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Neolignans from *Piper schmidtii* and Reassignment of the Structure of Schmiditin

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A new neolignan, (7*R*,8*S*,1′*S*)-Δ$^{8'}$-1′,4′-dihydro-3,4,5′-trimethoxy-4′-oxo-8.1′,7.*O*.2′-lignan [(2*R*,3*S*,3a*S*)-2-(3,4-dimethoxyphenyl)-3,3a-dihydro-5-methoxy-3-methyl-3a-(2-propenyl)-2-benzofuran-6(2*H*)-one] (**1**), together with five known neolignans and a known alkaloid were isolated from the stems of *Piper schmidtii* Hook f. The known compounds were identified as kadsurin B (**3**), piperenone (**4**), (7*R*,8*S*,1′*S*)-Δ$^{8'}$-1′,4′-dihydro-5′-methoxy-3,4-methylenedioxy-4′-oxo-8.1′,7.*O*.2′-lignan (**5**), lancifolin C (**6**), lancifolin D (**7**) and an alkaloid, 1-cinnamoylpyrrolidine (**2**). The earlier proposed structure of schmiditin (**12**) was revised to (7*S*,8*R*,3′*S*,4′*R*,6′*S*)-Δ$^{8'}$-3′,4′,5′,6′-tetrahydro-6′-hydroxy-3′,4′-dimethoxy-3,4-methylenedioxy-8.3′,7.*O*.4′-lignan [(2*S*,3*R*,3a*S*,6*S*,7a*R*)-2-(1,3-benzodioxol-5-yl)-2,3,3a,6,7,7a-hexahydro-3a,7a-dimethoxy-3-methyl-5-(2-propenyl)-2-benzofuran-6-ol = kadsurin B] (**3**) on the basis of spectral data and chemical transformations. Reassignment of the ^{1}H NMR data of lancifolin C (**6**), the absolute stereochemistry of kadsurin A (**10**) and ^{13}C NMR data of piperenone (**4**) and lancifolin C (**6**) are also reported. In addition, methyl piperate (**8**) was isolated from the fruits.

In our research programme, seeking naturally occurring insecticides from Indian *Piper* species,[1–7] *Piper schmidtii* Hook f. has been investigated. Previously,[4] we have isolated two new compounds, a lignan and a neolignan along with known compounds. We report herein the isolation of (7*R*,8*S*,1′*S*)-Δ$^{8'}$-1′,4′-dihydro-3,4,5′-trimethoxy-4′-oxo-8.1′,7.*O*.2′-lignan [(2*R*,3*S*,3a*S*)-2-(3,4-dimethoxyphenyl)-3,3a-dihydro-5-methoxy-3-methyl-3a-(2-propenyl)-2-benzofuran-6(2*H*)-one] (**1**) and 1-cinnamoylpyrrolidine (**2**)[8] from the dichloromethane extract of stems. In addition kadsurin B (**3**),[9] piperenone (**4**),[10,11] (7*R*,8*S*,1′*S*)-Δ$^{8'}$-1′,4′-dihydro-5′-methoxy-3,4-methylenedioxy-4′-oxo-8.1′,7.*O*.2′-lignan (**5**),[6,12] lancifolin C (**6**)[13] and lancifolin D (**7**)[13] were isolated from the petrol extract of stems. Methyl piperate (**8**)[14] was isolated from the methanol extract of fruits. The biogenetic nomenclature and numbering of neolignans follow the rules outlined in a review[15] and the systematic names are given in parentheses.

Compound **1** is a new neolignan structurally related to the earlier described neolignan **5**.[6,12] The spectral data of **3** are identical with the data published for schmiditin,[16,†] a neolignan reported from *P. schmidtii*. However, the proposed structure of schmiditin as **12**[16] is not in accordance with the spectroscopic data, and we propose it to be (7*S*,8*R*,3′*S*,4′*R*,6′*S*)-Δ$^{8'}$-3′,4′,5′,6′-tetrahydro-6′-hydroxy-3′,4′-dimethoxy-3,4-methylenedioxy-8.3′,7.*O*.4′-lignan [(2*S*,3*R*,3a*S*,6*S*,7a*R*)-2-(1,3-benzodioxol-5-yl)-2,3,3a,6,7,7a-hexahydro-3a,7a-dimethoxy-3-methyl-5-(2-propenyl)-2-benzofuran-6-ol] (**3**), the structure for kadsurin B.[9] Thus, the name schmiditin has to be removed from the literature. The ^{1}H NMR data of lancifolin C (**6**)[13] are reassigned on the basis of ^{1}H–^{1}H COSY NMR spectral data.

†Comparison of the physical data of an authentic sample of schmiditin, generously donated by Dr D. S. Bhakuni, with those of compound **3** (TLC, Co-TLC, m.p., mixed m.p., IR, ^{1}H and ^{13}C NMR) confirmed the identity of the two compounds.

