Pergamon

PII: S0031-9422(96)00502-X

Phytochemistry, Vol. 43, No. 6, pp. 1355–1360, 1996

0031-9422/96 $15.00 + 0.00

NEOLIGNANS AND ALKALOIDS FROM *PIPER ARGYROPHYLUM*

SANJAY K. SINGH, ASHOK K. PRASAD, CARL E. OLSEN,* AMITABH JHA,† SUBHASH C. JAIN,† VIRINDER S. PARMAR† and JESPER WENGEL‡

Department of Chemistry, Odense University, DK-5230 Odense M, Denmark; *Department of Chemistry, Royal Veterinary and Agricultural University, DK-1871 Frederiksberg C, Copenhagen, Denmark; †Department of Chemistry, University of Delhi, Delhi 110 007, India

(*Received* 24 *April* 1996)

Key Word Index—*Piper argyrophylum*; Piperaceae; stem; neolignans; 4-(2-piperonyl-2-hydroxy-1-methylethyl)-2,5-dimethoxy-2-(2-propenyl)-3,5-cyclohexadien-1-one; alkaloids.

Abstract—Twenty-three compounds, a novel neolignan nine known neolignans and 13 known alkaloids, were isolated from a methanol extract of stems of *Piper argyrophylum*. The structure of the new neolignan, 4-(2-piperonyl-2-hydroxy-1-methylethyl-2,5-dimethoxy-2-(2-propenyl)-3,5-cyclohexadien-1-one, was elucidated on the basis of its spectral data, whereas the known neolignans and alkaloids were identified by comparsion of their spectral data with those reported earlier. All compounds are new from *P. argyrophylum*. Copyright © 1996 Elsevier Science Ltd

INTRODUCTION

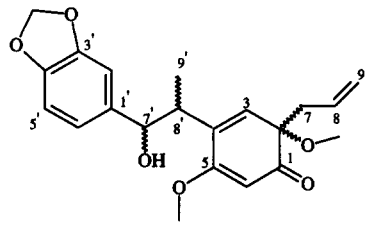
Phytochemical investigation of species from the Piperaceae has led to the isolation of many physiologically active compounds [1–6]. We wish to report herein the investigation of a methanol extract of stems of *Piper argyrophylum*, which has resulted in the isolation of 23 compounds, viz. a novel neolignan, 4-(2-piperonyl-2-hydroxy-1-methylethyl)-2,5-dimethoxy-2-(2-propenyl)-3,5-cyclohexadien-1-one (**1**), nine known neolignans, futoquinol (**2**) [7, 8], isodihydrofutoquinol B (**3**) [8, 9], 6-2-piperonyl-1-methylethyl)-3,4-dimethoxy-6-(2-propenyl)-2,4-cyclohexadien-1-one (**4**) [10], lancifolin C (**5**) [11–13], lancifolin D (**6**) [12–14],(2*R*,3*S*,3a*S*)-2-piperonyl-3,3a-dihydro-5-methoxy-3-methyl-3a-(2-propenyl)-6(2*H*)-benzofuranone (**7**) [15–18], (2*R*,3*R*,5*S*)-2-piperonyl-3,5-dihydro-5-methoxy-3-methyl-5-(2-propenyl)-6(2*H*)-benzofuranone (**8**) [19, 20], kadsurin A (**9**) [8, 15], kadsurin B (**10**) [11, 15] and 13 known alkaloids, *N*-formylnornuciferin as a mixture of *Z*- and *E*-isomers (**11**) [21], formauregine as a mixture of *Z*- and *E*-isomers (**12**) [22], 1-cinnamoylpyrrolidine (**13**) [11, 23], 10-amino-4-hydroxy-3-methoxyphenanthrene-1-carboxylic acid lactam (**14**) [24], 10-amino-2-hydroxy-3,4-dimethoxyphenanthrene-1-carboxylic acid lactam (**15**) [24–26], 10-amino-4-hydroxy-2,3-dimethoxyphenanthrene-1-carboxylic acid lactam (**16**) [26], 10-amino-2,3,4-trimethoxyphenanthrene-1-carboxylic acid lactam (**17**) [24], 10-amino-3,4-dimethoxyphenanthrene-1-carboxylic acid lactam (**18**) [24, 27], ceparadione A (**19**) [27], cepharadione B (**20**) [24, 27], (*E*)-*N*-feruloyltyramine (**21**) [28], (*Z*)-*N*-feruloyltyramine (**22**) [28] and *N*-*p*-coumaroyltyramine (**23**) [29,30].

