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XANTHONES, XANTHONOLIGNOIDS AND OTHER CONSTITUENTS OF THE ROOTS OF *VISMIA GUARAMIRANGAE**

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Key Word Index—*Vismia guaramirangae*, Guttiferae, roots, prenylated benzophenones, prenylated anthranoids, xanthones, xanthonolignoids, syringaresinol

Abstract—A new prenylated benzophenone, vismiaphenone C, has been isolated from the root bark of *Vismia guaramirangae* together with the known vismiaphenone A, chrysophanic acid, γ-hydroxyferruginin A and γ-anthrone A_3 The woody part of the roots has been shown to contain 10 xanthones, three xanthonolignoids and syringaresinol Three of the xanthones and one of the xanthonolignoids are described for the first time The co-occurrence of xanthones, xanthonolignoids and syringaresinol is of biogenetic significance

INTRODUCTION

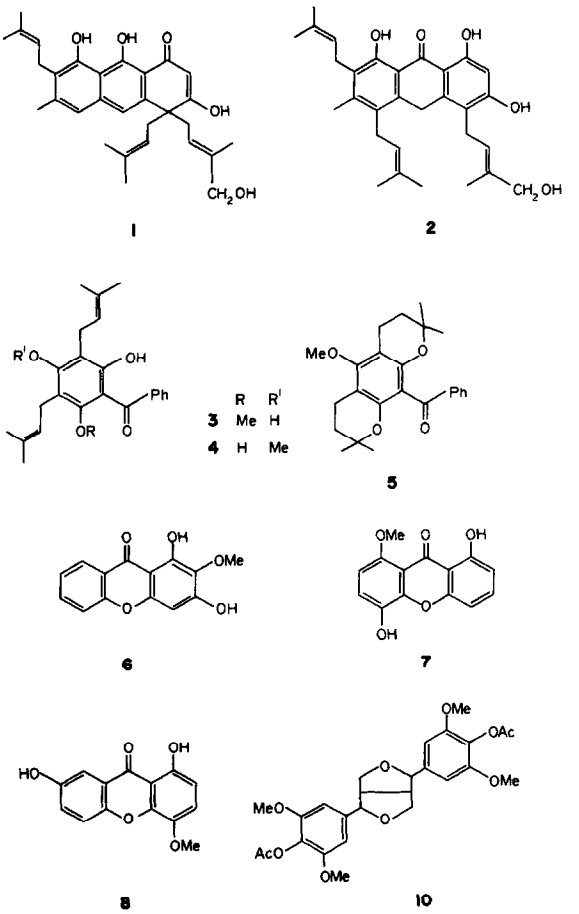
According to Engler [1] the *Vismia* genus belongs to the family, Guttiferae, subfamily, Hypericoideae, tribe, Vismieae In the last three years, besides common sesquiterpenes, we have isolated many new prenylated anthranoids and benzophenones [2] from the fruits of *V baccifera* var *dealbata*, *V baccifera* var *ferruginea*, *V macrophylla*, *V lindeniana*, *V falcata*, *V decipiens*, *V guianensis* and *V guaramirangae*, and also from the leaves [3] and the bark [4] of the latter two species, respectively In addition, dammaradienol and two lignans, sesamin and 5, 5′-dimethoxysesamin, were found in the bark Recently anthranoids have been also isolated by De Lourdes *et al* [5] from the leaves of *V reichardtiana* (syn *V guaramirangae* [6]) and by Do Carmo *et al* [7] from the wood of *V cayennensis* and *V japurensis* Xanthones, characteristic secondary metabolites of Guttiferae, have so far not been reported in the genus *Vismia*, but they occur in *Harungana madagascariensis* [8] and in *Psorospermum febbrifugum* [9], both of which belong to the tribe Vismieae

The present investigation on the roots of *V guaramirangae* has led to the isolation of two prenylated benzophenones, 10 xanthones, three xanthonolignoids, γ-hydroxyferruginin A, γ-hydroxyanthrone A_3, syringaresinol and chrysophanic acid Three xanthones, one benzophenone and one xanthonolignoid are here described for the first time

RESULTS

The extracts of the bark and the woody part of the roots revealed a different composition on TLC and were separately processed

Chromatographic separation of the root bark extract gave chrysophanic acid, γ-hydroxyferruginin A (**1**), γ-hydroxyanthrone A_3 (**2**), vismiaphenone A (**3**) and a new prenylated benzophenone (**4**), which we have named vismiaphenone C γ-Hydroxyferruginin A was previously found in the fruits of the same species [10] and vismiaphenone A in the fruits of *V decipiens* [2] γ-



*Part 9 in the series "Chemistry of the *Vismia* Genus" For Part 8 see ref [4]

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Hydroxyanthrone A_3, previously described [10] as a product of the thermal rearrangement of **1**, was isolated as a natural product The UV and MS (ion at *m/z* 105) data of vismiaphenone C, $C_{24}H_{28}O_4$ ($[M]^+$ 380) were indicative of a benzophenone with one unsubstituted ring The ^1H NMR spectrum, in addition to a complex multiplet (5H) in the aromatic region, showed signals due to one methoxyl group, two equivalent γ, γ'-dimethylallyl chains and two equivalent chelated hydroxyl groups, consequently vismiaphenone C was an isomer of vismiaphenone A (**3**) The bathochromic shift of the UV maxima after addition of aluminium chloride (but not of sodium acetate), the shift to low-field of the CH_2 signal in the ^1H NMR spectrum in pyridine-d_5 [11], as well as the acid-catalysed cyclization of the chain to give **5**, establish the structure **4** for vismiaphenone C