Results and discussion

The dichloromethane extract of stems of *P. schmidtii* was fractionated by sequential flash column chromatography (CC), preparative thin layer chromatography (TLC) and reversed-phase HPLC techniques. It resulted in the isolation of a novel neolignan **1** and a known alkaloid, 1-cinnamoylpyrrolidine (**2**).[8] Compound **1** showed an $[M]^+$ peak at *m/z* 356 in the EI mass spectrum and accurate mass determination led to the molecular formula $C_{21}H_{24}O_5$. A neolignan of the burchellin type[17] was suggested by the fragmentation pattern [*m/z*: 356, 315, 178, 165, 151, 135]. The ^1H NMR data of **1** were found in close agreement with those of a known diastereomer of burchellin (**5**)[6,12] except that **1** exhibited the signals for a veratryl instead of a piperonyl unit, thus suggesting structure **1**. The relative configuration of **1** was confirmed by NOE results. A *cis*-relationship between the methyl group (H-9) and the aryl ring was suggested from the NOEs between the methyl and the aromatic protons and between H-8 and H-7; no NOE was observed between H-9 and H-7. Further, no NOE could be observed between the methyl and H-7′ suggesting a *trans*-relationship of the methyl and the allyl group. Compound **1** showed a CD curve similar to that of **5**[6] indicating its absolute stereochemistry to be identical with that of **5**. Thus, **1** was identified as (7*R*,8*S*,1′*S*)-$\Delta^{8'}$-1′,4′-dihydro-3,4,5′-trimethoxy-4′-oxo-8.1′,7.*O*.2′-lignan.

Compound **3** exhibited a molecular ion in the EI mass spectrum at *m/z* 374, which by accurate mass measurement gave a molecular formula of $C_{21}H_{26}O_6$. The fragment ions in the EI mass spectrum at *m/z* 162, 149 and 135 indicated it to be a benzofuranoid neolignan[17] having a structural unit Ar-CH-CH-Me (Ar = 3,4-methylenedioxyphenyl). This was confirmed by the ^1H and ^1H–^1H COSY NMR spectra. The presence of an allyl unit was revealed by typical signals in the ^1H NMR spectrum [δ 3.10 (2 H, t), 5.16 (2 H, m), 5.92 (1 H, m)] and was confirmed by the ^1H–^1H COSY NMR spectrum showing the expected cross peaks. A structural unit, -CH_2-CHOH-, was suggested by signals in the ^1H NMR spectrum [δ 1.90 (1 H, dd), 2.68 (1 H, m), 4.07 (1 H, m), 3.24 (1 H, br s)] and their corresponding cross peaks in the ^1H–^1H COSY NMR spectrum. The presence of a hydroxy group was further confirmed by acetylation, as its acetate **9** showed an $[M]^+$ peak at *m/z* 416 in the EI mass spectrum and a deshielding effect (Δ 1.33 ppm) for the carbinol proton in the ^1H NMR spectrum. Two singlets at δ 3.27 and 3.54 in the ^1H NMR spectrum could be assigned to two methoxy groups. The above results point to structure **3**, similar to kadsurin A (**10**)[4] with the only difference that **3** is not a ketone, but an alcohol. To confirm the proposed structure **3** and its stereochemistry, the reduction of kadsurin A (**10**, our earlier isolate[4]) was accomplished with $LiAlH_4$ to afford two epimeric alcohols **3** and **11**, one of which was found to be identical with the natural compound **3**. The CD curves of kadsurin A (**10**) and piperenone (**4**) were identical, which establishes identical absolute stereochemistry of kadsurin A (**10**) with that reported for piperenone (**4**).[10,11] Consequently, the absolute configuration at C-3′, C-4′, C-7 and C-8 positions in **3** and **11** is as in kadsurin A (**10**), and NOE results (Tables 2 and 3) are also in agreement. The configuration at the C-6′ position in **3** and **11** was established on the basis of NOE results: in the ^1H NMR spectrum of **3**, the signals at δ 1.90 and 2.68 were assigned to H_α-5′ and H_β-5′, respectively, as irradiation of the mixed signals of the 3′-OCH_3 and the 6′-OH gave an NOE on the signal at δ 1.90 and the 4′-OCH_3 gave an NOE on the signal at δ 2.68. An enhancement was also observed on the signal of H-7 on irradiation of 3′-OCH_3 and the 6′-OH group together; this was attributed to the 6′-OH group being in β-position. Thus, in **3** and **11**, the 6′-OH must have a β- and an α-configuration, respectively. The α-configuration of 6′-OH in **11** was also confirmed by analysis of NOE results (Table 3). In conclusion, **3** and **11** were assigned the structures (7*S*,8*R*,3′*S*,4′*R*,6′*S*)-$\Delta^{8'}$-3′,4′,5′,6′-tetrahydro-6′-hydroxy-3′,4′-dimethoxy-3,4-methylenedioxy-8.3′,7.*O*.4′-lignan and (7*S*,8*R*,3′*S*,4′*R*,6′*R*)-$\Delta^{8'}$-3′,4′,5′,6′-tetrahydro-6′-hydroxy-3′,4′-dimethoxy-3,4-methylenedioxy-8.3′,7.*O*.4′-lignan, respectively. The spectral and physical data of **3** were identical with those of schmiditin reported from the same source by Joshi *et al.*,[16] but their proposed structure **12** was different. In the reported structure **12**[16] the hydroxy group was believed to be tertiary and located at C-4′ because no deshielding effect for the carbinol proton could be observed in the ^1H NMR spectrum on acetylation. In con-

