 2*S*,3*S*,3-(6-methoxy 1,3-benzodioxol 5-yl)methyl 4-(1,3-benzodioxol 5-yl)methyl tetrahydrofuran-2-ol and 2*S*,3*S*,2-(6-methoxy 1,3-benzodioxol 5-yl)methyl 3-(1,3-benzodioxol 5-yl)methyl butan 1,4-diol

INTRODUCTION

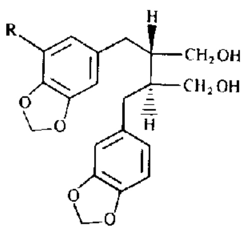
Previous work on the stems [1–4] and the leaves [5, 6] of *Piper trichostachyon* DC have shown the presence of aromatic and acyclic and cyclic long chain amides, e.g. trichostachine and cyclostachine, besides other common aliphatic compounds [7]. Our chemical investigations on the fruits of this plant have shown it to be devoid of such amides. Instead, we have isolated and identified six lignans (**1–6**), three of which [dehydrotrichostin (**2**), trichostin (**4**) and dihydrotrichostin (**6**)] are new to the literature.

RESULTS AND DISCUSSION

Lignan **2** had the molecular formula $C_{21}H_{20}O_7$ (M^+ m/z 384) and its IR spectrum showed a characteristic band for a γ-lactone carbonyl at 1775 cm^{-1}. Its ^{1}H NMR spectrum displayed signals characteristic of a diaryl butyrolactone. Signals for methylenedioxy protons were observed as a singlet at δ5.90 and for an aromatic methoxyl at δ3.90 Aromatic protons were observed as a singlet at δ6.26 (2H) for H-2 and H-6 and a multiplet at δ6.29 to 6.73(3H) for H-2′, H-5′ and H-6′ A multiplet centred at δ4.0 was assigned to the methyleneoxy protons of the lactone Two methine protons (β,β′) of the butyrolactone system were observed alongwith the protons of one of the benzylic groups centred at δ2.50 as a multiplet A signal for the other benzylic protons was observed as a narrow envelope centred at δ2.80. The ^{1}H NMR data of hinokinin and compound **2** were very similar except for the appearance in **2** of an extra signal attributed to one methoxyl at δ3.90. This was supported by mass spectrum, which differed from that of hinokinin by 30 The *trans* stereochemistry of the two benzyl groups was established by ^{1}H NMR, ^{13}C NMR, CD and optical rotation when compared with hinokinin [8–11] Both showed negative Cotton effect in CD (287, 240 and 285, 243 nm respectively) and both were optically laevorotatory In the ^{13}C NMR spectrum of **2** the β,β′ carbons were located at δ46.5 and 41.4 which was in accordance with the values of these carbons in hinokinin [12]. The mass spectrum proved helpful in establishing the position of the aryl moiety carrying a methoxyl group towards the carbonyl in the lactone ring The formation of the ion at m/z 222 and its further fragmentation to the ion at m/z 192 confirmed unambiguously the position of the two ligands in trichostin (Fig. 2) The diognostic fragments for the other part of the molecule appeared at m/z 162 and 132.



	R¹	R²
1	=O	H
2	=O	OMe
3	OH	H
4	OH	OMe



	R
5	H
6	OMe

The second new substance (**4**) had a molecular formula $C_{21}H_{22}O_7$ (M^+ m/z 386) and its IR spectrum contained a broad band at 3400–3420 cm^{-1} for a hydroxyl function In its ^{1}H NMR spectrum, signals for methoxyl and methylenedioxy protons were observed at δ3.86 and 5.80 respectively and for five aromatic protons at δ6.0–6.68 as a multiplet A broad singlet at δ5.10 showed the presence of a hemi-acetalic proton which on acetylation was shifted downfield and merged with the signal of the methylenedioxy protons, while the other signals remained practically unchanged. This was also supported by the ^{13}C NMR data where the hemi-acetalic carbon was observed at δ103.3 as a doublet The compound showed

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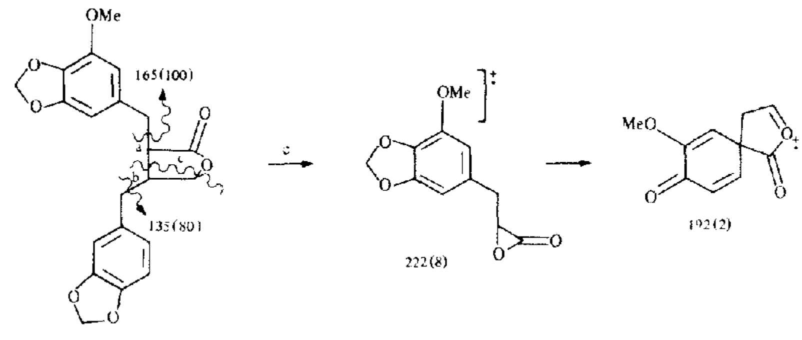