RESULTS AND DISCUSSION

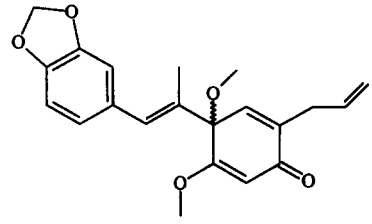
A methanol extract of stems of *P. argyrophylum* was subjected to silica gel flash column chromatography with successive gradient solvent systems of petrol–chloroform and chloroform–methanol. All compounds **1–23** were purified by repetitive preparative TLC.

Compound **1**, isolated as an oil, analysed for $C_{21}H_{24}O_6$ from its $[M]^+$ peak at *m/z* 372 in mass spectrum and from hydrogen and carbon counts in its ^1H and ^{13}C NMR spectra. Its IR spectrum suggested the presence of carbonyl (1730 cm^{-1}), hydroxyl (3401 cm^{-1}) and a benzene ring. The ^1H NMR spectrum indicated the presence of a piperonyl function (δ 5.90, 2H, *s*, OCH_2O and 6.70–6.85, 3H, *m*, Ar-H), a CH_3–CH–CH–OH unit (δ 1.11, 3H, *d*; 2.85, 1H, *br s*; 3.09–3.24, 1H, *m* and 4.82, 1H, *d*) and an allyl group (δ 2.44–2.62, 2H, *m*; 4.98–5.06, 2H, *m* and 5.30–5.43, 1H, *m*), which were all further confirmed by the expected cross-peaks in the ^1H–^1H COSY NMR spectrum. In addition, four singlets were identified in the ^1H NMR spectrum at δ 2.96 (OCH_3), 3.79 (OCH_3), 5.68 (=CH-) and 6.11 (=CH-). On this basis, we propose the structure of **1** as 4-(2-piperonyl-2-hydroxy-1-methyl-

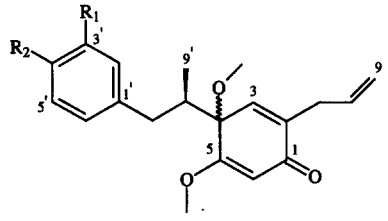
‡ Author to whom correspondence should be addressed.



1



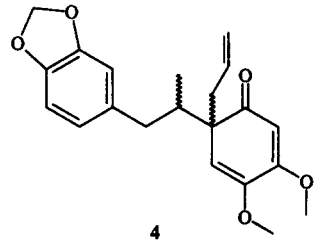
2



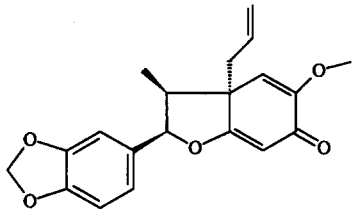
3 R_1 - R_2 = OCH_2O, 4*S*

5 R_1 = R_2 = OCH_3, 4*S*

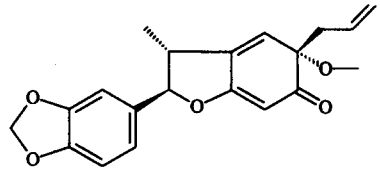
6 R_1 = R_2 = OCH_3, 4*R*



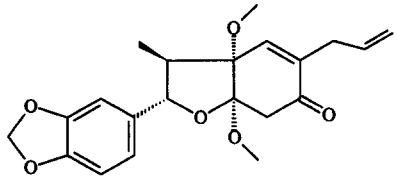
4



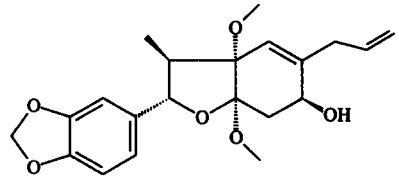
7



8



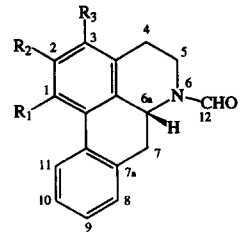
9



10

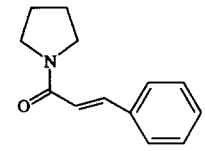
ethyl)-2,5-dimethoxy-2-(2-propenyl)-3,5-cyclohexadien-1-one. In NOE experiments, the protons at δ 1.11 and 6.11 gave mutual NOEs of 8 and 2%, whereas irradiation of the proton at δ 5.68 gave no NOE for the protons at δ 1.11 and vice versa. Furthermore, irradiation of the protons at δ 3.79 (3H, *s*) and 5.68 (1H, *s*) gave mutual NOEs of 13 and 3%, respectively. Thus, the two singlets at δ 6.11 and 5.68 were assigned to 3-H and 6-H, respectively. The structure assigned to **1** was also supported by its ^{13}C NMR spectrum and comparsion of its spectral data with those of the known neolignans, 4-(2-piperonyl-2-hydroxy-1-methylethyl)-4,5-dimethoxy-2-(2-propenyl)-3,5-cyclohexadien-1-one [13] and **8** [19, 20]. The stereochemistry of **1** could not be assigned from the available spectroscopic data.