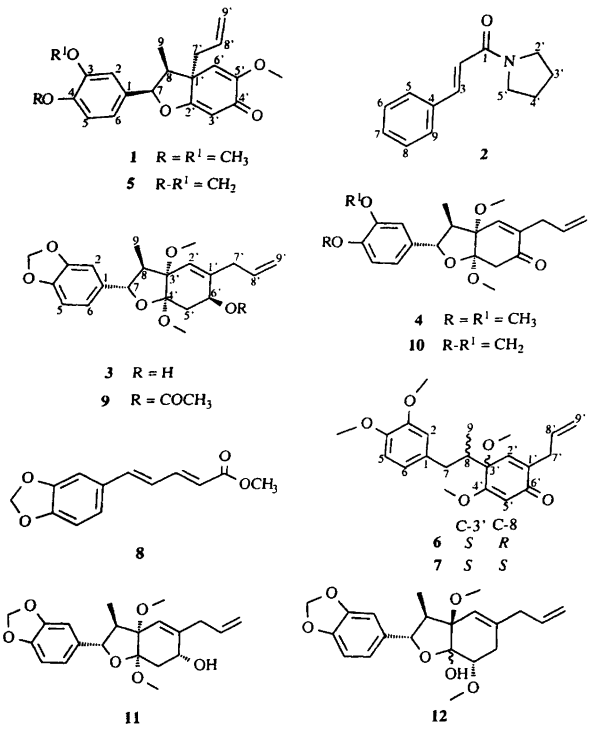

Fig. 1.

Table 1. NOE results[21] of compound **1**.

Proton irradiated	% Enhancement								
	H-9	H-8	H-7	H-8′	H-7′$_a$	H-7′$_b$	H-6′	5′-OCH_3	Ar-H
H-9	–	10.5	–	–	–	–	7.5	–	4.5
H-8 and H-7′$_b$	+	–	+	+	+	–	+	–	–
H-7	–	+	–	–	4.0	+	–	–	6.5
H-7′	–	+	9.0	7.5	–	+	–	–	–
H-6′ [a]	2.0	4.5	–	–	–	–	–	4.0	–
H-3′	–	–	–	–	–	–	–	–	–
5′-OCH_3	–	–	–	–	–	–	19.0	–	–
Ar-H	2.0	–	8.0	–	–	–	–	2.5	–

Table 2. NOE results[21] of compound **3**.

Proton irradiated	% Enhancement								
	H-9	H-8	H-7	H-7′	H_α-5′	H_β-5′	H-2′	4′-OCH_3	Ar-H
H-9	–	7.5	5.0	–	–	–	8.0	–	–
H-8 and H_β-5′	+	–	–	–	+	–	–	+	+
H-7	1.0	–	–	–	–	–	–	–	3.5
H-6′	–	–	–	1.0	3.0	2.5	–	–	–
H_α-5′	–	–	–	–	–	22.0	–	–	–
H-2′	1.5	–	–	1.0	–	–	–	–	–
3′-OCH_3 and 6′-OH	–	+	+	–	+	–	+	–	–
4′-OCH_3	–	–	–	–	–	5.0	–	–	2.0
Ar-H	–	3.0	4.5	–	–	–	–	–	–

Table 3. NOE results[21] of compound **11**.

Proton irradiated	% Enhancement										
	H-9	H-8	H-7	H-8′	H-7′	H-6′	H_α-5′	H_β-5′	H-2′	4′-OCH_3	Ar-H
H-9	–	6.5	4.0	–	–	–	–	–	7.5	–	–
H-8	1.0	–	–	–	–	–	–	–	–	–	2.5
H-7	0.5	–	–	–	–	–	–	–	1.0	–	4.0
H-7′	–	–	–	3.0	–	–	–	–	4.0	–	–
H-6′	–	–	–	–	–	–	–	4.0	–	–	–
H_α-5′ and 6′-OH	–	–	–	–	–	+	–	+	–	–	–
H_β-5′	–	–	–	–	–	5.0	18.0	–	–	1.5	–
H-2′	1.0	–	–	–	1.5	–	–	–	–	–	–
3′-OCH_3	–	0.5	–	–	–	–	1.5	–	2.0	–	–
4′-OCH_3	–	0.5	–	–	–	–	0.5	4.0	–	–	1.5
Ar-H	–	5.0	6.0	–	–	–	–	–	–	–	–

trast, on acetylation of **3**, we observed a deshielding effect of 1.33 ppm for the carbinol proton, thus proving the secondary nature of the alcoholic group. This was also evident from a clear cross peak for the hydroxy and the carbinol proton in the ^1H–^1H COSY NMR spectrum of **3**. In addition, Joshi *et al.*[16] placed one of the methoxy groups at C-5′ on biogenetic reasoning; but oxygenation at C-6′ is equally feasible as evident from the occurrence of several natural C-6′ oxygenated neolignans.[12,18] Thus, we propose that the structure of schmiditin (**12**) be revised to (7*S*,8*R*,3′*S*,4′*R*,6′*S*)-$\Delta^{8'}$-3′,4′,5′,6′-tetrahydro-6′-hydroxy-3′,4′-dimethoxy-3,4-methylenedioxy-8.3′,7.*O*.4′-lignan (**3**). This structure **3** has earlier been assigned to kadsurin B[9] based on X-ray data. The limited reported spectral and physical data[9] matched well with those for compound **3** suggesting them to be identical. Hence, the name schmiditin should be removed from the literature.