TLC of the extract of the woody part showed the presence of well over a dozen compounds of varying polarity, whose fractionation was achieved by combined extraction with aqueous sodium carbonate and sodium hydroxide, CC, fractional crystallization and prep TLC (see Experimental) As a result, 10 xanthones, three xanthonolignoids and one lignan were isolated in quantities sufficient for their complete characterization Seven of the xanthones isolated (i e 2-hydroxy-, 2-methoxy-, 1,7-dihydroxy-, 1-hydroxy-7-methoxy-, 2-hydroxy-1-methoxy-, 3-hydroxy-2-methoxy- and 1,5-dihydroxy-3-methoxyxanthone) were compounds known to occur in Guttiferae [12] Their identification was based on the spectral (UV, ^1H NMR, and MS) data and mps of the compounds and their derivatives and by comparison with the data available in the literature (see Experimental) The remaining three isomeric xanthones, $C_{13}H_5O_2(OH)_2(OMe)$ ($[M]^+$ 258), the structures which were determined as 1,3-dihydroxy-2-methoxy-xanthone (**6**), 1,5-dihydroxy-8-methoxyxanthone (**7**) and 1,7-dihydroxy-4-methoxy-xanthone (**8**) are described here for the first time

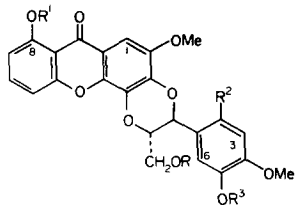
Xanthone **6**, mp 176–178°, had to be trisubstituted in the same ring since the ^1H NMR spectrum exhibited an isolated aromatic proton signal (δ 6 45) It gave a dimethyl-derivative, identical in all respects to 1,2,3-trimethoxyxanthone [13], thus establishing the oxygenation pattern The presence of a chelated hydroxyl group was indicated by a sharp singlet (δ 13 0) in the ^1H NMR spectrum and by a bathochromic shift with aluminium chloride in the UV spectrum The second hydroxyl group was located at C-3 because of the bathochromic shift of the UV maxima in the presence of sodium acetate Consequently, the natural product was 1,3-dihydroxy-2-methoxyxanthone (**6**), a structure which was in accord with the stability of xanthones in alkaline medium

Also in the second xanthone (**7**), mp 230–231°, one of the hydroxyl groups could be placed at C-1 (or C-8), since the ^1H NMR spectrum showed a sharp singlet at δ 12 97 Examination of the aromatic region of the spectrum revealed the presence of two *ortho*-coupled protons (doublets at δ 7 26 and 6 66, J = 9 Hz) and three vicinal protons (triplet at δ 7 56, J = 8 5 and 8 Hz, double doublet at δ 6 96, J = 1 5 and 8 5 Hz, double doublet at δ 6 76, J = 1 5 and 8 Hz) The UV maxima were shifted by addition of aluminium chloride and sodium methoxide (stable during the period of the experiment) but the chromophore system remained unaltered with sodium acetate Consequently, the C-3 and C-6 positions for the second hydroxyl group could be excluded, as well as the possibility that the two hydroxyls were on the same ring in an *ortho* or *para* relationship With these limitations three possible structures were compatible with the ^1H NMR data, i e 1-methoxy-2,8-dihydroxyxanthone, 1,5-dihydroxy-6-methoxyxanthone and 1,5-dihydroxy-8-methoxyxanthone (**7**) The first one was that of a known xanthone, isolated for the first time [14] from *Kielmeyera petiolaris* (Guttiferae) However, the reported mps of the compound (197–199°) and its dimethyl (153–155°) and diacetyl derivatives (165–167°), as well as the spectral data, were very different from those of the recorded xanthone A 1,5-dihydroxy-6-methoxy structure was ruled out since an *ortho*-coupled H-8 proton should be at *ca* δ 8 Therefore, the structure of 1,5-dihydroxy-8-methoxyxanthone (**7**) was proposed Moreover, the chemical shifts expected [15] for this oxygenation pattern were well in accordance with the observed values while the MW loss of 18 from the molecular ion in the mass spectrum supported the C-8 location of the methoxy group [16]

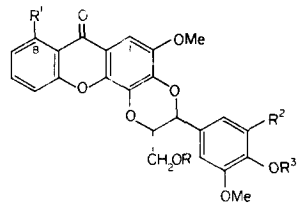
The third xanthone (**8**), mp 239 5–240 5°, exhibited shifts of the UV maxima with aluminium chloride and sodium methoxide (stable during the period of the experiment), but not in the presence of sodium acetate The ^1H NMR spectrum showed signals for two *ortho*-coupled protons (δ 7 17 and 6 53, *d*, J = 8 5 Hz) and a set of peaks (3H) between δ 7 60 and 7 20 from which the substitution pattern could not be deduced In the ^1H NMR spectrum of the diacetyl derivative one *meta*-coupled proton appeared (δ 7 90) and this was attributable to H-8 of a C-7 mono-substituted ring The downfield shift of this proton signal after acetylation also indicated that the C-7 substituent was originally a hydroxyl group The above data suggested either 1,7-dihydroxy-4-methoxy or 1,7-dihydroxy-2-methoxy substitution for the xanthone, with a definite preference for the former alternative (**8**) on the basis of the provided [15] chemical shifts of the *ortho*-coupled protons An attempt was made to confirm this by use of the Gibbs test However, it gave a positive result which indicated 1,7-dihydroxy-2-methoxy substitution This frequently used test has been reported to be sometimes misleading, therefore we checked its validity in the present case with model compounds, i e 1-hydroxy-4-methoxybenzene (hydroquinone monomethylether) and 2-hydroxy-5-methoxy methyl benzoate Both compounds gave a positive test, thus establishing that this test cannot be used to distinguish between these two possible substitution patterns and structure **8** was proposed for our compound

Four additional compounds were isolated from the fractions with lower R_f The UV data and mass fragmentation pattern (ions at m/z 274 and 180) of the first compound, $C_{24}H_{20}O_9$ ($[M]^+$, 452), suggested a xanthonolignoid structure [17] with a chelated hydroxyl group However, owing to its low solubility it did not furnish a significant ^1H NMR spectrum On acetylation it gave more soluble di- and triacetyl derivatives, both containing *inter alia* two methoxyl groups and one isolated aromatic proton From the available data the compound was identified with cadensin A (**9**), previously isolated by Castelão *et al* [17] from *Kielmeyera* and *Caraipa* spp Diacetyl- (**9a**) and triacetyl-cadensin A (**9b**) have not previously been described

