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NAPHTHALENES AND NAPHTHOQUINONES FROM *VENTILAGO* SPECIES

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Key Word Index—*Ventilago maderaspatana*; *V. calyculata*; Rhamnaceae; naphthalene derivatives; naphthoquinones; cordeauxione; isocordeauxione; maderone; ventilaginone; ventilagol; calyxanthone.

Abstract—Two new naphthalene derivatives and three naphthoquinones have been found in the root bark of *Ventilago maderaspatana*. Their structures are 2-acetyl-6,7-dimethoxy-3-methyl-1,8-methylenedioxynaphthalene (ventilaginone) and 1,3-dihydro-6,9-dihydroxy-7,8-dimethoxy-1-methylnaphtho[2,3-c]furan-3-one (ventilagol), 2(2′-acetoxypropyl)-3-hydroxy-5,7,8-trimethoxy-1,4-naphthoquinone (maderone), cordeauxione and isocordeauxione. The root bark of *V. calyculata* contains 2-methoxystypandrone and 1-hydroxy-6-methoxy-3-methylxanthone-8-carboxylic acid (calyxanthone).

INTRODUCTION

In continuation of our earlier investigations [1–3] on *Ventilago* spp., we report the structural elucidation of new naphthalenes and naphthoquinones from *V. calyculata* and *V. maderaspatana* (Rhamnaceae).