The nine known neolignans **2**–**10** and 13 alkaloids **11**–**23** were identified by analysis of their spectral data and by comparsion with those reported [7–30].

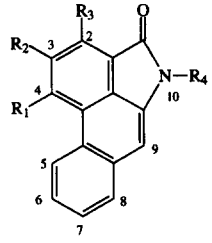


11 $R_1 = R_2 = OCH_3$, $R_3 = H$

12 $R_1 = R_2 = R_3 = OCH_3$



13



14 $R_1 = OH$, $R_2 = OCH_3$, $R_3 = R_4 = H$

15 $R_1 = R_2 = OCH_3$, $R_3 = OH$, $R_4 = H$

15a $R_1 = R_2 = OCH_3$, $R_3 = OH$, $R_4 = COCH_3$

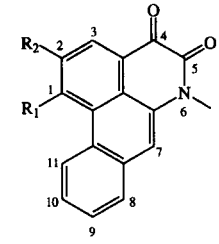
16 $R_1 = OH$, $R_2 = R_3 = OCH_3$, $R_4 = H$

16a $R_1 = OH$, $R_2 = R_3 = OCH_3$, $R_4 = COCH_3$

16b $R_1 = OCOCH_3$, $R_2 = OCH_3$, $R_4 = COCH_3$

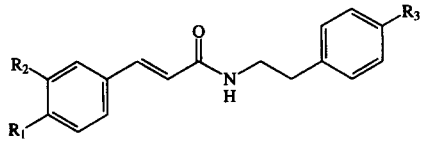
17 $R_1 = R_2 = R_3 = OCH_3$, $R_4 = H$

18 $R_1 = R_2 = OCH_3$, $R_3 = R_4 = H$



19 $R_1 - R_2 = OCH_2O$

20 $R_1 = R_2 = OCH_3$

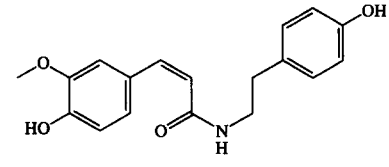


21 $R_1 = R_3 = OH$, $R_2 = OCH_3$

21a $R_1 = R_3 = OCOCH_3$, $R_2 = OCH_3$

23 $R_1 = R_3 = OH$, $R_2 = H$

23a $R_1 = R_3 = OCOCH_3$, $R_2 = H$



22

The aporphine alkaloids, **11** and **12**, were isolated as mixtures of *Z*- and *E*-isomers in ratios of 1.7:1 and 2.1:1, respectively. Comparsion of ^1H NMR spectral data for both isomeric pairs indicated that **12** differs from **11** only by the substituent at position 3. Using the reported ^1H NMR data for **11** [21], we were able to assign the ^1H NMR data for both isomers of **12**. This analysis was confirmed by the presence of the expected cross-peaks in the ^1H–^1H COSY NMR spectrum. We have performed an X-ray diffraction analysis of the isolated *N*-formylnornuciferin; it is in complete agreement with the structure assigned to **11** [31].

The structures of **15**, **16**, **21**, and **23** were further confirmed by acetylation using acetic anhydride (2.5 equivalents) and anhydrous pyridine. Thus, **15** gave **15a** (a monoacetate, not a diacetate) [24] due to the presence of the chelated hydroxyl group, whereas **16** gave **16a** (a monoacetate) and **16b** (a known diacetate) [24–26], confirming the presence of a free hydroxyl group in **16**. Compounds **21** and **23** afforded the known diacetates **21a** [28] and **23a** [29, 30], respectively.

EXPERIMENTAL

General. Mp are uncorr. IR were recorded as KBr pellet or as films. ^1H, ^{13}C and 2D NMR, and NOE spectra were recorded in $CDCl_3$, MeOH-d_4, DMSO-d_6 or ME_2CO-d_6 on a Brucker AC-250 spectrometer.

Chemical shifts are reported in δ units with TMS as int. standard for all solvents. Silica gel (230–400 mesh, Merck) was used for flash CC and analyt. TLC was performed on Merck silica gel 60 F_{254} plates. Prep. TLC was performed on silica gel 60 $F_{254+336}$. Spots were visualized under UV light or by spraying (analyt. TLC) with 10% H_2SO_4 in EtOH, followed by heating for a few min. Compound **1** turned grey when heated after H_2SO_4 spraying.

Plant material. Stems of *P. argyrophylum* Miq. were collected from Bonaccord forest (Trivandrum, India) in 1993 and were identified with the help of the Tropical Botanic Garden and Research Institute (TBGRI, Trivandrum).