Compounds **4** and **5** were found to be piperenone[10,11] and (7*R*,8*S*,1′*S*)-$\Delta^{8'}$-1′,4′-dihydro-5′-methoxy-3,4-methylenedioxy-4′-oxo-8.1′,7.*O*.2′-lignan[6,12] having spectral data as published.

On the basis of spectral data (^1H and ^{13}C NMR, EIMS and CD), compound **6** was found to be (+)-lancifolin C[13] but there were some discrepancies in assigning its ^1H NMR data. Diaz *et al.*[13] reported the proton signals in the region δ 1.5 to 3.5 ($CDCl_3$) as 1.91 (1 H, d, *J* 13.0, H_a-7), 2.17 (1 H, dd, *J* 13.0 and 5.0, H_b-7), 2.12–2.40 (1 H, m, H-8), 3.00–3.20 (2 H, m, H-7′), 3.12 (3 H, s, OCH_3-3′), whereas for the same re-

gion we observed the corresponding signals ($CDCl_3$) as 2.05 (1 H, dd, *J* 11.7 and 11.9, H_a-7), 2.28 (1 H, m, H-8), 3.15 (2 H, m, H-7'), 3.17 (3 H, s, 3'-OCH_3) and 3.38 (1 H, d, *J* 12.7, H_b-7). The main difference was in the chemical shifts of the two protons of the methylene group (H-7) for which our assignment was confirmed by its ^1H–^1H COSY NMR spectrum showing the expected signals. Similar shift values for methylene protons in related compounds have been reported.[4,19] The remaining reported ^1H NMR spectral data were identical with our observed data.

On basis of the same spectral data as above, compound **7** was found to be (–)-lancifolin D[13,20] but the observed Cotton effects in the CD spectrum were the opposite of those of the CD data of lancifolin D reported by Diaz *et al.*[13] confirming **7** as an enantiomer of the reported compound.[13] The same enantiomer of lancifolin D (**7**) has earlier been reported[20] with the sign of optical rotation the opposite of our observation, but on comparison of maxima and minima of the CD data they seem to be identical. The other spectral data (^1H and ^{13}C NMR, EI Mass, UV and IR) of **7** were comparable to the published data.[13,20]

Compound **8** was isolated from the methanol extract of fruits and identified as methyl piperate with spectral data as reported.[14]

Experimental

Melting points were determined on a Bùchi 535 hot oil apparatus and are uncorrected. IR spectra were recorded (KBr pellet or film) on a Perkin-Elmer 1720 FT-IR spectrophotometer and UV spectra on a Shimadzu UV 160 A spectrophotometer. ^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ on a Bruker AC-250 or Varian Unity 500 spectrometer at 250 or 500 and 62.9 or 125.7 MHz, respectively. Coupling constants (*J*) are in Hz. EIMS and HRMS were recorded on a Varian Mat 311A mass spectrometer at 70 eV. Optical rotations and circular dichroism (CD) spectra were recorded on a Perkin Elmer 141 polarimeter and a custom built spectrometer, respectively. Silica gel 60 (230–400 mesh, art 9385, Merck) was used for flash CC and analytical TLC was performed on Merck silica gel 60 F_{254} plates. The spots were visualized under UV light or by spraying with 10% concentrated H_2SO_4 in ethanol followed by heating at around 120°C for a few minutes. Preparative TLC was performed on plates coated with silica gel 60 $PF_{254+366}$ or on Merck preparative plates precoated (2 mm) with Kieselgel 60 F_{254} or with aluminium oxide 60 F_{254} plates. A Delta Pak C_{18}-300 Å (5 cm × 30 cm, 15 μm) column was used for reversed-phase preparative HPLC with Waters-486 UV detector.

Plant material. Leaves and stems of the plant *Piper schmidtii* Hook f. were collected from Doddabetta, Ooty (Tamil Nadu, India), in November 1990 and fruits were collected from the same place in January 1992. Voucher specimens have been deposited in the herbarium of Botanical Survey of India (BSI), Southern Circle, TNAU Campus, Coimbatore (Tamil Nadu, India).

Extraction and isolation. The air-dried and crushed leaves (1.24 kg), stems (4.50 kg) and fruits (1.10 kg) were extracted separately and successively with petrol (b.p. 60–80°C), dichloromethane and methanol in a Soxhlet apparatus. The extracts were concentrated *in vacuo*. The dichloromethane extract (37 g) of stems was flash column chromatographed (I) on silica gel (480 g) using a gradient solvent system of petrol and ethyl acetate with stepwise increasing concentration of ethyl acetate. The fraction (450 mg) eluted with 50% petrol in ethyl acetate was found to be a complex mixture which was again subjected to flash CC (II) on silica gel (48 mg) using petrol and chloroform with a stepwise increasing amount of chloroform. Compounds **1** and **2** were purified from the fractions of flash CC II (eluted with 60 and 65% chloroform in petrol, respectively) on a silica gel coated Merck preparative TLC plate in 20% EtOAc in benzene. The petrol extract (53.9 g) of stems of *P. schmidtii* was macerated with cold petrol and the petrol-soluble portion (26 g) was fractionated into 75 fractions by silica gel (495 g) flash CC (III) with petrol and chloroform with stepwise increasing concentration of chloroform. Compounds **6** and **7** were isolated from fraction 67 (of flash CC III) eluted with 70% chloroform in petrol by silica gel preparative TLC in 5% methanol in benzene. Fractions 61 to 65 (of flash CC III), eluted with 60% chloroform in petrol were mixed and the mixture (1.1 g) was further subjected to silica gel (43 g) flash CC (IV) using a gradient solvent system of petrol and chloroform with increasing order of polarity. Compound **3** was crystallized from fraction 8 (of flash CC IV) and **4** and **5** were isolated by reversed-phase HPLC using 35% aqueous ethanol as the eluant from fractions 16 and 20 (of flash CC IV), respectively. The methanol extract (160 g) of fruits of *P. schmidtii* was macerated with chloroform and the chloroform-insoluble portion (90 g) was again macerated with ethyl acetate. The ethyl acetate soluble portion (9 g) was subjected to CC on silica gel (520 g) with a solvent system of petrol–chloroform and chloroform–methanol increasing the concentration of chloroform and methanol, respectively; compound **8** crystallized from a fraction eluted with 20% methanol in chloroform.