RESULTS AND DISCUSSION

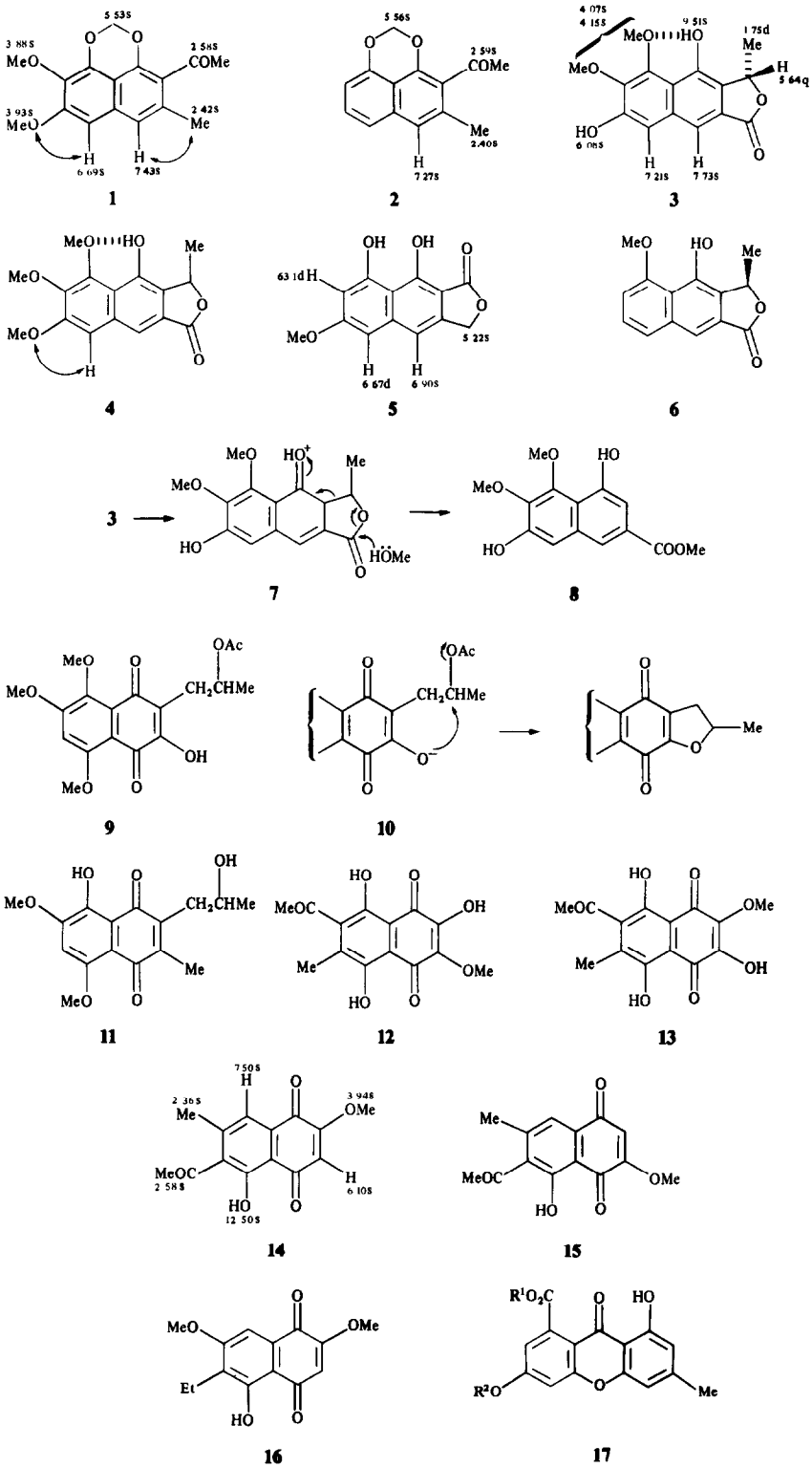
Naphthalenes

Two naphthalene derivatives have been isolated from the acetone extract of the root bark of *V. maderaspatana*. Ventilagone (**1**) analysed for $C_{16}H_{16}O_5$, showed ν_{CO} at 1687 cm^{-1}, and the UV spectrum suggested a naphthalene chromophore. Analysis of the ^1H NMR spectrum was straightforward (see **1**) except for a 2H singlet at δ5.53. This appeared to arise from a methylenedioxy group (ν_{max} 930 cm^{-1} [4]) which usually resonates near δ6 (6.12 in 1,2-methylenedioxy- and 6.01 in 2,3-methylenedioxynaphthalene). However we found that in 1,8-methylenedioxynaphthalene the methylene signal appears at δ5.50, and the spectrum of **1** accords well with that of musizin methylene ether (**2**). Irradiation of the aromatic methyl protons in ventilaginone resulted in a substantial NOE on the lower field aromatic singlet (signal enhancement 37%) which confirmed the arrangement of substituents in ring B. Similarly, irradiation of the methoxy protons at δ3.93 increased the intensity of the higher field aromatic proton signal by 18% showing that one methoxy group is adjacent to a ring proton. In agreement, when the ^1H NMR spectrum was run in C_6D_6, one methoxy signal shifted significantly upfield to δ3.27 whereas the other only moved to 3.77; the methylenedioxy resonance shifted from 5.53 to 4.82. The data are consistent with structure **1** which is preferred to the 5,6-dimethoxy alternative as the aromatic singlet at δ6.69 is too lowfield for a β-proton between two oxygens in a naphthalene system (usually in the region 6.5–6.3, e.g. **5**). The general substitution pattern is common to a number of natural naphthalene derivatives (musizin [5], torachrysone [6]) but so far as we are aware, a 1,8-methylenedioxy group has not been observed previously in natural products.

The other new naphthalene derivative, ventilagol (**3**), $C_{15}H_{14}O_6$, is optically active, and forms a diacetate and a dimethyl ether (Me_2SO_4–K_2CO_3–Me_2CO) but only a monomethyl ether with diazomethane. A strong IR band at 1750 cm^{-1} indicates the presence of a γ-lactone. The ^1H NMR spectrum can be assigned as shown in **3**, and in the MS major peaks at *m/z* 275 and 247 probably derive from fragmentation of the molecular ion with losses of Me· and of MeCO· with hydrogen transfer, respectively, from the lactone ring [7].

Support for structure **3** was obtained in several ways. The UV spectrum does not undergo a bathochromic shift in the presence of NaOAc–H_3BO_3 showing that the hydroxyls are neither *ortho* nor *peri* to each other [8]. When the methoxy protons in **3** were irradiated no NOE was observed but irradiation of the monomethyl ether **4** at δ3.99 increased the intensity of the higher field aromatic proton by 19%. Thus the β-hydroxyl in ventilagol is adjacent to a ring proton. (That the other hydroxyl failed to react with diazomethane in ether is consistent with its position *peri* to methoxyl, and so is its chemical shift [9].) This was confirmed when the ^1H NMR spectrum of **3** was run in DMSO-d_6; addition of NaOD shifted the H-5 signal upfield by 0.52 ppm while the H-4 singlet moved upfield by 0.64 ppm in accord with its position *para* to hydroxyl [10]. Furthermore, conversion of **4** to its acetate resulted in a downfield shift of the H-4 signal by 0.48 ppm. Finally the arrangement of the lactone ring in ventilagol must be as represented in **3** (cf. eleutherol, **6** [11]) to account for the downfield chemical shift of H-4 at δ7.73 in contrast to that of α-sorigenin (**5**) [12] at 6.90 (in $CDCl_3$).