Extraction and isolation. Crushed and dried stems (2.46 kg) were extracted successively with petrol and MeOH. The MeOH extract was subjected to flash CC with gradient solvent systems of first petrol–$CHCl_3$ and then $CHCl_3$–MeOH, increasing the concn. of $CHCl_3$ and MeOH stepwise. In total, 23 frs. were collected. Frs 4–7, eluted with $CHCl_3$–petrol (1:1) were combined and subjected to prep. TLC using EtOAc–C_6H_6 (3:7) resulting in 2 frs. Compounds **2–4**, **9** and **10** were isolated by prep. TLC of the first fr. with EtOAc–C_6H_6 (1:4) (double run). Prep. TLC of the second fr. with EtOAc–C_6H_6 (1:3) (double run) yielded pure **1** and **5–8**. Furthermore, frs 10–15, eluted with $CHCl_3$ and $CHCl_3$–MeOH (1:99), were combined and subjected to prep. TLC with MeOH–$CHCl_3$ (1:49) (triple run) affording pure **7** and **11–20**. Frs 18–22 eluted with $CHCl_3$–MeOH (1:50), were combined and subjected to prep. TLC with MeOH–$CHCl_3$ (1:24) (double run) giving pure **21–23**. All prep. bands after development were located by UV light and the compounds recovered from silica gel with EtoAc.

4-(2-*piperonyl*-2-*hydroxy*-1-*methylethyl*)-2,5-*dimethoxy*-2-(2-*propenyl*)-3,5-*cyclohexadien*-1-*one* (**1**). Oil (4 mg) (R_f 0.35 in EtOAc–C_6H_6 3:7) EIMS *m/z* (rel. int.): 372 ($[M]^+$, 3), (7), 341 (4), 340 (4), 331 (2), 300 (3), 282 (13), 223 (34), 194 (6), 191 (44), 182 (13), 181 (100), 177 (5), 164 (5), 151 (9), 150 (7), 149 (16), 121 (4), 93 (9), 91 (5), 77 (2), 69 (2), 65 (5), 43 (3). IR ν_{max}^{KBr}: 3401 (OH), 1730 (C=O), 1692, 1661, 1607, 1556, 1504, 1487, 1443, 1372, 1221, 1171, 1088, 1037, 989, 928, 849, 814. ^{1}H NMR ($CDCl_3$, 250 MHz): δ 1.11 (3H, *d*, J = 7.1 Hz, 9′-Me), 2.44–2.62 (2H, *m*, 7-H), 2.85 (1H, *br s*, 7′-OH), 2.96 (3H, *s*, 2-OMe), 3.09–3.24 (1H, *m*, 8′-H), 3.79 (3H, *s*, 5-OMe), 4.82 (1H, *d*, J = 4.4 Hz, 7′-H), 4.98–5.06 (2H, *m*, 9-H), 5.30–5.43 (1H, *m*, 8-H), 5.68 (1H, *s*, 6-H), 5.90 (2H, *s*, OCH_2O), 6.11 (1H, *s*, 3-H), 6.70–6.85 (3H, *m*, Ar-H). ^{13}C NMR ($CDCl_3$, 62.5 MHZ): δ 13.7 (C-9′), 41.3, 42.8, (C-7, C-8), 52.4 (2-OMe), 56.0 (5-OMe), 75.3 (C-7′), 77.2 (C-2), 100.9 (OCH_2O), 105.2, 106.9, 107.8 (C-6, C-2′, C-5′), 119.2, 119.5 (C-9, C-6′), 131.3 (C-8) 136.9 (C-4), 142.9 (C-3), 143.1 (C-1′), 146.6, 147.5 (C-3′, C-4′), 172.5 (C-5), 187.6 (C-1).

Futoquinol (**2**). Crystals (6 mg) (R_f 0.47 in EtOAc–C_6H_6 3:7). Mp 97–98° (lit. [8] mp 97–98°). Spectral data (^{1}H NMR, ^{13}C NMR, IR, UV and EIMS as reported earlier [7, 8].

Isodihydrofutoquinol B (**3**). Oil (312 mg) (R_f 0.44 in EtOAc–C_6H_6 3:7). $[\alpha]_D^{22}$ + 123.3°; MeOH, *c* 0.45 (lit. [8] $[\alpha]_D^{22}$ + 108.5°; MeOh, *c* 0.15). Spectral data (^{1}H NMR, ^{13}C NMR, IR, UV and EIMS) as reported earlier [8, 9].