Fig 2

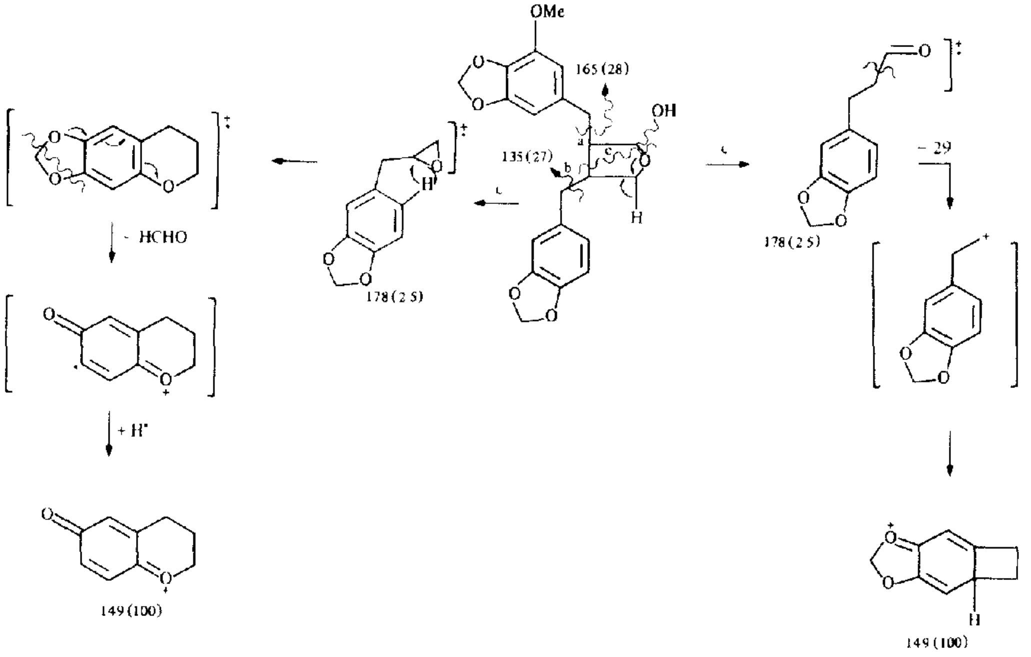

Fig 3

negative rotation Since this compound differs from cubebin by a methoxyl group, the former was oxidized by PCC in methylene chloride and the oxidized compound as expected, was identical with compound **2** (co-TLC, IR, ^{1}H NMR and CD) and showed laevorotation and a negative Cotton effect (CD) From the above observations, the stereochemistry of the two benzyl substituents should therefore be *trans* in **4** as in hinokinin The mass spectrum showed a base peak at *m/z* 149 which can be explained only when the methoxy bearing ligand is flanked towards the hemi-acetalic side (Fig 3) The double cleavage in the lactone ring may follow two pathways with the formation of either phenyl propionaldehyde or oxirane species which after cyclization and loss of formaldehyde, stabilize either to a cyclobutane system or to a pyran system by addition of a proton

The third new substance (**6**) had the molecular formula $C_{21}H_{24}O_7$ (M^+ *m/z* 388) Its IR spectrum showed a prominent band at 3420–3400 cm^{-1} indicating the presence of a hydroxyl function In its ^{1}H NMR spectrum, signals for methylenedioxy, methoxyl and methyleneoxy protons appeared at δ5 90, 3 86 and 3 4 3 76 respectively The two methine protons were observed as a multiplet at δ1.6–2 03 and the benzylic protons at δ2 46–2 76 The structure and stereochemistry of **6** at C(2) C(3) as *trans* was confirmed by the demonstration that $LiAlH_4$ reduction product of lactone **2** was identical with **6** In the ^{13}C NMR spectrum, the methine carbons appear at δ44 0 which compare well with those of (−)-dihydro cubebin where these signals are observed at δ43 8 and which has *trans* stereochemistry The ^{13}C NMR data of compounds **2–6** are given in Table 1

EXPERIMENTAL

Mps uncorr IR KBr, CD spectra, MeOH, ^{1}H NMR 60 and 90 MHz, ^{13}C NMR 22 5 MHz MS 70 eV, $[\alpha]_D^{20}$ MeOH