Further support for the lactone ring orientation was obtained unexpectedly in an attempt to effect partial demethylation of ventilagol with boron tribromide. The product, obtained in low yield after quenching in methanol, was the ester **8**. This represents a reversed Friedel–Crafts alkylation which might be summarised as



shown in **7**, the protons for catalysis arising from interaction of **3** with boron tribromide.

The first sample (a) of ventilagol was optically active, $[\alpha]_D$ −101° ($CHCl_3$) which suggests the (1*S*)-configuration for **3** by comparison with (1*R*)-eleutherol (**6**) which has $[\alpha]_D$ +90° ($CHCl_3$). A second sample (b) was optically inactive, and a third (c) had a lower rotation than (a) and was apparently partially racemised. Unfortunately none of (a) remains and an attempt to run a CD curve (for comparison with eleutherol) on a dilute

solution containing the remaining trace of (c) showed no significant dichroism.

Naphthoquinones

Maderone (**9**), $C_{18}H_{20}O_8$, is soluble in aqueous sodium bicarbonate and is decolourised by dithionite suggesting a hydroxyquinone structure, while the IR spectrum provides evidence for ester (1737 cm^{-1}) and quinone (1652 cm^{-1}) functions as well as hydroxyl (3240 cm^{-1}). The ^1H NMR spectrum includes signals for a methyl singlet (δ1.95), a hydroxyl (7.78), three methoxyl groups, and a 1H singlet at 6.67. In addition decoupling experiments established that a methyl doublet at δ1.28 was coupled to a methine multiplet at 5.23 which in turn was coupled to a methylene doublet at 2.84. Hence a side chain $-CH_2\underset{|}{C}H-CH_3$ is present which can be expanded to $-CH_2CH(OAc)CH_3$ taking account of peaks in the MS at $[M-42]^+$, $[M-60]^+$ (100%) and $[M-101]^+$ ($CH_2CH(OAc)Me$).

The orientation of the substituents as shown in **9** can be deduced as follows. Two methoxyls are assigned to *peri* positions as neither the hydroxyl nor the isolated proton can be *peri* to carbonyl, and all the naphthoquinones in *Ventilago* are juglone or naphthazarin derivatives. That the third methoxyl is also in the aromatic ring is suggested by the chemical shift of the lone (aromatic) proton at δ6.67 (cf. 6.78 for H-6 in 2,5,7,8-tetramethoxy-1,4-naphthoquinone [13]). The acidity of the hydroxyl group shows that it must be in the quinonoid ring and its absence from the aromatic ring is confirmed by the fact that the chemical shift of the isolated proton suffers little change when maderone is acetylated. It follows that the acetoxypropyl side chain must be adjacent to the hydroxyl which explains another observation. On addition of sodium acetate the peak in the VIS spectrum at $\lambda_{425\,nm}$ undergoes a hypsochromic shift of 43 nm instead of the expected bathochromic shift. This indicates that a new compound is formed, probably as a result of nucleophilic cyclization (see **10**; formation of an *o*-quinone isomer is also possible). Unfortunately lack of material precluded further investigation. The position of the β-methoxyl has not been established and is assigned to C-7 on biogenetic grounds, and by analogy to the polyketide pigments, javanicin, solaniol and their derivatives, e.g. **11** [14].

The other quinone obtained from *V. maderaspatana* proved to be a mixture of isomers, $C_{17}H_{12}O_7$. The spectroscopic data revealed the presence of methyl, methoxyl and C-acetyl groups, two *peri*-hydroxyls and a β-hydroxyl group showing that the pigment was a fully substituted naphthazarin very closely resembling cordeauxione (**12**) found in *Cordeauxia edulis* (Leguminosae) [15]. In the ^1H NMR spectrum however there are *two* pairs of *peri*-hydroxyl singlets (ratio ~ 2:1) and the ring methyl signal is broadened and asymmetrical indicating the presence of two compounds. These were just detectable by multiple development TLC but with the small amount available separation was not attempted. Instead the mixture was treated with diazomethane which gave a single compound identical with cordeauxione 2-*O*-methyl ether. We conclude that the mixture consisted of cordeauxione (**12**) and isocordeauxione (**13**).