The other three compounds constituted a mixture which could not be resolved by chromatographic methods After acetylation four products were separated, two of which were identified with diacetylsyringaresinol (**10**) and diacetylkielcorin (**11**) Kielcorin occurs in



	R	R^1	R^2	R^3
9	H	H	H	H
9a	Ac	H	H	Ac
9b	Ac	Ac	H	Ac
12	H	H	OMe	H
12a	Ac	Ac	OMe	Ac



	R	R	R^2	R^5
11	Ac	H	H	Ac
13	H	OH	OMe	H
13a	Ac	OH	OMe	Ac
13b	Ac	OAc	OMe	Ac

Kielmeyera and *Caraipa* spp [17], as well as in four *Hypericum* spp [18] The last two products, $C_{29}H_{26}O_{10}$ and $C_{31}H_{28}O_{11}$, were clearly the diacetyl and the triacetyl derivatives, respectively, of the same compound, $C_{25}H_{22}O_8$ (^{1}H NMR evidence) Other outstanding features of the ^{1}H NMR spectra were *inter alia* singlets for three methoxyl groups and for one isolated aromatic proton The mass fragmentation pattern of the diacetyl derivative was similar to those of **9a** and **11** (Table 1), and suggested a xanthonolignoid structure which possessed, with respect to cadensin A, an additional methoxyl in the C_9-unit The third known [17] xanthonolignoid, cadensin B (**12**), has very similar UV and mass spectral data, but significant differences were observed in the aromatic region of the ^{1}H NMR spectra of the triacetyl derivatives In fact, triacetylcadensin B (**12a**) is reported to exhibit two one proton singlets (δ 7 07 and 6 69) attributed to H-6′ and H-3′ respectively, while in our compound one two-proton singlet (δ 6 60) was present Notably, the chemical shift of these protons was comparable to the chemical shift of the aromatic protons of diacetylsyringaresinol (δ6 57, 2H) Therefore for our compound ($C_{25}H_{22}O_8$) we propose the structure **13** and the name of cadensin C

Table 1 Mass spectral fragmentation patterns of diacetylxanthonolignoids

Ion		**11**	**9a**	**13a**
$[M]^+$		520 (96)	536 (70)	566 (27)
$[M-CH_2=CO]^+$	(a)	478 (38)	494 (25)	524 (30)
$[(a)-MeCOOH]^+$	(b)	418 (58)	434 (95)	464 (12)
$[(b)-15]^+$		403 (5)	419 (14)	449 (5)
$[M-ArCH_2]^+$		341 (15)	357 (13)	357 (9)
$[(a)-ArC\equiv C-CH_2OAc]^+$	(x)	258 (34)	274 (100)	274 (14)
$[(x)-Me]^+$		243 (11)	259 (49)	259 (7)
$[(x)-CHO]^+$		229 (19)	245 (13)	245 (11)
$[ArCH=CH-CH_2OAc]^+$	(y)	222 (100)	222 (95)	252 (100)
$[ArCH_2]^+$	(c)	179 (68)	179 (16)	209 (40)
$[(y)-60]^+$		162 (43)	162 (32)	192 (35)
$[(c)-CH_2=CO]^+$		137 (19)	137 (10)	167 (22)

DISCUSSION

Hypericoideae include three tribes, Vismieae, Cratoxyleae and Hypericeae Although Engler [1] considers the Hypericoideae to be a subfamily of the Guttiferae, for Hutchinson [19] the taxon represents a separate family Xanthones, the characteristic secondary metabolites of Guttiferae, occur in Cratoxyleae [20] and Hypericeae [21], as well as in Vismieae (*Psorospermum* [9], *Harungana* [9] and now *Vismia*) Moreover, xanthonolignoids are found both in Kielmeyeroideae (Guttiferae) [17] and in Hypericoideae (*Hypericum* [18] and now in *Vismia*) All these findings recommend the inclusion of the Hypericoideae in the family Guttiferae

The isolation of 1,5-dihydroxy-8-methoxyxanthone (**7**) and of 1,7-dihydroxy-4-methoxyxanthone (**8**) is exceptional, because 1,4-substitution (or the equivalent 5,8 alternative) in the form of 1,3,4,5, 1,3,5,8, 1,2,3,4,7 or 1,3,4,5,8 has until now been found only in xanthones from the family Gentianaceae [12, 22] Finally, the co-occurrence of xanthones, xanthonolignoids and syringaresinol in *Vismia* is of importance from the biosynthetic view-point

EXPERIMENTAL

Plant material The roots of *V guaramirangae* Huber were collected in Dec 1979 in Brazil (Serra de Pacatuba, near Fortaleza, Ceará) from the plant used as the source of berries and barks in the previous studies [9, 4]

Extraction and fractionation of the root bark Air-dried finely ground bark (0 5 kg) of the roots was extracted with cold EtOH (twice) and the extracts evaporated Part (2 2 g) of the residue (RB, 60 g) was chromatographed on Si gel to give four subfractions RB_1 ($CHCl_3$), RB_2 ($CHCl_3$–MeOH, 49 1), RB_3 ($CHCl_3$–MeOH, 19 1), RB_4 ($CHCl_3$–MeOH, 4 1) On extended purification RB_1 gave vismiaphenone A (60 mg), vismiaphenone C (100 mg), chrysophanic acid (95 mg) and a mixture of triglycerides, RB_2 gave γ-hydroxyanthrone A_3 (120 mg) and RB_3 gave γ-hydroxyferruginin A (234 mg) RB_4 was not further examined

Extraction and fractionation of the root wood Air-dried finely ground wood (3 kg) of the roots was extracted with cold C_6H_6 ($\times$ 3) and EtOH (twice) successively The last extract was not further examined Part (13 g) of the residue from the C_6H_6 extract (22 g) was dissolved in Et_2O–EtOAc (1 1) and washed successively with 10% aq $NaHCO_3$, 10% aq Na_2CO_3, and 1 M NaOH The residual organic layer was evaporated (5 8 g, residue A) The $NaHCO_3$, Na_2CO_3 and NaOH solns were separately acidified (2 M HCl) and extracted with Et_2O–EtOAc Evaporation of the solvents yielded three residues, B (0 37 g), C (2 60 g) and D (2 65 g), respectively During the Na_2CO_3 and the NaOH extraction a dark-brown ppt (1 3 g) was discarded