Dried fruits of *Piper trichostachyon* DC (500 g) collected from Palghat District of Kerala at an altitude of 3500 feet (deposited at Bhartiyar Univ Coimbatore and International Institute of Ayurvedia Coimbatore Herb No IIAH-1325) were extracted with petrol (60–80°) and the solvent removed to give a resineous mass (35 g) Repeated CC of the extract (15 g) on silica gel yielded six compounds in the order of **1**, **4**, **2**, **5**, **3** and **6** after

Table 1. ^{13}C NMR data of compound **2**, **4**, **5** and **6**

C	**2**	**4**	**5**	**6**
α	38 5	39 0	35.5	35.5
α'	35 4	38 5	35 5	36.0
β	46 5	52 9	43.8	44.0
β'	41 4	45 7	43 8	44 0
γ	178 3	103.3	59 6	60 4
γ'	71 0	71 9	59.6	60.4
1	131 6	134 3	134 6	134 3
1′	132 2	135 4	134.6	135 2
2	108 8	107 7	108 0	107 5
6	103 0	102 5	122 0	102 8
2′	108 3	108 6	108.0	108 5
5′	109 0	108.4	109.0	109 0
6′	121 5	121 3	122 0	121 4
3	144 0	143 4	145.8	143 5
4	132 2	134.3	147 6	134 3
5	149 2	148 9	109 0	149 2
3′	146 5	145.8	145 8	146 0
4′	148 0	147 5	147 6	147.0
OMe	56 8	56 5	—	56.5
OCH_2O	100 6	100 5	100.6	100 2
	101 0	100 6		100.6

eluting with C_6H_6 and C_6H_6–EtOAc in increasing proportions and monitoring on TLC (C_6H_6–EtOAc, 17 3).

Compound 1 Gummy solid analysed for $C_{20}H_{18}O_6$ (M^+ at *m/z* 354) [observed 68.37, H 5 43 requires C 67.69, H 5 12%], $[\alpha]_D^{20}$ −23 3° Identified as hinokinin by comparison with an authentic sample [10] (co-TLC, IR and ^{1}H NMR)

Compound **2**. Semi-solid, M^+ at *m/z* 384 analysed for $C_{21}H_{20}O_7$ (observed C 66 30, H 5 84 requires C 65.61, H 5 24%), $[\alpha]_D^{20}$ 10 2° (0 5 *c*) Negative Cotton effect in CD 287 and 240 nm, UV λ_{max}^{MeOH} nm 318, 260 and 240; IR ν_{max}cm^{-1} 1775, 1620, 1500, 1480, 1365, 1310, 1244, 1190, 1133, 1090, 1035, 920 and 800, ^{1}H NMR (CCl_4) δ2 50 (4H, *m*, Ar–CH_2– and β,β' methine protons), 2 80 (2H, *m*, Ar–CH_2–), 3 90 (3H, *s*, Ar–OMe), 4 0 (2H, *m*, –OCH_2–), 5 9 (4H, *s*, 2 × –OCH_2O–), 6 26 (2H, *s*, Ar-2 and 6) and 6 29–6 73 (3H, *m*, Ar-2′5′ and 6′); MS 384 $[M]^+$, 248, 235, 222, 208, 203, 192, 166, 165 (100%) 162, 135, 132, 109, 84, 71, 55 and 43

Compound 3 Crystalline solid, mp. 132°$[M]^+$, *m/z* 356, analysed for $C_{21}H_{20}O_6$ (observed C 68 30, H 6 0 requires C 67 40, H 5.65%) $[\alpha]_D^{20}$ −28.0° (1). The compound was identified as (−)-cubebin by comparison with an authentic sample (lit [13]) mp. 131°) (co-TLC, IR and ^{1}H NMR)