Another naphthoquinone, $C_{14}H_{12}O_9$, was isolated from the root bark of *V. calyculata* after extensive CC and PLC. The UV-VIS spectrum and the presence of one *peri*-hydroxyl group indicated a juglone derivative; it formed a monomethyl ether. The ^1H NMR spectrum is a series of singlets corresponding to aromatic methyl, acetyl methyl, methoxy and *peri*-hydroxy groups, an isolated aromatic and a quinonoid proton, readily assigned as shown in **14** by analogy with the spectrum of stypandrone (**14** without the methoxyl) [16]. The arrangement of the substituents in the benzenoid ring was confirmed by NOE experiments; irradiation of the aromatic methyl protons enhanced the signal at δ7.50 by 12% while irradiation of the acetyl methyl had no effect. Irradiation at δ3.94 enhanced the signal at δ6.10 by 15%. The large upfield shift in benzene of the methoxy signal ($\Delta^{CDCl_3}_{C_6H_6} = 1.13\delta$) supports the location of that group on the quinone ring [17] but does not distinguish between **14** and the isomer **15**. In the proton-coupled ^{13}C NMR spectrum the chelated carbonyl carbon (C-4) signal is a doublet at δ190.0 (J = 2.4 Hz) due to coupling with H-3 while the C-1 carbonyl carbon signal is a double doublet arising from coupling with H-3 (J = 7.6 Hz) and H-8 (J = 4.2 Hz) [18]. These data are consistent only with structure **14** and not with **15**. Similar J values have been reported for the related fungal metabolite **16** [19].

This pigment is therefore 2-methoxystypandrone (**14**), a compound previously isolated [20] from the roots of *Polygonum cuspidatum* (Polygonaceae) and from *Rhamnus fallax* (Rhamnaceae) [21]. Another quinone with very similar physical properties is orientalone, found in the roots of *Rumex orientalis* (Polygonaceae), to which structure **15** was assigned [22] on unconvincing IR evidence. Structure **15** has been synthesized unambiguously by Jung *et al.* [23], and by P. Brassard *et al.* [personal communication]. Direct comparison with orientalone was not possible but spectroscopic comparison cast doubt on the orientalone structure. Direct comparison of the Brassard synthetic material with our 2-methoxystypandrone confirmed that they were different so it seems likely that orientalone is actually **14**.

Calyxanthone

Finally the methanol extract of the root bark of *V. calyculata* yielded a very polar, pale yellow compound, $C_{15}H_{10}O_6$, which was not a quinone. It had a typical xanthone UV spectrum [24] while the IR spectrum provided evidence for carboxyl (3300–2600 and 1680 cm^{-1}) and chelated carbonyl (1640 cm^{-1}) functions. The ^1H NMR spectrum showed signals for two pairs of *meta*-coupled protons, of which one pair showed fine coupling to a methyl group. As calyxanthone forms a monomethyl ether-methyl ester with diazomethane it is evidently a dihydroxymethylxanthone-carboxylic acid and the orientations shown in **17** ($R^1 = R^2 = H$) were suggested by the chemical shifts of the aromatic protons. In confirmation the spectroscopic data for the dimethyl derivative are in excellent agreement with those reported for **17** ($R^1 = R^2 = Me$) isolated [25] from *Aspergillus wentii*. The same compound has also been derived from isosulochrine [26] and direct comparison (TLC, IR, MS) established its identity.

EXPERIMENTAL

Silica gel G and silica gel (100–200 mesh) (Acme, India) were used for TLC and CC, respectively, unless stated otherwise.