6-(2-*Piperonyl*-1-*methylethyl*)-3,4-*dimethoxy*-6-(2-*propenyl*)-2,4-*cycliohexadien*-1-*one* (**4**). Oil (15 mg) (R_f 0.41 in EtOAc C_6H_6 3:7). $[\alpha]_D^{22}$ −2.04°; $CHCl_3$, *c* 0.61 (lit. [10] $[\alpha]_D^{24}$ −2.26°; $CHCl_3$, *c* 1.03). Spectral data (^{1}H NMR, ^{13}C NMR, IR, UV and EIMS) as reported earlier [10].

(+)-*Lancifolin C* (**5**). Oil (10 mg) (R_f 0.29 in EtOAc–C_6H_6 3:7. $[\alpha]_D^{22}$ +70.7°; $CHCl_3$, *c* 0.3 (lit. [11] $[\alpha]_D^{22}$ +75.0°; $CHCl_3$, *c* 0.95). Spectral data (^{1}H NMR, ^{13}C NMR, IR, UV and EIMS) as reported earlier. [11–13].

(−)-*Lancifolin D* (**6**). Oil (10 mg) (R_f 0.28 in EtOAc C_6H_6, 3:7). $[\alpha]_D^{22}$ −25.8°; Me_2CO, *c* 0.6 (lit. [13] $[\alpha]_D^{24}$ −26.8°; Me_2CO, *c* 1.47). Spectral data (^{1}H NMR, ^{13}C NMR, IR, UV and EIMS) as reported earlier [12–14].

(2R,3S,3aS)-2-*Piperonyl*-3,3a-*dihydro*-5-*methoxy*-3-*methyl*-3a-2-*propenyl*)-6(2H)-*benzofuranone* (**7**). Oil (250 mg) (R_f 0.19 in EtOAc–C_6H_6 3:7). $[\alpha]_D^{22}$ −75.6°; MeOH, *c* 0.75 (lit. [15] $[\alpha]_D^{22}$ −67.4°; MeOH, *c* 0.49). Spectral data (^{1}H NMR, ^{13}C NMR, IR, UV and EIMS) as reported earlier [15–18].

(2R,3R,5S)-2-*Piperonyl*-3,5-*dihydro*-5-*methoxy*-3-*methyl*-5-(2-*propenyl*)-6(2H)-*benzofuranone* (**8**). Oil (5 mg) (R_f 0.31 in EtOAc–C_6H_6 3:7). $[\alpha]_D^{22}$ −82.3°; MeOH, *c* 0.2 (lit. [19] $[\alpha]_D^{22}$ −84.3°; MeOH, *c* 1.5). Spectral data (^{1}H NMR, ^{13}C NMR, IR, UV and EIMS) as reported earlier [19, 20].

Kadsurin A (**9**). Oil (60 mg) (R_f 0.47 in EtOAc–C_6H_6 3:7). $[\alpha]_D^{22}$ −101.4°; $CHCl_3$, *c* 0.4) (lit. [8] $[\alpha]_D^{22}$-104.4°; $CHCl_3$, *c* 0.46). Spectral data (^{1}H NMR, ^{13}C NMR, IR, UV and EIMS) as reported earlier [8, 15].

Kadsurin B (**10**). Crystals (35 mg) (R_f 0.38 in EtOAc–C_6H_6 3:7). Mp 101–102° (lit. [15] mp 101–102°. $[\alpha]_D^{22}$ −221.7°; MeOH, *c* 0.18 (lit. [15] $[\alpha]_D^{22}$ −218.4°; MeOH, *c* 0.4). Spectral data (^{1}H NMR, ^{13}C NMR, IR, UV and EIMS) as reported earlier [11, 15].

N-*Formylnornuciferin* (*mixt. of* Z- *and* E-*isomers*, 1.7:1, **11**). Needles (7 mg) (R_f 0.63 in MeOH–$CHCl_3$, 1:24). Mp 147° (lit. [21] mp 140°). $[\alpha]_D^{22}$ −423°; $CHCl_3$, *c* 0.17 (lit. [21] $[\alpha]_D^{20}$ −413.9°; $CHCl_3$). Spectral data (^{1}H NMR, ^{13}C NMR, IR and UV) as reported earlier [21].

Formauregine (*mixt. of* Z- *and* E-*isomers*, 2.1:1, **12**). Solid (8 mg) (R_f 0.66 in MeOH–$CHCl_3$ 1:24). Mp 78°. $[\alpha]_D^{24}$ −220.6°; EtOH, *c* 0.27 (lit. [22] $[\alpha]_D$-146°; EtOH, *c* 0.2). ^{1}H NMR ($CDCl_3$, 250 MHz) of *Z*-isomer: δ 2.54–2.65 (2H, *m*, 4-H_{eq}; 7-H_{ax}), 2.74–2.85 (1H, *m*, 4-H_{ax}), 2.95–3.20 (1H, *m*, 7-H_{eq}), 3.33 (1H, *ddd*, J = 12.6, 12.6, 2.9 Hz, 5-H_{ax}), 3.74 (3H, *s*, 1-OMe), 3.84 (1H, *ddd*, J = 12.8, 4.8, 1.8 Hz, 5-H_{eq}),