A portion (1 7 g) of residue A was chromatographed on Si gel yielding the following useful fractions with the indicated solvents C_6H_6 (A_1), C_6H_6–EtOAc (19 1, A_2) Chromatography on Si gel of B (C_6H_6–EtOAc, 4 1) gave 3-hydroxy-2-methoxyxanthone (90 mg) Chromatography on Si gel of C yielded the following fractions with the indicated solvents C_6H_6–EtOAc (4 1, C_1, C_2, C_3, C_4, C_5), C_6H_6–EtOAc (1 1, C_6, C_7) Chromatography on Si gel of D with the indicated solvent gave the following fractions C_6H_6 (D_1), C_6H_6–EtOAc (19 1, D_2 D_3), C_6H_6–EtOAc (4 1, D_4, D_5, D_6), C_6H_6–EtOAc (1 1, D_7)

Crystallization of A_1 (190 mg) from Me_2CO gave 1-hydroxy-7-methoxyxanthone (140 mg) and of A_2 (120 mg) from heptane, 2-methoxyxanthone (96 mg) C_1 (201 mg) showed the presence of

fatty acids and small quantities of 1-hydroxy-7-methoxyxanthone and 2-methoxyxanthone C_2 was washed with cold CCl_4 and crystallized from C_6H_6 yielding 1,3-dihydroxy-2-methoxyxanthone (291 mg) Chromatography on Si gel of C_3 (235 mg) with $CHCl_3$ gave 1,5-dihydroxy-3-methoxyxanthone (65 mg), 2-hydroxyxanthone (130 mg) and 1,7-dihydroxy-4-methoxyxanthone (40 mg) successively

C_4 (260 mg) was dissolved in Et_2O–EtOAc and washed with 10% aq Na_2CO_3 and 1 M NaOH The two aq solns were separately acidified (2 M HCl), extracted and evaporated giving two residues Crystallization of the first one from MeOH gave 3-hydroxy-2-methoxyxanthone (160 mg), crystallization of the second one from CH_2Cl_2–heptane yielded 2-hydroxy-1-methoxyxanthone (60 mg) C_5 (310 mg) was washed with cold CCl_4 and crystallized from $CHCl_3$ giving 1,5-dihydroxy-4-methoxyxanthone (180 mg), the CCl_4 washings showed two spots on TLC corresponding to 1,5-dihydroxy-4-methoxyxanthone and to 3-hydroxy-2-methoxyxanthone C_6 (210 mg) contained 'impure' cadensin A, while C_7 (270 mg) contained 'impure' cadensin C Chromatography of D_1 (200 mg) on Si gel with C_6H_6–$CHCl_3$ (1 1) gave chrysophanic acid (55 mg) and 1-hydroxy-7-methoxyxanthone D_2 (400 mg) was washed with CCl_4 and crystallized from MeOH giving 1,7-dihydroxyxanthone (210 mg), the CCl_4 washings were evaporated and crystallized from C_6H_6 yielding 1,3-dihydroxy-2-methoxyxanthone (124 mg) Crystallization of D_3 (220 mg) from CH_2Cl_2 gave 1,5-dihydroxy-3-methoxyxanthone (170 mg) D_4 (560 mg) was chromatographed on Si gel with $CHCl_3$ giving 2-hydroxy-1-methoxyxanthone (230 mg), 3-hydroxy-2-methoxyxanthone (30 mg), 2-hydroxyxanthone (150 mg) and 1,7-dihydroxy-4-methoxyxanthone (75 mg) successively Crystallization of D_5 (260 mg) from $CHCl_3$ gave 1,5-dihydroxy-8-methoxyxanthone (230 mg) D_6 (250 mg) was washed with Me_2CO the insoluble part of which was found to be constituted of pure cadensin A (180 mg) D_7 (400 mg) was washed with MeOH the insoluble part of which was found to be constituted of 'impure' cadensin C

γ-Hydroxyferruginin A (**1**), *γ-hydroxyanthrone* A_3 (**2**), *vismiaphenone A* (**3**), *chrysophanic acid and syringaresinol* These compounds were identified by comparison (^{1}H NMR, TLC, mmp) with authentic specimens previously isolated in this laboratory

Vismiaphenone C Oil, UV λ_{max}^{MeOH} nm 257, 298, λ_{max}^{NaOAc} nm unchanged, $\lambda_{max}^{AlCl_3}$ nm 270, 334 (after 20 min), ^{1}H NMR ($CDCl_3$) δ 8 42 (2H, *s*), 7 75–7 30 (5H, *m*), 5 15 (2H, *br t*, J = 7 Hz), 3 70 (3H, *s*), 3 30 (4H, *br t*, J = 7 Hz), 1 70 (12 H, *br s*), $\Delta\delta = \delta$ (C_5D_5N) $-\delta$($CDCl_3$) = +0 32 (CH_2), EIMS (probe) 70 eV, *m/z* (rel int) 380 $[M]^+$ (100), 365 $[M-15]^+$ (32), 325 $[M-55]^+$ (22), 324 $[M-56]^+$ (20), 309 (8), 303 $[M-77]^+$ (8), 247 (10), 105 $[C_6H_5-C\equiv O]^+$ (25), 77 (32)

Vismiaphenone C (55 mg) in $CHCl_3$ (4 ml) and TFA (1 ml) was left to stand overnight Evaporation and chromatographic purification (Si gel, C_6H_6) afforded oily dicyclovismiaphenone C (**5**), ^{1}H NMR ($CDCl_3$) δ 7 90–7 65 (2H, *m*), 7 50–7 25 (3H, *m*), 3 73 (3H, *s*), 2 70 (4H, *t*, J = 7 Hz), 1 70 (4H, *t*, J = 7 Hz), 1 08 (12H, *s*)

