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TRITERPENOIDS AND COUMARINS FROM THE LEAVES OF *CALOPHYLLUM CORDATO-OBLONGUM*

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Key Word Index—*Calophyllum cordato-oblongum*; Guttiferae; leaves; 28-hydroxy-D:A-friedo-oleanan-3-one; canophyllol; cordatolide A; cordatolide B; oblongulide; pyranocoumarins.

Abstract—The hot light petrol extractives of the leaves of *Calophyllum cordato-oblongum* gave D:A-friedo-oleanan-3-one, 28-hydroxy-D:A-friedo-oleanan-3-one (canophyllol) and three new coumarins: cordatolides A and B and oblongulide.

INTRODUCTION

Bark and timber extracts of *Calophyllum cordatooblongum* Thw. gave [1] cordato-oblongic acid (**1**), 1,6-dihydroxy-5-methoxyxanthone, 4-hydroxyxanthone, 3-hydroxy-4-methoxyxanthone, cordato-oblonguxanthone (**2**), 1,5,6-trihydroxyxanthone, jacareubin (**3**) and scriblitifolic acid (**4**). The leaves of *C. cordato-oblongum* have now been investigated and have been shown to contain coumarins and triterpenoids.

RESULTS AND DISCUSSION

The hot light petrol extracts of the leaves of *C. cordato-oblongum* yielded D:A-friedo-oleanan-3-one, 28-hydroxy-D:A-friedo-oleanan-3-one (canophyllol) and three new coumarins named cordatolide A (**5**), cordatolide B (**6**) and oblongulide (**7**).

The first two coumarins were found to be isomeric having the formula $C_{20}H_{22}O_5$. Both had similar mass spectral fragmentations with the base peaks each at m/z 327 $[M - Me]^+$. Their IR spectra showed the presence of hydroxyl, carbonyl (coumarin) and olefinic groups. Comparison of the ^1H NMR spectral data (Table 1) suggested that cordatolides A and B are stereoisomers having the following structural features: –CH=CH–; Me–C=CH; –CHOH; $(Me)_2$–C–O; 2 × Me–CH–. The ^{13}C NMR chemical shifts of cordatolide A (see Fig. 1) confirmed the presence of: a conjugated carbonyl group, five methyl groups, four olefinic carbon atoms, six singlet aromatic carbon atoms and one tertiary carbon.

Acetylation of cordatolide B gave a monoacetate whilst oxidation (Cr_2O_3–pyridine, 5°) gave a ketone (**8**), $C_{20}H_{20}O_5$ ($[M]^+$, 340.1316), mp 165°, $[\alpha]_D$ −23.7° ($CHCl_3$). These data confirmed the presence of a –CHOH group in cordatolide B. Reduction of **8** with sodium borohydride gave a mixture, the components of which were separated and identified as cordatolides A and B.

Table 1. ^1H NMR data for compounds **5** and **6** ($CDCl_3$) [Coupling constants (Hz) are given in parentheses]

H No	Cordatolide A (**5**)	Cordatolide B (**6**)
3	5.48 *d* (10)	5.51 *d* (10)
4	6.58 *d* (10)	6.63 *d* (10)
6	3.93 *octet* (8)	4.30 *octet* (10)
7	2.00	1.9 *m*
8	4.65 *d* (7)	4.96 *d* (3)
11	5.86 *s*	5.90 *s*
Me-2	1.49 *s*	1.48 *s*
Me-6	1.43 *d* (3.5)	1.43 *d* (5)
Me-7	1.11 *d* (6.2)	1.15 *d* (7)
Me-12	2.55	2.56

Hence, cordatolides A and B had a similar skeleton and differed only in the stereochemistry of the –CHOH group. Cordatolide A on hydrogenation (palladium/charcoal) gave two products which were identified as deoxydihydrocordatolide (**9**), mp 247° ($[M]^+$ 328.1681, $C_{20}H_{24}O_4$), $[\alpha]_D$ +56.6° ($CHCl_3$) and deoxytetrahydrocordatolide (**10**) ($[M]^+$ 330.1835, $C_{20}H_{26}O_4$), $[\alpha]_D$ +44.5° ($CHCl_3$). The ready deoxygenation during catalytic hydrogenation showed that the hydroxyl group might be attached to a benzylic carbon atom. The ^1H NMR chemical shifts of the –CHOH (Table 1) for both cordatolides confirmed this. The formation of dihydro and tetrahydro derivatives showed the presence of two types of olefinic system in the cordatolides. The marked differences in the UV spectra of cordatolide A and the dihydro and tetrahydro derivatives showed that the olefinic systems are conjugated with the aromatic nucleus. In addition, the UV spectrum of deoxydihydrocordatolide was similar to those reported for a number of 5,7-dioxygenated coumarins. The absence