Isolation of the constituents. The plant material *Ventilago maderaspatana* was collected from Srisailam forest (Andhra

Pradesh, India). Air dried, powdered root bark (2.5 kg) was extracted with Me_2CO (Soxhlet, 10 syphonings). Part of the dark brown residue (50 g) was subjected to CC on silica gel (300 g). The column was eluted with C_6H_6–petrol (1:1) (fractions 1–90), C_6H_6 (fractions 91–172), C_6H_6–EtOAc (9:1) (fractions 173–212), C_6H_6–EtOAc (4:1) (fractions 213–240). Initial fractions (1–32) contained only waxy material. Fractions 66–90 were rechromatographed (CC: C_6H_6–petrol, 2:1) and the fraction containing **1** was purified by prep. TLC (C_6H_6). It formed plates from C_6H_6–petrol, mp 136° (Found: C, 66.59; H, 5.69. $C_{16}H_{16}O_5$ requires C, 66.66; H, 5.59%); UV $\lambda_{max}^{CHCl_3}$ nm (log ε): 276 (3.87), 352 (3.70); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 930, 1604, 1631, 1687; ^1H NMR (220 MHz, $CDCl_3$): see **1**; (220 MHz, C_6D_6): δ2.42 (3H, *s*), 2.45 (3H, *s*), 3.27 (3H, *s*), 3.77 (3H, *s*), 4.82 (2H, *s*), 6.50 (1H, *s*), 7.62 (1H, *s*); MS *m/z* (rel. int.): 288 (80), 273 (100), 258 (33), 245 (45), 243 (17), 230 (33), 228 (18), 215 (35), 144 (*m/2z*) (3 5), 136.5 (*m/2z*) (3), 129 (*m/2z*) (7).

Fractions 173–196 were rechromatographed (CC: C_6H_6–EtOAc, 9:1 and 4:1). The C_6H_6–EtOAc (4:1) eluate gave **3** after crystallization from Me_2CO. It formed needles, mp 215°, $[\alpha]_D^{25}$ −101° ($CHCl_3$, c 0.099) (Found: C, 62.38; H, 4.84. $C_{15}H_{14}O_6$ requires C, 62 07; H, 4.86%); UV λ_{max}^{MeOH} nm (log ε): 233 (4.48), 262 (4.56), 290 sh (3.64), 302 (3.74), 315 sh (3.56), 355 sh (3.48), 370 (3 53), unaffected by NaOAc and NaOAc–H_3BO_3; IR ν_{max}^{KBr} cm^{-1}: 1603, 1750, 3300, 3410; ^1H NMR (100 MHz, $CDCl_3$): see **3**, (220 MHz, DMSO-d_6): δ1.65 (3H, *d*, *J* = 7 Hz, Me), 3.92 (3H, *s*, OMe), 4.10 (3H, *s*, OMe), 5.74 (1H, *q*, *J* = 7 Hz, CH Me), 7.22 (1H, *s*, H-5), 7.74 (1H, *s*, H-4); DMSO-d_6–DO^-): 1.61 (3H, *d*), 3.90 (3H, *s*), 3.97 (3H, *s*), 5.60 (1H, *q*), 6.70 (1H, *s*), 7.09 (1H, *s*); MS (Found: $[M]^+$ 290.0784. $C_{15}H_{14}O_6$ requires M, 290.0790); *m/z* (rel. int.): 290 (100), 275 (82) (Found: 275.0553. $C_{14}H_{11}O_6$ requires 275.0555), 247 (42) (Found. 247.0591, $C_{13}H_{11}O_5$ requires 247.0606), 233 (27), 219 (12), 217 (10), 205 (14), 204 (10).