1-Hydroxy-7-methoxyxanthone Mp 132–133° (white needles, CH_2Cl_2–C_7H_{16}) (lit [23] 130–131°) UV λ_{max}^{MeOH} nm 261, 288, 383, $\lambda_{max}^{AlCl_3}$ nm 279, 309, 442, ^{1}H NMR ($CDCl_3$) δ 12 6 (1H, *s*), 7 70–7 20 (4H, *m*), 6 83 (1H, *dd*, J = 8 and 2 Hz, H-4), 6 73 (1H, *dd*, J = 8 and 2 Hz, H-2), 3 87 (3H, *s*), EIMS (probe) 70 eV, *m/z* (rel int) 242 $[M]^+$ (100), 227 (47), 213 (29), 212 (29), 199 (38), 171 (67), 143 (27), 115 (62) Acetylation gave 1-acetoxy-7-methoxyxanthone, mp 188–90° (white needles, C_7H_{16}) ^{1}H NMR ($CDCl_3$) δ 7 75–7 2 (5H, *m*), 6 93 (1H, *dd*, J = 8 and 2 Hz, H-4), 3 87 (3H, *s*), 2 50 (3H, *s*)

2-Methoxyxanthone Mp 128–130° (light yellow needles, C_7H_{16}) (lit [24] 130°) UV λ_{max}^{MeOH} nm 238, 250, 298, 360, λ_{max}^{NaOMe} nm unchanged, ^{1}H NMR ($CDCl_3$) δ 8 35 (1H, *dd*, J = 8 and 2 Hz, H-1), 7 80–7 20 (6H, *m*), 3 90 (3H, *s*)

1,3-Dihydroxy-2-methoxyxanthone (**6**) Mp 176–178° (yellow-orange needles, C_6H_6) UV λ_{max}^{MeOH} nm 250, 313, 349, (sh), λ_{max}^{NaOAc} nm 245, 371, unchanged with H_3BO_3, λ_{max}^{NaOMe} nm 245, 272, 362, unchanged during the period of the expt, $\lambda_{max}^{AlCl_3}$ nm 246, 264, 338, 412, ^{1}H NMR ($CDCl_3$) δ 13 0 (1H, *s*), 8 18 (1H, *dd*, J = 8 and 2 Hz, H-8), 7 75–7 05 (3H, *m*), 6 63 (1H, *br s*, OH), 6 45 (1H, *s*, H-4), 4 0 (3H, *s*), EIMS (probe) 70 eV, *m/z* (rel int) 258 $[M]^+$ (87), 244 (74), 241 (23), 229 (6), 228 (9), 215 (100), 211 (11), 200 (2), 187 (4), 184 (4), 171 (3) Acetylation gave 1,3-diacetoxy-2-methoxyxanthone mp 144–145° (light yellow prisms, CH_2Cl_2–C_7H_{16}), ^{1}H NMR ($CDCl_3$) δ 8 20 (1H, *dd*, J = 8 and 2 Hz, H-8), 7 80–7 20 (3H, *m*), 7 18 (1H, *s*, H-4), 3 88 (3H, *s*), 2 50 (3H, *s*), 2 38 (3H, *s*)

Methylation gave 1,2,3-trimethoxyxanthone, mp 127–128° (white needles, CH_2Cl_2–C_7H_{16}) (lit [13] 129–130°), UV λ_{max}^{MeOH} nm 254, 278, 301, 332, ^{1}H NMR ($CDCl_3$) δ 8 18 (1H, *dd*, J = 8 and 2 Hz, H-8), 7 70–7 10 (3H, *m*), 6 63 (1H, *s*, H-4), 4 02 (3H, *s*), 3 95 (3H, *s*), 3 90 (3H, *s*)

1,5-Dihydroxy-3-methoxyxanthone (*mesuaxanthone*) Mp 273–275° (yellow needles, EtOH) (lit [25] 270–272°) UV λ_{max}^{MeOH} nm 244, 308, 355, λ_{max}^{NaOAc} nm 246, 276, 306, $\lambda_{max}^{AlCl_3}$ nm 266, 336, 408 ^{1}H NMR (DMSO–$CDCl_3$, 2 1) δ 12 80 (1H, *s*), 10 2 (1H, *br s*, OH), 7 75–7 0 (3H, *m*), 6 55 (1H, *d*, J = 2 5 Hz, H-4), 6 27 (1H, *d*, J = 2 5 Hz, H-2), 3 90 (3H, *s*) Acetylation gave the corresponding mono- and di-acetyl derivative 1-Hydroxy-3-methoxy-5-acetoxyxanthone, mp 191–194° (light yellow needles, CH_2Cl_2–C_7H_{16}), UV λ_{max}^{MeOH} nm 236, 250 (sh), 303, 345 (sh), UV $\lambda_{max}^{AlCl_3}$ nm 234, 265, 328, 398, ^{1}H NMR ($CDCl_3$) δ 12 62 (1H, *s*), 8 08 (1H, *dd*, J = 2 7 and 6 8 Hz, H-8), 7 70–7 10 (2H, *m*), 6 35 (2H, *s*, H-2, H-4), 3 87 (3H, *s*), 2 43 (3H, *s*) 1,5-Diacetoxy-3-methoxyxanthone ^{1}H NMR ($CDCl_3$) δ 8 08 (1H, *dd*, J = 2 8 and 6 8 Hz, H-8), 7 70–7 10 (2H, *m*), 6 73 (1H, *d*, J = 2 5 Hz, H-2), 6 55 (1H, *d*, J = 2 5 Hz, H-4), 3 90 (3H, *s*), 2 50 (6H, *s*)

2-Hydroxyxanthone Mp 240–241° (yellow needles, $CHCl_3$) (lit [13] 240–242°) UV λ_{max}^{MeOH} nm 236, 250 (sh), 300, 362, unchanged with $AlCl_3$ or NaOAc, ^{1}H NMR (DMSO–$CDCl_3$) δ 8 15 (1H, *dd*, J = 2 and 8 Hz, H-8), 7 85–7 05 (6H, *m*), EIMS (probe) 70 eV, *m/z* (rel int) 212 $[M]^+$ (100), 184 (20), 155 (10), 128 (15) Methylation gave 2-methoxyxanthone, identical to the natural product