(7R,8S,1'S)-$\Delta^{8'}$-1',4'-Dihydro-3,4,5'-trimethoxy-4'-oxo-8.1',7.O.2'-lignan [(2R,3S,3aS)-2-(3,4-dimethoxyphenyl)-3,3a-dihydro-5-methoxy-3-methyl-3a-(2-propenyl)-2-benzofuran-6(2H)-one] (**1**). Viscous oil (4.5 mg). $[\alpha]_D^{22}$ −20.8 (*c* 0.063, MeOH). $C_{21}H_{24}O_5$ (M^+ 356.1629, Calcd. 356.1624). IR ν_{max} ($CHCl_3$): 1657, 1614, 1505, 1493, 1447, 1387, 1241, 1214, 1192, 1167, 1104, 1059, 1040, 1016 and 965 cm^{-1}. UV λ_{max} (MeOH): 258 and 206 nm. ^1H NMR (250 MHz, $CDCl_3$): δ 0.50 (3 H, d, *J* 7.3, H-9), 2.55 (1 H, dd, *J* 14.0 and 7.0, H_a-7'), 2.68–2.77

(2 H, m, H_b-7′ and H-8), 3.68 (3 H, s, 5′-OCH_3), 3.90 (6 H, s, 3-OCH_3 and 4-OCH_3), 5.19 (2 H, m, H-9′), 5.50 (1 H, s, H-3′), 5.75 (1 H, m, H-8′), 5.88 (1 H, s, H-6′), 5.95 (1 H, d, *J* 5.0, H-7), 6.72 (1 H, d, *J* 1.7, H-2), 6.78 (1 H, dd, *J* 8.3 and 1.7, H-6) and 6.87 (1 H, d, *J* 8.3, H-5). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 12.0 (C-9), 43.9 (C-7′), 44.6 (C-8), 53.9 (C-1′), 55.1, 55.2 and 55.9 (3-OCH_3, 4-OCH_3 and 5′-OCH_3), 87.3 (C-7), 102.0 (C-3′), 108.7 and 109.0 (C-2 and C-6′), 111.1 (C-5), 117.9 (C-9′), 120.1 (C-6), 129.1 (C-1), 131.8 (C-8′), 148.8 and 149.1 (C-3 and C-4), 152.9 (C-5′), 181.5 (C-2′) and 182.6 (C-4′). EIMS *m/z* (rel. int.): 356 (M^+, 100), 340 (66), 325 (18), 315 (52), 267 (31), 265 (24), 178 (82), 177 (54), 165 (31), 164 (38), 163 (90), 162 (52), 151 (55), 135 (63), 121 (20), 107 (20), 91 (18), 69 (20), 55 (16), 41 (21), 28 (19) and 18 (46). CD (3.0 mg/100 ml MeOH; 230–400 nm): $[\theta]_{230}$ +17395, $[\theta]_{240}$ +9448, $[\theta]_{252}$ 0, $[\theta]_{266}$ −15813, $[\theta]_{275}$ −15813, $[\theta]_{298}^{min}$ −110693, $[\theta]_{325}$ 0, $[\theta]_{330}$ +12651, $[\theta]_{335}^{min}$ +15813, $[\theta]_{316}$ +9488, $[\theta]_{380}$ +3953 and $[\theta]_{400}$ 0.

1-Cinnamoylpyrrolidine (**2**). Crystals (20 mg), m.p. 99–101°C (Lit.[8] m.p. 101–103°C). ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.91 and 2.01 (2 H each, m, H-3′ and H-4′), 3.64 (4 H, m, H-2′ and H-5′), 6.73 (1 H, d, *J* 15.8, H-2), 7.36 (3 H, m, H-6, H-7 and H-8), 7.53 (2 H, m, H-5 and H-9) and 7.70 (1 H, d, *J* 15.8, H-3). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 24.2 and 26.0 (C-3′ and C-4′), 45.9 and 46.5 (C-2′ and C-5′), 118.8 (C-2), 127.7 (C-6 and C-8), 128.7 (C-5 and C-9), 129.4 (C-7), 135.3 (C-4), 141.6 (C-3) and 164.6 (C-1). EI mass, UV and IR spectral data were similar to literature values.[8]