6-O-Methyl ether **4** (CH_2N_2). Plates (C_6H_6), mp 164°; ^1H NMR (220 MHz, $CDCl_3$): δ1.76 (3H, *d*, *J* = 7 Hz, Me), 3.99 (6H, *s*, 2 × OMe), 4.18 (3H, *s*, OMe), 5.69 (1H, *q*, *J* = 7 Hz, CH Me), 7.05 (1H, *s*, H-5), 7 75 (1H, *s*, H-4), 9.75 (1H, *s*, exchangeable with D_2O, *peri*-OH): MS (Found: 304.0966. $C_{16}H_{16}O_6$ requires 304.0947); *m/z* (rel. int.): 304 (100), 289 (82) (Found: 289.0711. $C_{15}H_{13}O_6$ requires 289.0712), 261 (40) (Found: 261.0761. $C_{14}H_{13}O_5$ requires 261.0763), 247 (25), 233 (11), 219 (20); *6-O-Methyl ether 1-acetate* (Ac_2O–pyridine): needles (petrol), mp 205° (Found. C, 62.60; H, 5.12 $C_{18}H_{18}O_7$ requires C, 62.42; H, 5.24%); ^1H NMR (100 MHz, $CDCl_3$): δ1.66 (3H, *d*, *J* = 7 Hz, Me), 2.44 (3H, *s*, OAc), 3.95 (3H, *s*, OMe), 4.0 (6H, *s*, 2 × OMe), 5.64 (1H, *q*, *J* = 7 Hz, CH Me), 7.12 (1H, *s*, H-5), 8.16 (1H, *s*, H-4) *Dimethyl ether* (Me_2SO_4–K_2CO_3–Me_2CO): needles (petrol), mp 121° (Found: C, 64.00; H, 5.80. $C_{17}H_{18}O_6$ requires C, 64.14; H, 5 70%); ^1H NMR (100 MHz, $CDCl_3$): δ1.78 (3H, *d*, *J* = 7 Hz, Me), 3.96 (6H, *s*, 2 × OMe), 4.01 (3H, *s*, OMe), 4.05 (3H, *s*, OMe), 5.76 (1H, *q*, *J* = 7 Hz, CH Me), 7.12 (1H, *s*, H-5), 8.04 (1H, *s*, H-4). *Diacetate* (Ac_2O–pyridine): needles (petrol), mp 113–115° (Found: C, 60.90; H, 4.84. $C_{19}H_{18}O_8$ requires C, 60.96; H, 4.85%); ^1H NMR (100 MHz, $CDCl_3$): δ1.68 (3H, *d*, *J* = 7 Hz, Me), 2.40 (3H, *s*, OAc), 2.45 (3H, *s*, OAc), 3 95 (3H, *s*, OMe), 3.98 (3H, *s*, OMe), 5.64 (1H, *q*, *J* = 7 Hz, CH Me), 7.51 (1H, *s*, H-5), 8.22 (1H, *s*, H-4).

Reaction of ventilagol with boron tribromide. To a suspension of ventilagol (**3**; 20 mg) in $CHCl_3$ (5 ml) cooled to −78° was added BBr_3 (1 ml). After 30 min at −78° the mixture was allowed to warm to ambient temp. After addition of MeOH (5 ml) the mixture was evaporated *in vacuo*, and the residual solid was purified by prep TLC on silica in $CHCl_3$, and finally sublimed at 160°/0.001 mmHg to give the ester **8** (2 mg); IR ν_{max}^{KBr} cm^{-1}: 1260, 1695, 3410; ^1H NMR (220 MHz, $CDCl_3$). δ3 95, 4.06, 4.12 (each 3H, *s*, OMe), 6.00 (1H, *s* (*br*), exchanged with D_2O, OH-6), 7.16 (1H, *s* (*br*), H-2), 7.28 (1H, *s*, H-5), 7.90 (1H, *s* (*br*), H-4), 9.25 (1H, *s*, exchanged with D_2O, OH-1); MS (Found: $[M]^+$, 278.0793, $C_{14}H_{14}O_6$ requires M, 278.0790); *m/z* (rel. int.): 278 (100), 263 (45), 247 (13), 235 (21), 220 (22), 213 (12), 189 (18), 176 (17), 161 (11).

Fractions 213–216 were subjected to CC (C_6H_6–EtOAc, 9:1 and 4:1). The C_6H_6–EtOAc (9:1) eluate was purified by repeated prep. TLC ($CHCl_3$) on Kieselgel 60 F_{254} plates impregnated with 3% $(COOH)_2$ to give **12** and **13**. Red solid, mp 190°; UV λ_{max}^{MeOH} nm: 250, 305 sh, 489, 528 sh; IR ν_{max}^{KBr} cm^{-1}: 3350 br, 1700 br, 1640 sh, 1620 sh, 1590 sh; ^1H NMR (220 MHz, $CDCl_3$): δ2.21 (3H, unsymm. *s*, ArMe), 2.54 (3H, *s*, COMe), 4.19 (3H, *s*, OMe), 6.7–7.3 (1H, *br*, exchanged with D_2O, OH), 11.78 and 12.90/11.97 and 12.69 (2:1, total 2H, *peri*-OH): MS (Found: $[M]^+$, 292.0570. $C_{14}H_{12}O_7$ requires M, 292.0582); *m/z* (rel. int.): 292 (100), 277 (84), 249 (20), 221 (5), 43 (38). Treatment with CH_2N_2 in MeOH gave an orange crystalline solid; UV λ_{max}^{MeOH} nm: 214, 238 sh, 305, 470 sh, 494, 524 sh; ^1H NMR (220 MHz, $CDCl_3$): δ2.24 (3H, *s*, ArMe), 2.59 (3H, *s*, COMe), 4.15 (6H, *s*, OMe), 12.63 and 12.82 (each 1H, *s*, *peri*-OH) identical with cordeauxione-2-O-methyl ether prepared in the same way from cordeauxione.