1,7-Dihydroxy-4-methoxyxanthone (**8**) Mp 239 5–240 5° (orange needles, CH_2Cl_2–C_7H_{16}) UV λ_{max}^{MeOH} nm 236, 266, 323, 397, unchanged with NaOAc, λ_{max}^{NaOMe} nm 256, 275 (sh), 430, unchanged during the time, $\lambda_{max}^{AlCl_3}$ nm 238, 286, 355, 465, Gibbs test λ_{max} 677 nm (hydroquinone monomethyl ether, λ_{max} 600 nm, 2-hydroxy-5-methoxy-methylbenzoate, λ_{max} 645 nm), ^{1}H NMR (DMSO–$CDCl_3$) δ 12 0 (1H, *br s*), 7 60–7 20 (3H, *m*), 7 17 (1H, *d*, J = 8 5 Hz, H-3), 6 53 (1H, *d*, J = 8 5 Hz, H-2), 3 88 (3H, *s*), ^{1}H NMR (C_5D_5N) δ 7 95 (1H, *d*, J = 2 Hz, H-8), 7 60–7 50 (2H, *m*), 7 26 (1H, *d*, J = 8 5 Hz, H-3), 6 80 (1H, *d*, J = 8 5 Hz, H-2), 3 83 (3H, *s*), EIMS (probe) 70 eV, *m/z* (rel int) 258 $[M]^+$ (41), 243 (100), 229 (4), 215 (13), 187 (6) Acetylation gave 1,7-diacetoxy-4-methoxyxanthone mp 173–176° (white needles), CH_2Cl_2–C_7H_{16}), ^{1}H NMR ($CDCl_3$) δ 7 90 (1H, *dd*, J = 2 4 and 1 Hz, H-8), 7 65–7 40 (2H, *m*), 7 15 (1H, *d*, J = 8 5 Hz, H-3), 6 85 (1H, *d*, J = 8 5 Hz, H-2), 3 97 (3H, *s*), 2 43 (3H, *s*), 2 30 (3H, *s*) Methylation gave the corresponding mono- and di-methyl derivatives 1-Hydroxy-4,7-dimethoxyxanthone mp 188–189° (yellow needles, CH_2Cl_2–C_7H_{16}), UV λ_{max}^{MeOH} nm 236, 265, 322, 392, $\lambda_{max}^{AlCl_3}$ nm 240, 288, 360 (sh), 465, Gibbs test λ_{max} 684 nm, ^{1}H NMR ($CDCl_3$) δ 12 05 (1H, *s*), 7 62 (1H, *d*, J = 2 5 Hz, H-8), 7 50–7 20 (2H, *m*), 7 18 (1H, *d*, J = 9 Hz, H-3), 6 68 (1H, *d*, J

= 9 Hz, H-2), 3 95 (3H, *s*), 3 90 (3H, *s*) 1,4,7-Trimethoxyxanthone mp 158–159° (light yellow needles, CH_2Cl_2–C_7H_{16}), UV λ_{max}^{MeOH} nm 238, 260, 320, 378, ^{1}H NMR ($CDCl_3$) δ7 69 (1H, *d*, *J* = 2 5 Hz, H-8), 7 48 (1H, *d*, *J* = 8 5 Hz, H-5), 7 23 (1H, *dd*, *J* = 8 5 and 2 5 Hz, H-6), 7 13 (1H, *d*, J = 9Hz, H-3), 6 68 (1H, *d*, *J* = 9 Hz, H-2), 3 97 (6H, *s*), 3 90 (3H, *s*)

3-*Hydroxy*-2-*methoxyxanthone* Mp 233–235° subl (white prisms, MeOH) (lit [26] 225–230°) UV λ_{max}^{MeOH} nm 249, 276 (sh), 311, 347, unchanged with $AlCl_3$, UV λ_{max}^{NaOAc} nm 245, 270 (sh), 379, negative Gibbs test, ^{1}H NMR (DMSO–$CDCl_3$, 2 1) δ10 60 (1H, *br s*, OH), 8 13 (1H, *dd*, *J* = 8 and 2 Hz, H-8), 7 90–7 25 (3H, *m*), 7 50 (1H, *s*, H-1), 6 90 (1H, *s*, H-4), 3 90 (3H, *s*), EIMS (probe), 70 eV, *m/z* (rel int) 242 $[M]^+$ (100), 227 (72), 213 (25), 199 (44), 171 (37), 150 (52), 137 (32) Acetylation gave 3-acetoxy-2-methoxyxanthone, mp 189–191° (light yellow needles, CH_2Cl_2–C_7H_{16}), ^{1}H NMR ($CDCl_3$) δ8 28 (1H, *m*, H-8), 7 76 (1H, *s*, H-1), 7 90–7 30 (3H, *m*), 7 23 (1H, *s*, H-4), 3 93 (3H, *s*), 2 35 (3H, *s*) Methylation gave 2,3-dimethoxyxanthone, mp 155–159° (light yellow prisms, CH_2Cl_2–C_7H_{16}), λ_{max}^{MeOH} nm 250, 270 (sh), 304, 345, ^{1}H NMR ($CDCl_3$) δ8 30 (1H, *m*, H-8), 7 80–7 20 (3H, *m*), 7 63 (1H, *s*, H-1), 6 87 (1H, *s*, H-4), 4 0 (6H, *s*)