(7S,8R,3′S,4′R,6′S)-Δ$^{8'}$-3′,4′,5′,6′-Tetrahydro-6′-hydroxy-3′,4′-dimethoxy-3,4-methylenedioxy-8.3′,7.O.4′-lignan [(2S,3R,3aS,6S,7aR)-2-(1,3-benzodioxol-5-yl)-2,3,3a,6,7,7a-hexahydro-3a,7a-dimethoxy-3-methyl-5-(2-propenyl)-2-benzofuran-6-ol = kadsurin B] (**3**). Colourless crystals (200 mg), m.p. 101–102°C (Lit.[9] m.p. 101–102°C). $[\alpha]_D^{22}$ −217.1 (*c* 0.47, MeOH) (Lit.[9] $[\alpha]_D^{22}$ −18.5°; Lit.[16] $[\alpha]_D$ −21.0, MeOH). $C_{21}H_{26}O_6$ (M^+ 374.1711, Calcd. 374.1729). IR ν_{max} (KBr): 3490, 2963, 2932, 1718, 1637, 1506, 1493, 1450, 1412, 1385, 1259, 1247, 1198, 1101, 1049, 1011, 998 and 965 cm^{-1}. UV λ_{max} (MeOH): 213, 234 and 285 nm. ^{1}H NMR (250 MHz, $CDCl_3$): δ 0.93 (3 H, d, *J* 7.0, H-9), 1.90 (1 H, dd, *J* 14.6 and 4.9, H_α-5′), 2.68 (2 H, m, H_β-5′ and H-8), 3.10 (2 H, t, *J* 6.7, H-7′), 3.24 (1 H, br s, 6′-OH), 3.27 (3 H, s, 3′-OCH_3), 3.54 (3 H, s, 4′-OCH_3), 4.07 (1 H, m, H-6′), 4.16 (1 H, d, *J* 10.6, H-7), 5.16 (2 H, m, H-9′), 5.39 (1 H, s, H-2′), 5.92 (1 H, m, H-8′), 5.95 (2 H, s, OCH_2O) and 6.74–6.86 (3 H, m, H-2, H-5 and H-6). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 9.3 (C-9), 34.1 (C-5′), 39.1 (C-7′), 49.0, 49.1 and 51.8 (C-8, 3′-OCH_3 and 4′-OCH_3), 65.8 (C-6′), 81.3 (C-3′), 84.9 (C-7), 101.1 (OCH_2O), 104.5 (C-4′), 107.5 and 107.9 (C-2 and C-5), 117.3 (C-9′), 120.4 (C-2′), 121.2 (C-6), 134.1 (C-1), 135.3 (C-8′), 146.2 (C-1′) and 147.6 and 148.0 (C-3 and C-4). EIMS *m/z* (rel. int.): 374 (M^+, 6), 343 (17), 342 (64), 327 (33), 301 (19), 272 (17), 271 (83), 230 (34), 211 (100), 207 (17), 162 (68), 149 (34), 135 (85), 123 (18), 105 (17), 91 (42), 79 (17), 67 (21), 59 (26), 45 (15), 43 (22), 41 (23) and 18 (9). CD (7.2 mg/100 ml MeOH; 230–400 nm): $[\theta]_{230}^{max}$ +3096, $[\theta]_{240}$ 0, $[\theta]_{251}^{min}$ −8599, $[\theta]_{260}$ −4127, $[\theta]_{270}^{max}$ −2750, $[\theta]_{280}$ −3784, $[\theta]_{290}^{min}$ −5847, $[\theta]_{302}$ 0, $[\theta]_{328}^{max}$ +2064, $[\theta]_{352}$ +1720, $[\theta]_{369}$ +1376, $[\theta]_{400}$ 0.

(7S,8R,3′S,4′R,6′S)-Δ$^{8'}$-3′,4′,5′,6′-Tetrahydro-6′-acetoxy-3′,4′-dimethoxy-3,4-methylenedioxy-8.3′,7.O.4′-lignan [(2S,3R,3aS,6S,7aR)-2-(1,3-benzodioxol-5-yl)-2,3,3a,6,7,7a-hexahydro-6-acetoxy-3a,7a-dimethoxy-3-methyl-5-(2-propenyl)benzofuran], acetate of kadsurin B (**9**). Compound **3** (10 mg) was refluxed in acetic anhydride (1 ml) and pyridine (0.25 ml) for 4 h. The resulting reaction mixture was poured into ice-cold water and extracted with ethyl acetate. The extract was dried over Na_2SO_4. Upon removal of solvent the resulting oily residue was subjected to preparative TLC in 20% ethyl acetate in benzene to afford the corresponding acetate (9.5 mg). ^{1}H NMR (250 MHz, $CDCl_3$): δ 0.90 (3 H, d, *J* 7.0, H-9), 1.85 (1 H, dd, *J* 15.3 and 5.4, H_α-5′), 2.02 (3 H, s, $COCH_3$), 2.60 (1 H, m, H-8), 2.70 (1 H, dd, *J* 15.3 and 1.4, H_β-5′), 2.93 (2 H, m, H-7′), 3.26 (3 H, s, 3′-OCH_3), 3.50 (3 H, s, 4′-OCH_3), 4.19 (1 H, d, *J* 10.8, H-7), 5.20 (2 H, m, H-9′), 5.40 (1 H, d, *J* 4.3, H-6′), 5.58 (1 H, s, H-2′), 5.84 (1 H, m, H-8′), 5.93 (2 H, s, OCH_2O) and 6.73–6.88 (3 H, m, H-2, H-5 and H-6). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 9.0 (C-9), 21.2 ($COCH_3$), 33.7 (C-5′), 38.9 (C-7′), 48.8, 49.4 and 51.7 (C-8, 3′-OCH_3 and 4′-OCH_3), 67.2 (C-6′), 81.5 (C-3′), 83.9 (C-7), 100.8 (OCH_2O), 102.5 (C-4′), 107.3 and 107.7 (C-2 and C-5), 117.3 (C-9′), 120.9 (C-2′), 125.6 (C-6), 134.5 (C-1), 134.6 (C-8′), 140.7 (C-1′), 147.3 and 147.9 (C-3 and C-4) and 170.9 (CO). EIMS *m/z* (rel. int.): 416 (M^+, 4), 375 (16), 356 (10), 315 (18), 283 (13), 272 (20), 271 (100), 230 (10), 211 (10), 190 (13), 165 (14), 162 (17), 151 (22), 149 (15), 135 (38), 105 (5), 91 (7), 43 (26), 28 (10) and 18 (46).