Compound **4** Gummy mass M^+ at *m/z* 386, analysed for $C_{21}H_{22}O_7$ (observed C 66.21, H 6.09 requires C 65 27, H 5.73%) $[\alpha]_D^{20}$ −62.25 (0 8C) UV λ_{max}^{MeOH} nm 238, 260 and 315, IR ν_{max}cm^{-1} 3460−3420, 1620, 1610, 1500, 1490, 1440, 1315, 1245, 1190, 1132, 1090, 1040, 920 and 800; ^{1}H NMR (CCl_4) δ2 00–2 80 (6H, *m*, 2x, Ar–CH_2– and β,β' methine protons), 3 53 −4 0 (2H, *m*, –OCH_2–), 3 86 (3H, *s*, Ar-OMe), 5 10 (1H, *br s*, $\text{H}-\overset{|}{\underset{|}{\text{C}}}-\text{OH}$), 5 80 (4H, *s*, 2 × –$OCH_2O$–), 6.00–6 68 (5H, *m*, Ar–2,6,2′,5′ and 6′) Acetylation with C_5H_5N–Ac_2O gave monoacetate **4a**, semi-solid, M^+ at *m/z* 428 analysed for $C_{23}H_{24}O_8$ (observed C 65.36, H 5 99 requires C 64 49, H 5.64%). IR showed prominent bands at 1728 and 1243 cm^{-1} [due to –O–C(O)–Me]. ^{1}H NMR (CCl_4) δ2 06 [3H, *s*, O–C(O)Me], 2 28–2 88 (6H, *m*, 2 × Ar–CH_2– and β,β' methine protons), 3 83 (3H, *s*, Ar–OMe) 3 73–4.13 (2H, *m*, –OCH_2–), 5.96 (5H, *s*, 2 × –OCH_2O and $\overset{|}{\text{C}}$H–OAc), 6.30–6 80 (5H, *m*, Ar 2,6,2′,5′ and 6′), MS *m/z* 386 $[M]^+$, 368, 356, 205, 203, 178, 166, 165, 149, (100%), 135, 126, 84, 77, 55 and 43

Oxidation of **4** To a stirred soln of **4** (0 05 g) in CH_2Cl_2, PCC reagent was added in small proportions and the mixture monitored by TLC until completion of the reaction Usual work-up afforded a resinous mass which after CC over silica gel yielded a gummy mass (12 mg), analysed for $C_{21}H_{20}O_7$ (M^+ *m/z* 384) $[\alpha]_D^{20}$ −14.2° Negative Cotton effect at 286 and 240 nm From the spectral data the compound was identified as **2**.

Compound **5** Solid, mp 102°, M^+ at *m/z* 358 analysed for $C_{20}H_{22}O_6$ (observed C 68 61, H, 6.77 requires 67.21, H 6 20%) identified as (−)-dihydrocubebin by comparison with an authentic sample of dihydrocubebin (Lit [14] mp 101–102°) (co-TLC, IR and ^{1}H NMR)

Compound **6** Semi-solid, M^+ at *m/z* 388, analysed for $C_{21}H_{24}O_7$ (observed C 65.86 H, 6 73 requires 64 91, H 6 23%) $[\alpha]_D^{20}$ − 13 3 (0 6C). UV λ_{max}^{MeOH} nm 235 and 260, IR ν_{max}cm^{-1} 3400–3420, 2920, 1626, 1505, 1490, 1440, 1310, 1245, 1180, 1130, 1080, 1040, 920, 840 and 800, ^{1}H NMR (CCl_4) δ1 6–2.03 (2H, *m*, β,β' methine protons), 2 46–2 76 (4H, *m*, 2 × Ar–CH_2–), 3 4–3.76 (4H, *d*, *J* = 8 Hz, 2 × –CH_2–OH) 3.86 (3H, *s*, Ar–OMe), 5 90 (4H, *s*, 2 × –OCH_2O–), 630 (2H, *s*, Ar–2 and 6) and 6 63 (3H, *br s*, Ar–2′, 5′ and 6′) Acetylation with C_5H_5N–Ac_2O gave diacetate **6a**, a semi-solid, analysed for $C_{25}H_{28}O_9$ (observed C 64 66, H 6 12 requires C 63 55 H 5 97%) M^+ at *m/z* 472 IR showed absence of a band at 3420 cm^{-1} and appearance of two prominent bands at 1722 and 1243 cm^{-1} due to –O–C(O)–Me), ^{1}H NMR (CCl_4) δ2 06 (6H, *s*, 2 × OC(O)Me), 1 8–2 26 (2H, *m*, methine protons), 2 53–2 89 (4H, *m*, 2 × Ar–CH_2–), 3 86 (3H, *s*, Ar–OMe) 3.83–4 16 (4H, *m*, 2 × –OCH_2–), 5 93 (4H, *s*, 2 × –OCH_2O–), 6 33 (2H, *s*, Ar-2 and 6) and 6.66 (CH, *br s*, Ar-2′,5′ and 6′), MS *m/z* 388 $[M]^+$, 370, 358, 339, 234, 223, 218, 209 204, 166, 165, 149, 135, 105 77, 55, and 43 (100%)

$LiAlH_4$ *reduction of* **2** To an ethereal soln of **2** (30 mg), $LiAlH_4$ (12 mg) was added and the contents stirred for 6 hr Usual work-up of the reaction mixture and purification by CC over silica gel afforded a compound (17 mg), M^+ at *m/z* 388 (analysed for $C_{21}H_{24}O_7$), identical with **6** (superimposable IR)

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