2-*Hydroxy*-1-*methoxyxanthone* Mp 173–174° (yellow needles, CH_2Cl_2–C_7H_{16}) (lit [23] 171–173°) UV λ_{max}^{MeOH} nm 242, 256, 370, unchanged with NaOAc or $AlCl_3$, λ_{max}^{NaOMe} nm 254, 275, 427, ^{1}H NMR ($CDCl_3$–CD_3OD, 19 1) δ8 30 (1H, *dd*, *J* = 8 and 2 Hz), 7 8–7 1 (5H, *m*), 3 98 (3H, *s*), EIMS (probe) 70 eV, *m/z* (rel int) 242 $[M]^+$ (43), 224 (100), 213 (21), 199 (43), 196 (28), 184 (8), 168 (56) Acetylation gave 2-acetoxy-3-methoxyxanthone, mp 142–145° (light yellow prisms, MeOH), ^{1}H NMR ($CDCl_3$) δ8 33 (1H, *dd*, *J* = 8 and 2 Hz, H-8), 7 90–7 10 (5H, *m*), 3 98 (3H, *s*)

1,5-*Dihydroxy*-8-*methoxyxanthone* (**7**) Mp 230–231° (yellow needles, $CHCl_3$) UV λ_{max}^{MeOH} nm 252, 336, 382 (sh), unchanged with NaOAc, λ_{max}^{NaOMe} nm 252, 319, 364, 415 (sh) unchanged during the time, $\lambda_{max}^{AlCl_3}$ nm 272, 384, 435 (sh), Gibbs test, λ_{max} 678 nm, ^{1}H NMR ($CDCl_3$–CD_3OD, 9 1) δ12 97 (1H, *s*), 7 56 (1H, *dd*, *J* = 8 5 and 8 Hz, H-3), 7 26 (1H, *d*, *J* = 9 Hz, H-6), 6 96 (1H, *dd*, *J* = 8 5 and 1 5 Hz, H-4), 6 76 (1H, *dd*, *J* = 8 and 1 5 Hz, H-2), 6 66 (1H, *d*, *J* = 9 Hz, H-7), 3 85 (3H, *s*), EIMS (probe) 70 eV, *m/z* (rel int) 258 $[M]^+$ (83), 240 (100), 229 (28), 212 (50), 201 (38), 200 (41), 187 (6), 184 (5), 171 (5) Acetylation gave the corresponding mono- and di-acetyl derivatives 1-Hydroxy-5-acetoxy-8-methoxyxanthone, mp 200–203° (light yellow needles, CH_2Cl_2–C_7H_{16}), ^{1}H NMR ($CDCl_3$) δ12 77 (1H, *s*), 7 53 (1H, *dd*, *J* = 8 5 and 8 Hz, H-3), 7 43 (1H, *d*, *J* = 9 Hz, H-6), 6 95–6 65 (3H, *m*), 4 03 (3H, *s*), 2 42 (3H, *s*) 1,5-Diacetoxy-8-methoxyxanthone, mp 185–186° (white needles, CH_2Cl_2–C_7H_{16}), ^{1}H NMR ($CDCl_3$) δ7 65 (1H, *dd*, *J* = 8 8 and 7 6 Hz, H-3), 7 35 (1H, *d*, *J* = 9 2 Hz, H-6), 7 28 (1H, *dd*, *J* = 8 8 and 1 5 Hz, H-4), 6 95 (1H, *dd*, *J* = 7 6 and 1 5 Hz, H-2), 6 73 (1H, *d*, *J* = 9 2 Hz, H-7), 3 97 (3H, *s*), 2 46 (3H, *s*), 2 38 (3H, *s*) Methylation gave 1,5,8-trimethoxyxanthone mp 221–222° (white crystals, CH_2Cl_2–C_7H_{16}), UV λ_{max}^{MeOH} nm 246, 316, 360, ^{1}H NMR ($CDCl_3$) δ7 53 (1H, *dd*, *J* = 8 5 and 8 Hz, H-3), 7 08 (1H, *d*, *J* = 9 Hz, H-6), 7 05 (1H, *dd*, *J* = 8 and 1 5 Hz, H-4), 6 77 (1H, *dd*, *J* = 8 5 and 1 5 Hz, H-2), 6 63 (1H, *d*, *J* = 9 Hz, H-7), 3 95 (3H, *s*), 3 90 (6H, *s*)

1,7-*Dihydroxyxanthone* (*euxanthone*) Mp 240–241° (yellow needles, $CHCl_3$) (lit [27] 240–241°) UV λ_{max}^{MeOH} nm 238, 261, 288, 315 (sh), 388, unchanged with NaOAc, λ_{max}^{NaOMe} nm 251, 345, 424, $\lambda_{max}^{AlCl_3}$ 279, 310, 449 Acetylation gave the corresponding mono- and di-acetyl derivatives 1-Hydroxy-7-acetoxyxanthone, mp 159–162° (yellow-green needles, CH_2Cl_2–C_7H_{16}), ^{1}H NMR ($CDCl_3$) δ12 40 (1H, *s*), 7 95 (1H, *d*, *J* = 1 5 Hz), 7 60 (1H, *dd*, *J* = 8 and 7 5 Hz, H-3), 7 50 (2H, *m*), 6 93 (1H, *dd*, *J* = 7 5 and 1 5 Hz, H-4), 6 80 (1H, *dd*, *J* = 8 and 1 5 Hz, H-2), 2 35 (3H, *s*) 1,7-Diacetoxyxanthone mp 185–186° (white prisms, CH_2Cl_2–C_7H_{16}), ^{1}H NMR ($CDCl_3$) δ7 90 (1H, *d*, *J* = 1 5 Hz, H-8), 7 70 (1H, *dd*, *J* = 7 5 and 8 Hz, H-3), 7 43 (2H, *m*), 7 33 (1H, *dd*, *J* = 1 5 and 8 Hz, H-2), 6 97 (1H, *dd*, *J* = 1 5 and 7 5 Hz, H-4), 2 47 (3H, *s*), 2 30 (3H, *s*)