Reduction of kadsurin A (**10**) *with $LiAlH_4$.* To a solution of kadsurin A (20 mg) in dry ether was added $LiAlH_4$ (2 mg). After 15 min of stirring at room temperature, the reaction was quenched by addition of ethyl acetate (2 ml) and a small amount of ice-cold water, and the mixture was extracted with ether. The organic phase was washed with water, dried ($MgSO_4$) and evaporated *in vacuo*. The residue (20 mg) was purified by preparative TLC in 25% ethyl acetate in benzene on an aluminium oxide coated plate, to yield two compounds. The less polar compound (10 mg) was found to be identical with the natural compound **3** in relation to m.p., mixed m.p., EIMS, IR, ^{1}H and ^{13}C NMR and specific rotation. The more polar compound obtained as a viscous material (5 mg) was identified as *(7S,8R,3′S,4′R,6′R)-Δ$^{8'}$-3′,4′,5′,6′-tetrahydro-6′-hydroxy-3′,4′-dimethoxy-3,4-methylenedioxy-8.3′,7.O.4′-lignan [(2S,3R,3aS,6R,7aR)-2-(1,3-benzodioxol-5-yl)-2,3,3a,6,7,7a-hexahydro-3a,7a-dimethoxy-3-*

methyl-5-(2-propenyl)-2-benzofuran-6-ol] (**11**). $[\alpha]_D^{22}$ −80.0 (*c* 0.24, MeOH). $C_{21}H_{26}O_6$ (M^+ 374.1711, Calcd. 374.1729). IR ν_{max} (KBr): 3450, 3120, 3000, 1640, 1635, 1520, 1450, 1250, 1120, 1100, 985, 920, 850 and 810 cm^{-1}. UV λ_{max} (MeOH): 210, 234 and 286 nm. ^1H NMR (500 MHz, $CHCl_3$): δ 0.87 (3 H, d, *J* 7.0, H-9), 1.63 (1 H, dd, *J* 12.6 and 10.2, H_α-5′), 2.56 (1 H, dd, *J* 10.7 and 7.0, H-8), 2.82 (1 H, dd, *J* 12.6 and 6.2, H_β-5′), 3.10 (2 H, m, H-7′), 3.34 (3 H, s, 3′-OCH_3), 3.52 (3 H, s, 4′-OCH_3), 4.01 (1 H, d, *J* 10.7, H-7), 4.34 (1 H, br s, H-6′), 5.18 (2 H, m, H-9′), 5.32 (1 H, t, *J* 1.2, H-2′), 5.92 (1 H, m, H-8′), 5.94 (2 H, s, OCH_2O) and 6.73–6.86 (3 H, m, H-2, H-5 and H-6). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 9.2 (C-9), 36.4 (C-5′), 36.7 (C-7′), 48.6 (C-8), 48.7 (3′-OCH_3), 49.7 (4′-OCH_3), 51.9 (C-6′), 81.8 (C-3′), 85.4 (C-7), 100.8 (OCH_2O), 103.0 (C-4′), 107.1 (C-2), 107.6 (C-5), 116.8 (C-9′), 120.6 (C-2′), 120.8 (C-6), 134.4 (C-1), 135.9 (C-8′), 147.1 (C-1′) and 147.2 and 147.8 (C-3 and C-4). EIMS *m/z* (rel. int.): 374 (M^+, 12), 343 (22), 342 (62), 327 (31), 301 (16), 272 (15), 271 (80), 259 (16), 230 (22), 211 (100), 207 (16), 165 (19), 162 (42), 151 (18), 149 (28), 147 (26), 135 (53), 129 (82), 112 (46), 84 (13), 83 (19), 71 (31), 70 (34), 57 (38), 43 (17), 28 (17) and 18 (20). CD (5.8 mg/100 ml MeOH; 230–400 nm): $[\theta]_{230}$ +8278, $[\theta]_{240}^{max}$ +10136, $[\theta]_{250}$ 0, $[\theta]_{254}^{min}$ −1183, $[\theta]_{260}$ 0, $[\theta]_{266}^{min}$ +845, $[\theta]_{270}$ 0, $[\theta]_{288}^{min}$ −3885, $[\theta]_{302}$ 0, $[\theta]_{328}^{max}$ +1858, $[\theta]_{352}$ +1183, $[\theta]_{370}$ +1183, $[\theta]_{382}$ +2027 and $[\theta]_{400}$ 0.