3.91 (3H, *s*, 3-OCH_3), 3.96 (3H, *s*, 2-OMe), 4.93 (1H, *dd*, $J = 13.9$, 4.1 Hz, H-6a), 7.21–7.33 (3H, *m*, H-8; H-9, H-10), 8.25 (1H, *s*, CHO), 8.29–8.34 (1H, *m*, H-11). ^{1}H NMR ($CDCl_3$, 250 MHz) of *E*-isomer: δ 2.54–2.65 (1H, *m*, 7-H_{eq}), 2.74–2.85 (2H, *m*, 4-H_{ax}, 4-H_{eq}), 2.95–3.20 (2H, *m*, 5-H_{ax}, 7-H_{ax}), 3.74 (3H, *s*, 1-OMe), 3.91 (3H, *s*, 3-OMe), 3.96 (3H, *s*, 2-OMe), 4.35–4.53 (2H, *m*, 5-H_{eq}, H-6a), 7.21–7.33 (3H, *m*, H-8; H-9, H-10), 8.29–8.34 (1H, *m*, H-11), 8.37 (1H, *s*, CHO). Other spectral data (IR, UV and EIMS) as reported earlier [21, 22].

1-*Cinnamoylpyrrolidine* (**13**). Crystals (500 mg) (R_f 0.49 in MeOH–$CHCl_3$, 1:24). Mp 100–102° (lit. [11] mp 101–103°). Spectral data (^{1}H NMR, ^{13}C NMR, IR, UV and EIMS) as reported earlier [11, 23].

10-*Amino*-3-*hydroxy*-4-*methoxyphenanthrene*-1-*carboxylic acid lactam (piperolactam A*, **14**). Yellow crystals (10 mg) (R_f 0.28 in MeOH–$CHCl_3$, 1:24). Mp 305–307°; decomp. (lit. [24] mp 303–306°; decomp.). Spectral data (^{1}H NMR, ^{13}C NMR, IR, UV and EIMS) as reported earlier [24].

10-*Amino*-2-*hydroxy*-3,4-*dimethoxyphenanthrene*-1-*carboxylic acid lactam* (**15**). Yellow crystals (9 mg) (R_f 0.50 in MeOH–$CHCl_3$, 1:24). Mp 213–215° (lit. [24] mp 212–214°). Spectral data (^{1}H NMR, IR, UV and EIMS) as reported earlier [24–26].

10-*Acetylamino*-2-*hydroxy*-3,4-*dimethoxyphenanthrene*-1-*carboxylic acid lactam* (**15a**). Yellow crystals (4 mg, 64% yield) (R_f 0.68 in MeOH–$CHCl_3$ 1:24). Mp 185–186°. EIMS *m/z*: 337([M]$^+$, 37), 322 (8), 295 (12), 281 (15), 280 (100), 265 (19), 264 (15), 237 (4), 220 (10), 205 (8), 177 (4), 164 (19), 150 (4), 120 (1), 91 (2), 43 (7). ^{1}H NMR ($CDCl_3$, 250 MHz): δ 2.46 (3H, *s*, NCOMe), 4.09, 4.18 (3H, 2*s*, 3-OMe, 4-Me), 7.59–7.63 (2H, *m*, 6-H, 7-H), 7.86 (1H, *s*, 9-H), 7.88–7.92 (1H, *m*, 8-H), 9.11–9.18 (1H, *m*, 5-H).

10-*Amino*-4-*hydroxy*-2,3-*dimethoxyphenanthrene*-1-*carboxylic acid lactam* (**16**). Yellow crystals (10 mg) (R_f 0.47 in MeOH–$CHCl_3$ 1:24). Mp 223–224° (lit. [26] mp 222–224°). Spectral data (^{1}H NMR, ^{13}C NMR, IR, Uv and EIMS) as reported earlier [26].

10-*Acetylamino*-4-*hydroxy*-2,3-*dimethoxyphenanthrene*-1-*carboxylic acid lactam* (**16a**). Yellow crystals (2 mg, 33% yield) (R_f 0.65 in MeOH–$CHCl_3$, 1:24. Mp 195–197°. EIMS *m/z* (rel. int.): 337 ([M]$^+$, 55), 303 (4), 296 (13), 295 (100), 280 (93), 279 (12), 266 (16), 265 (15), 252 (28), 236 (23), 209 (12), 180 (16), 164 (16), 152 (18), 120 (12), 91 (11), 69 (3), 43 (27). ^{1}H NMR ($CDCl_3$, 250 MHz): δ 2.60 (3*H*, *s*, NCOMe), 3.98 (3H, *s*, 3-OMe), 4.52 (3H, *s*, 2-OMe), 7.13 (1H, *s*, 9-H), 7.51–7.56 (2H, *m*, 6-H, 7-H), 7.79–7.81 (1H, *m*, 8-H), 8.73–8.77 (1H, *m*, 5-H).