Cadensin A (**9**) **9** was obtained pure from the fraction D_6, mp 267–270° dec (lit [17] 264–267°), yellow prisms UV λ_{max}^{MeOH} nm 256, 277 (sh), 321, 376, unchanged with NaOAc or H_3BO_3, λ_{max}^{NaOMe} nm 243, 284, 399, $\lambda_{max}^{AlCl_3}$ 237, 267, 290 (sh), 348, 431, EIMS (probe) 70 eV *m/z* (rel int) 452 $[M]^+$ (12), 434 (5), 420 (20), 377 (6), 315 (5), 274 (90), 259 (53), 245 (9), 241 (5), 231 (33), 203 (18), 180 (67), 173 (7), 162 (14), 152 (12), 137 (100), 124 (77) Cadensin A (300 mg) from fractions C_6 and D_6 was acetylated (C_5H_5N–Ac_2O) and the resulting material purified on Si gel with C_6H_6–EtOAc (4 1) giving diacetylcadensin A (60 mg) and triacetylcadensin A (160 mg) *Diacetylcadensin A* (**9a**) mp 227–229°, yellow prisms (CH_2Cl_2–EtOH), UV λ_{max}^{MeOH} nm 256, 315, 374, $\lambda_{max}^{AlCl_3}$ nm 232, 266, 332, 428, ^{1}H NMR ($CDCl_3$) δ12 63 (1H, *s*), 7 50 (1H, *dd*, *J* = 8 5 and 8 Hz, H-6), 7 23 (1H, *s*, H-1), 7 05–6 70 (5H, *m*) 5 05 (1H, *br d*, *J* = 7 Hz), 4 60–4 10 (3H, *m*), 3 90 (3H, *s*), 3 83 (3H, *s*), 2 22 (3H, *s*), 2 08 (3H, *s*), EIMS (probe) 70 eV Table 1 *Triacetylcadensin A* (**9b**) mp 232–234° (white prisms, EtOH), UV λ_{max}^{MeOH} nm 253, 283, 315, 348 (sh), ^{1}H NMR ($CDCl_3$) δ7 63 (1H, *dd*, *J* = 8 5 and 8 Hz, H-6), 7 56–6 87 (5H, *m*), 7 26 (1H, *s*, H-1), 5 07 (1H, *br d*, *J* = 7 Hz), 4 65–4 05 (3H, *m*), 3 92 (3H, *s*), 3 83 (3H, *s*), 2 37 (3H, *s*), 2 29 (3H, *s*), 2 05 (3H, *s*), EIMS (probe) 70 eV, *m/z* (rel int) 578 $[M]^+$ (9), 536 (40), 494 (15), 434 (32), 419 (5), 406 (5), 357 (7), 274 (34), 259 (21), 245 (8), 244 (10), 231 (10), 222 (100), 180 (3), 179 (6), 162 (7), 151 (25), 137 (27)

Acetylation of 'impure' cadensin C Part of the material (480 mg) from fractions C_7 and D_7 was acetylated (C_5H_5N–Ac_2O) and the resulting material was separated on Si gel (C_6H_6–EtOAc, 4 1) Diacetylcadensin C (29 mg), diacetylkielcorin (27 mg), triacetylcadensin C (86 mg) and diacetylsyringaresinol (50 mg) were successively eluted Further amounts of the first three compound were obtained by prep TLC of the intermediate fractions

Diacetylsyringaresinol (**11**) ^{1}H NMR ($CDCl_3$) δ6 57 (4H), 4 70 (2H, *d*, *J* = 4 4 Hz, H-1, H-1'), 4 35–3 65 (4H, *dq*, *J* = 9 2, 7 2 and 3 8 Hz, H-3, H-4, H-3', H-4') 3 80 (12 H, *s*), 3 27–2 90 (2H, *m*, *J* = 7 2, 4 4 and 3 8 Hz), 2 30 (6H, *s*) The identification was completed by comparison (TLC, ^{1}H NMR, IR) with an authentic sample *Diacetylkielcorin* (**11**) mp 203–206° (lit [17] 206–208°) white microcrystals (EtOH), ^{1}H NMR ($CDCl_3$) δ8 30 (1H, *dd*, *J* = 8 and 2 Hz, H-8), 7 70–6 90 (6H, *m*), 7 35 (1H, *s*, H-1), 5 05 (1H, *br d*, *J* = 7 Hz), 4 60–4 05 (3H, *m*), 3 90 (3H, *s*), 3 80 (3H, *s*), 2 27 (3H, *s*), 2 03 (3H, *s*), EIMS (probe) 70 eV Table 1 *Diacetylcadensin C* (**13a**) mp 242–246°, yellow prisms (EtOH), UV λ_{max}^{MeOH} nm 248, 316, 369, $\lambda_{max}^{AlCl_3}$ nm 229, 265, 344, 428, ^{1}H NMR ($CDCl_3$) δ11 80 (1H, *s*), 7 42 (1H, *t*, *J* = 8 Hz, H-6), 7 20–6 60 (5H, *m*), 5 0 (1H, *br d*, *J* = 7 Hz), 4 60–4 0 (3H, *m*), 3 88 (3H, *s*), 3 73 (6H, *s*), 2 27 (3H, *s*), 2 0 (3H, *s*), EIMS (probe) 70 eV Table 1 *Triacetylcadensin C* (**13b**) mp 210–214°, white needles (EtOH), UV λ_{max}^{MeOH} nm 240, 316, 348 (sh), ^{1}H NMR ($CDCl_3$) 7 45 (1H, *dd*, *J* = 7 and 8 Hz, H-6), 7 25 (1H, *dd*, *J* = 8 and 2 Hz, H-5), 7 15 (1H, *s*, H-1), 6 90 (1H, *dd*, *J* = 7 and 2 Hz, H-7), 6 60 (2H, *s*, H-2', H-6'), 5 0 (1H, *br d*, *J* = 7 Hz), 4 60–4 05 (3H, *m*), 3 87 (3H, *s*), 3 75 (6H, *s*), 2 35 (3H, *s*), 2 20 (3H, *s*), 1 95 (3H, *s*), EIMS (probe) 70 eV *m/z* (rel int) 608 $[M]^+$ (14), 566 (22), 524 (38), 464 (10), 365 (10), 357 (8), 274 (14), 259 (14), 252 (100), 245 (12), 244 (16), 231 (8), 210 (32), 209 (34), 192 (30), 167 (24)

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