(7S,8R,3′S,4′R)-Δ$^{8'}$-3′,4′,5′,6′-Tetrahydro-3,3′,4,4′-tetramethoxy-6′-oxo-8.3′,7.O.4′-lignan (piperenone) (**4**). Viscous material (5 mg) (Lit.[10] m.p. 86–88°C). $[\alpha]_D^{22}$ −135.5° (*c* 0.14, MeOH) (Lit.[10] $[\alpha]_D^{20}$ −129.0°; *c* 1.16, MeOH). IR, UV, ^1H NMR and EI mass spectral data were in agreement with those reported previously.[10,11] ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 9.2 (C-9), 29.6 (C-7′), 33.4 (C-8), 43.3 (C-5′), 48.9 (3′-OCH_3), 52.5 (4′-OCH_3), 55.7 and 55.9 (3-OCH_3 and 4-OCH_3), 81.9 (C-3′), 85.5 (C-7), 101.9 (C-4′), 110.7 (C-2), 111.1 (C-5), 117.5 (C-9′), 120.1 (C-6), 132.4 (C-1), 134.7 (C-8′), 138.6 (C-2′), 143.3 (C-1′), 149.1 (C-4), 149.3 (C-3) and 194.0 (C-6′). CD (10.2 mg/100 ml MeOH; 226–400 nm): $[\theta]_{226}$ 0, −72145, $[\theta]_{272}$ 0, $[\theta]_{280}^{sh}$ +5010, $[\theta]_{290}$ +5018, $[\theta]_{324}^{max}$ +17034 and $[\theta]_{400}$ 0.

(7R,8S,1′S)-Δ$^{8'}$-1′,4′-Dihydro-5′-methoxy-3,4-methylenedioxy-4′-oxo-8.1′,7.O.2′-lignan (**5**). Colourless oil (25 mg). $[\alpha]_D^{22}$ −67.4 (*c* 0.49, MeOH) (Lit.[6] $[\alpha]_D^{22}$ −56.7; *c* 0.53, MeOH). ^1H and ^{13}C NMR, IR, UV and EI mass spectral data were as reported.[6,12]

Lancifolin C (**6**). Colourless oil (40 mg). $[\alpha]_D^{22}$ +75.0 (*c* 0.95, $CHCl_3$) (Lit.[5] $[\alpha]_D^{24}$ +77.7°; *c* 1.06, $CHCl_3$). ^1H NMR (250 MHz, $CDCl_3$): δ 0.59 (3 H, d, *J* 6.8, H-9), 2.05 (1 H, dd, *J* 11.7 and 11.9, H_a-7), 2.28 (1 H, m, H-8), 3.15 (2 H, m, H-7′), 3.17 (3 H, s, 3′-OCH_3), 3.38 (1 H, d, *J* 12.7, H_b-7), 3.77 (3 H, s, 4′-OCH_3), 3.85 and 3.87 (3 H each, s, 3-OCH_3 and 4-OCH_3), 5.16 (2 H, m, H-9′), 5.74 (1 H, s, H-5′), 5.89 (1 H, m, H-8′), 6.35 (1 H, s, H-2′) and 6.75 (3 H, m, H-2, H-5 and H-6). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 13.4 (C-9), 33.0 (C-7′), 36.6 (C-7), 43.3 (C-8), 52.63 (3′-OCH_3), 55.8 (4′-OCH_3), 55.83 and 55.9 (3-OCH_3) and 4-OCH_3), 80.3 (C-3′), 105.2 (C-5′), 111.0 (C-2), 112.2 (C-5), 117.0 (C-9′), 121.3 (C-6), 133.4 (C-1), 135.1 (C-8′), 138.7 (C-2′), 141.4 (C-1′), 147.3 and 148.8 (C-3 and C-4), 173.2 (C-4′) and 186.4 (C-6′). Its IR, UV and EI mass spectral data were found to be identical with the reported data.[13]

Lancifolin D (**7**). Colourless oil (30 mg). $[\alpha]_D^{22}$ −23.5 (*c* 1.1, Me_2CO) (Lit.[5] $[\alpha]_D^{22}$ −26.8; *c* 1.47, Me_2CO: Lit.[20] $[\alpha]_D^{22}$ +28.6; *c* 0.21, Me_2CO). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 13.8 (C-9), 32.9 (C-7′), 37.2 (C-7), 42.5 (C-8), 52.3 (3′-OCH_3), 55.6, 55.7 and 55.8 (4′-OCH_3, 3-OCH_3 and 4-OCH_3), 79.6 (C-3′), 105.7 (C-5′), 111.1 (C-2), 112.1 (C-5), 116.9 (C-9′), 120.9 (C-6), 132.7 (C-1), 135.1 (C-8′), 139.0 (C-2′), 141.1 (C-1′), 147.3 (C-4), 148.6 (C-3), 172.9 (C-4′) and 186.3 (C-6′). Its other spectral data (IR, UV, ^1H NMR and EIMS) were as published.[13,20]

Methyl piperate (**8**). Needles (120 mg), m.p. 142–143°C (Lit.[14] m.p. 141–142°C). ^1H and ^{13}C NMR, IR, UV and EI mass spectral data were as previously reported.[14]

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