10-*Acetylamino*-4-*acetoxy*-2,3-*dimethoxyphenanthrene*-1-*carboxylic acid lactam* (**16b**). Yellow needles (3 mg, 32% yield) (R_f 0.82 in MeOH–$CHCl_3$ 1:24. Mp 194–195° (lit. [26] mp 194–195°). Spectral data (1H NMR and EIMS as reported earlier [26].

10-*Amino*-2,3,4-*trimethoxyphenanthrene*-1-*carboxylic acid lactam (piperolactam C*, **17**). Yellow crystals (7 mg) (R_f 0.45 in MeOH–$CHCl_3$, 1:24). Mp 189–190° (lit. [24] mp 187–188°). Spectral data (^{1}H NMR, IR, UV and EIMS as reported earlier [24].

Cepharanone B (**18**). Pale yellow crystals (10 mg) (R_f 0.37 in MEOH–$CHCl_3$, 1:24). Mp 264–265° (lit. [27] mp 264–265°). Spectral data (^{1}H NMR, IR, UV and EIMS) as reported earlier [24, 27].

Cepharadione A (**19**). Orange needles (10 mg) (R_f 0.43 in MeOH–$CHCl_3$ 1:24), Mp >300° (lit. [27] mp >350°). ^{1}H NMR ($CDCl_3$; 250 MHz): δ 3.85 (3H, *s*, NMe), 6.45 (2H, *s*, OCH_2O), 7.52 (1H, *s*, 7-H), 7.64–7.69 (2H, *m*, H-9, H-10), 7.88–7.93 (1H, *m*, H-8), 8.15 (1H, *s*, 3-H), 8.98–9.35 (1H, *m*, H-11). Other spectral data (IR, UV and EIMS) as reported earlier [27].

Cepharadione B (**20**). Orange needles (8 mg) (R_f 0.55 in MeOH–$CHCl_3$ 1:24). Mp 264–266° (lit. [27] mp 267–268°). Spectral data (^{1}H NMR, IR, UV and EIMS) as reported earlier [24, 27].

(E)-N-*Feruloyltyramine* (**21**). Crystals (400 mg) (R_f 0.15 in MeOH–$CHCl_3$, 1:24). Mp 96° (lit [28] mp 91°). Spectral data (^{1}H NMR, ^{13}C NMR, IR, UV and EIMS) as reported earlier [28].

(E)-N-*Feruloyltyramine diacetate* (**21a**). Crystals (45 mg, 70% yield) (R_f 0.59 in MeOH–$CHCl_3$, 1:24). Mp 160–161° (lit. [28] mp 157–157.5°). Spectral data (^{1}H NMR, ^{13}C NMR, IR, UV and EIMS) as reported earlier [28].

(Z)-N-*Feruloyltyramine* (**22**). Oil (5 mg) (R_f 0.12 in MeOH–$CHCl_3$ 1:24). Spectral data (^{1}H NMR, ^{13}C NMR, IR and EIMS as reported earlier [28].

N-p-*Coumaroyltyramine* (**23**). Powder (40 mg) (R_f 0.06 in MeOH–$CHCl_3$ 1:24). Mp 244–246° (lit. [29] mp 240–245°). Spectral data (^{1}H NMR, ^{13}C NMR, IR, UV and EIMS) as reported earlier [29, 30].

N-p-*Coumaroyltyramine diacetate* (**23a**). Powder (6 mg, 75% yield) (R_f 0.48 in MeOH–$CHCl_3$ 1:24). Mp 160° (lit. [29] mp 160°). Spectral data (^{1}H NMR, ^{13}C NMR, IR, UV and EIMS) as reported earlier [29, 30].

Acknowledgements—We are grateful to DANIDA (Danish International Development Agency) for financial assistance and to the Tropical Botanic Garden and Research Institute (TBGRI, Trivandrum, India) for identification of plant material.

REFERENCES

1. Kirtikar, K. R. and Basu, B. D. (1993) *Indian Med. Plants* **3**, 2131.
2. Anon. (1963) *The Wealth of India*, Vol. 3, p. 83. CSIR Publication, New Delhi.
3. Raj, H. G., Gupta, S., Prasad, A. K., Boll, P. M., Wengel, J., Biswas, G., Singh, S. K., Sharma, N. K., Bisht, K. S. and Parmar, V. S. (1995) *Bioorg. Med. Chem. Letters* **5**, 1567.
4. Gervan, R. I., Greenberg, N. H., McDonald, M. M., Schumacher, A. M. and Affott, B. J. (1972) *J. Cancer Chemother. Rep.* **3**, 1.