The C_6H_6–EtOAc (4:1) eluate containing **9** was purified by prep. TLC (C_6H_6–EtOAc, 1:1). Compound **9** was obtained as orange red microcrystals (C_6H_6–petrol), mp 159°: $[\alpha]_D^{25}$ −159° ($CHCl_3$, c 0.31); UV λ_{max}^{MeOH} nm: 226, 265, 298, 425; $\lambda_{max}^{MeOH-AcO^-}$ nm: 224, 288, 382; IR ν_{max}^{KBr} cm^{-1}: 1652, 1737, 3240 br; ^1H NMR (220 MHz, $CDCl_3$): δ1.28 (3H, *d*, *J* = 7 Hz, Me), 1.95 (3H, *s*, OAc), 2.84 (2H, *d*, *J* = 7 Hz, CH_2), 3.87 (3H, *s*, OMe), 4.01 (3H, *s*, OMe), 4.04 (3H, *s*, OMe), 5.23 (1H, *m*, H-2'), 6.67 (1H, *s*, H-6), 7.78 (1H, *s*, exchangeable with D_2O, OH): MS (Found: M^+, 364.1146. $C_{18}H_{20}O_8$ requires M, 364.1158); *m/z* (rel. int.): 364 (4), 322 (Found: 322.1044. $C_{16}H_{18}O_7$ requires 332.1052, 16), 304 (Found: 304.0946. $C_{16}H_{16}O_6$ requires 304.0947, 100), 291 (20), 289 (61), 278 (36), 277 (24), 276 (44), 263 (32), 261 (43), 249 (15), 247 (23), 239 (16), 233 (18), 219 (9), 205 (10), 60 (19); *Acetate* (Ac_2O–pyridine) obtained as orange yellow needles (C_6H_6–petrol) (Found: C, 59.00; H, 5.48. $C_{20}H_{22}O_9$ requires C, 59.11; H, 5.46%); ^1H NMR (100 MHz, $CDCl_3$): δ1.29 (3H, *d*, *J* = 7 Hz, Me), 1.98 (3H, *s*, OAc), 2.41 (3H, *s*, OAc), 2.77 (2H, *d*, *J* = 7 Hz, CH_2), 3.89 (3H, *s*, OMe), 4.0 (6H, *s*, 2 × OMe), 5.14 (1H, *m*, H-2'), 6.73 (1H, *s*, H-6).

V. calyculata: *isolation of 2-methoxystypandrone.* The acetone extract of the root bark was fractionated by CC (see ref. [2]). Fractions 97–112 were chromatographed (CC) in C_6H_6 and C_6H_6–EtOAc (9:1). The C_6H_6 eluate on prep. TLC (C_6H_6–EtOAc, 19:1) gave compound **14** as brownish-red needles (C_6H_6–petrol), mp 187° (Found: C, 64.47; H, 4.68. $C_{14}H_{12}O_5$ requires C, 64.61, H, 4.65%); UV λ_{max}^{MeOH} nm (log ε): 225 (4.99), 288 (4.74), 425 (4.34); IR ν_{max}^{KBr} cm^{-1}: 1625, 1680; ^1H NMR (220 MHz, $CDCl_3$): δ2.36 (3H, *s*, Me), 2.58 (3H, *s*, Ac), 3.94 (3H, *s*, OMe), 6.10 (1H, *s*, H-3), 7.50 (1H, *s*, H-8), 12.50 (1H, *s*, exchangeable with D_2O, *peri*-OH); (C_6D_6): 1.97 (3H, *s*), 2.32 (3H, *s*), 2.81 (3H, *s*), 5.40 (1H, *s*), 7.30 (1H, *s*): MS (Found: $[M]^+$, 260.0676. $C_{14}H_{12}O_5$ requires M, 260.0684); *m/z* (rel. int.): 260 (80), 245 (100), 232 (17), 217 (22), 204 (11), 189 (7); *Methyl ether* (Me_2SO_4–K_2CO_3–Me_2CO): yellow needles (MeOH), mp 178–180° (Found: C, 65 48; H, 5.18. $C_{15}H_{14}O_5$ requires C, 65.69; H, 5.14%); ^1H NMR (100 MHz, $CDCl_3$): δ2.35 (3H, *s*, Me), 2.54 (3H, *s*, Ac), 3.85 (3H, *s*, OMe), 3.90 (3H, *s*, OMe), 6.10 (1H, *s*, H-3), 7.81 (1H, *s*, H-8).

Isolation of calyxanthone. The methanolic extract (50 g) of the root bark of *V. calyculata* was chromatographed on silica gel (300 g). The column was eluted with $CHCl_3$–MeOH (9:1) (fractions 1–50) (4:1) (fractions 51–62) and (1:1) (fractions

63–80). Fractions 12–16 were rechromatographed (CC, $CHCl_3$–MeOH, 9:1) to obtain **17** ($R^1 = R^2 = H$) which was purified by repeated crystallisation from MeOH and MeOH–$CHCl_3$. Calyxanthone was obtained as pale yellow needles, mp > 265°; UV λ_{max}^{MeOH} nm. 238, 252 sh, 267 sh, 307, 351; IR ν_{max}^{KBr} cm^{-1}: 3300–2600, 1680, 1640, 1605, 1575; ^1H NMR (360 MHz, DMSO-d_6): 2.38 (3H, *d*, *J* = 0.6 Hz, Me), 6.63 (1H, *dd*, *J* = 1.4, 0.6 Hz, H-2), 6.78 (1H, *d*, *J* = 2.3 Hz, H-5), 6.78 (1H, *dd*, *J* = 1.4, 0 6 Hz, H-4), 6.88 (1H, *d*, *J* = 2.3 Hz, H-7), 12.40 (1H, *s*, *peri*-OH); MS (Found: 286.0481. $C_{15}H_{10}O_6$ requires 286.0477); *m/z* (rel. int.): 286 (88), 268 (44) (Found: 268.0395. $C_{15}H_8O_5$ requires 268.0371), 242 (100) (Found: 242.0575. $C_{14}H_{10}O_4$ requires 242.0579), 239 (15), 213 (18) (Found: 213.0549. $C_{13}H_9O_3$ requires 213.0552); *Methyl ether-methyl ester* (CH_2N_2): pale yellow needles (MeOH), mp 183°; UV λ_{max}^{MeOH} nm (log ε): 236 (4.51), 254 (4 41), 267 (4.30), 304 (4.37), 352 (4.05); IR ν_{max}^{KBr} cm^{-1}. 1712, 1655, 1608; ^1H NMR (360 MHz, $CDCl_3$): δ2.38 (3H, *d*, *J* = 0.6 Hz, Me), 3.91 (3H, *s*, OMe), 4.00 (3H, *s*, OMe), 6.56 (1H, *dd*, *J* = 1.4, 0.7 Hz, H-2), 6.64 (1H, *dd*, *J* = 1.4, 0.6 Hz, H-4), 6 83 and 6.84 (each 1H, *d*, *J* = 2.3 Hz, H-5 and H-7), 12.25 (1H, *s*, *peri*-OH); MS (Found: 314.0790. $C_{17}H_{14}O_6$ requires 314.0790); *m/z* (rel. int.). 314 (56), 282 (100), (Found· 282 0540. $C_{16}H_{10}O_5$ requires 282.0528), 253 (11), 254 (11).

Methylenations 1,2-, 2,3- and 1,8-methylenedioxynaphthalenes are known compounds [27–29 respectively]. Compound **2** was obtained by treating musizin (2 mg) with CH_2I_2–K_2CO_3–Me_2CO (Found. $[M]^+$, 228.0786. $C_{14}H_{12}O_3$ requires 228.0786): MS *m/z* (rel. int.): 228 (45), 213 (100), 127 (20).

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