5. Dominguez, X, A. and Alcon, J. (1985) *J. Ethnopharmacol.* **13**, 139.
6. Loder, J. W., Moorhouse, A. and Russel, G. B. (1969) *Aust. J. Chem.* **22**, 1531.
7. Takahashi, S. and Ogiso, A. (1970) *Chem. Pharm. Bull.* **18**, 100.
8. Tyagi, O. D., Jensen, S., Boll, P. M., Sharma N. K. Bisht, K. S. and Parmar, V. S. (1993) *Phytochemistry* **32**, 445.
9. Matsui, K. and Munakata, K. (1976) *Tetrahedron Letters* 4371.
10. Prasad, A. K., Tyagi, O. D., Wengel, J., Boll, P. M., Olsen, C. E., Gupta, S., Sharma, N. K., Bisht, K. S. and Parmar, V. S. (1994) *Tetrahedron* **50**, 10579.
11. Tyagi, O. D., Prasad, A. K., Wengel, J., Boll, P. M., Olsen, C. E., Parmar, V. S., Sharma, N. K., Jha, A. and Bisht, K. S. (1995) *Acta Chem. Scand.* **49**, 142.
12. Diaz D., P. P., Yosida, M. and Gottlieb, O. R. (1980) *Phytochemistry* **19**, 285.
13. Prasad, A. K., Tyagi, O. D., Wengel, J., Boll, P. M., Olsen, C. E., Sharma, N. K., Bisht, K. S., Gupta, S. and Parmar, V. S. (1994) *Tetrahedron* **50**, 2231.
14. Arison, B. H. and Hwang, S. B. (1991) *Acta Pharm. Sin.* **26**, 345.
15. Tyagi, O. D., Wengel, J., Prasad, A. K., Boll, P. M., Olsen, C. E., Pati, H. N., Bisht, K. S. and Parmar, V. S. (1994) *Acta Chem. Scand.* **48**, 1007.
16. Jensen, S., Olsen, C. E., Tyagi, O. D., Boll, P. M., Hussaini, F. A. Gupta, S., Bisht, K. S. and Parmar, V. S. (1994) *Phytochemistry* **36**, 789.
17. Gottlieb, O. R., Silva, M. L. D. and Ferreira, Z. S. (1975) *Phytochemistry* **14**, 1825.
18. Wenkert, E., Gottlieb, H. E., Gottlieb, O. R., Pereira, M. O. da S. and Formiga, M. D. (1976) *Phytochemistry* **15**, 1547.
19. Prasad, A. K., Tyagi, O. D., Wengel, J., Boll, P. M., Olsen, C. E., Bisht, K. S., Singh, A., Sarangi, A., Kumar, R., Jain, S. C. and Parmar, V. S. (1995) *Phytochemistry* **39**, 655.
20. Khan, M. R., Gray, A. I. and Waterman, P. G. (1987) *Phytochemistry* **26**, 1155.
21. Pachaly, P., Adnan, A. Z. and Will, G. (1992) *Planta Med.* **58**, 184.
22. Cortes, D., Hocquemiller, R., Leboeuf, M., Cave, A. and Moretti, C. (1986) *J. Nat. Prod.* **49**, 878.
23. Achenbach, H. and Karl, W. (1970) *Chem. Ber.* **103**, 2535.
24. Desai, S. J., Prabhu, B. R. and Mulchandani, N. B. (1988) *Phytochemistry* **27**, 1511.
25. Desai, S. J., Chaturvedi, R. and Mulchandani, N. B. (1990) *J. Nat. Prod.* **53**, 496.
26. Olsen, C. E., Tyagi, O. D., Boll, P. M., Hussaini, F. A., Parmar, V. S., Sharma, N. K., Taneja, P. and Jain, S.C. (1993) *Phytochemistry* **33**, 518.
27. Akasu, M., Itokawa, H. and Fujita, M. (1974) *Tetrahedron Letters* 3609.
28. Fukuda, N., Yonemitsu, M. and Kimura, T. (1983). *Chem. Pharm. Bull.* **31**, 156.
29. Yoshihara, T., Takamatsu, S. and Sakamura, S. (1978) *Agric. Biol. Chem.* **42**, 623.
30. Zhao, G., Hui Y., Rupprecht, J. K., McLaughlin, J. L. and Wood, K. V. (1992) *J. Nat. Prod.* **55**, 347.
31. Simonsen, O., Singh, S. K., Wengel, J. and Parmar, V. S. (1996) *Acta Crystallogr. Sect. C* (in press).