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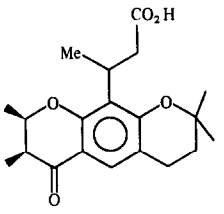
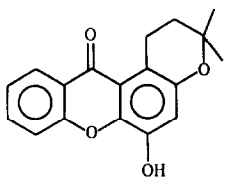


1 Cordato-oblongic acid



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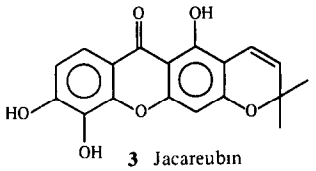
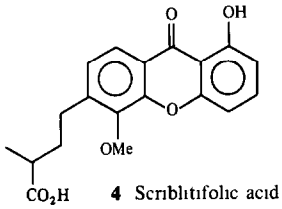
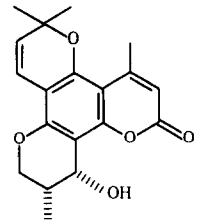


3 Jacareubin



4 Scriblitifolic acid



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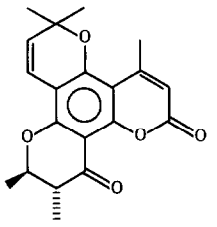

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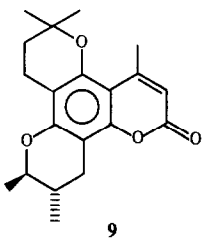

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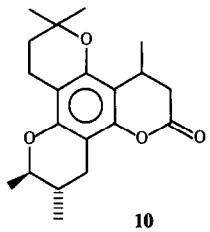

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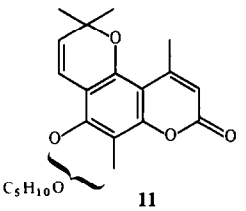

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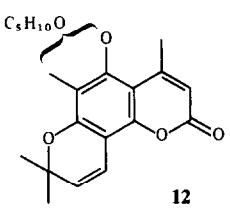

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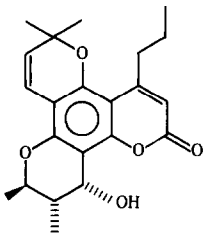

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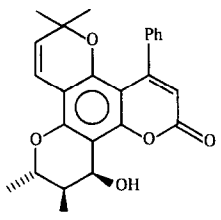

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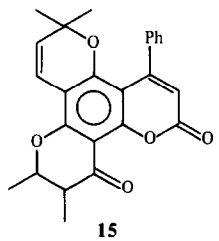

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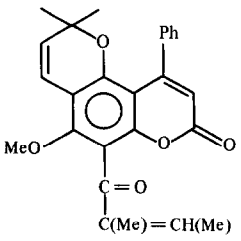

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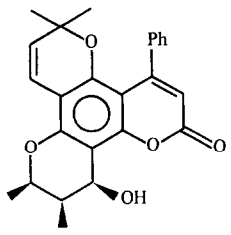

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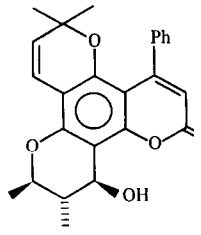

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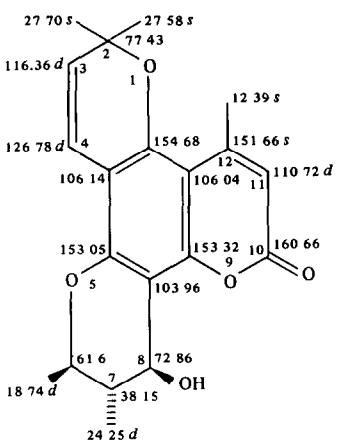
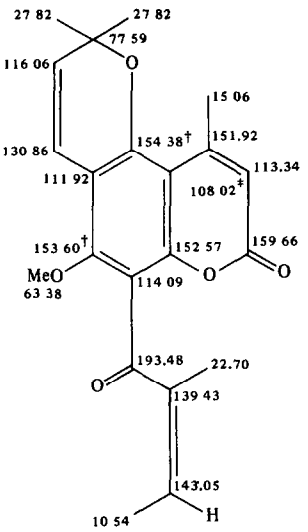


5 Cordatolide A



7 Oblongulide

Fig. 1 ^{13}C NMR data for compounds **5** and **7** ($CDCl_3$). †‡Not unambiguous assignments.

of any aromatic protons in the ^1H NMR spectra of the cordatolides and their derivatives showed that their aromatic rings are fully substituted.

The mass fragmentations of the cordatolides were typical of the compounds having the 2,2-dimethylchromene system where the $[M-15]^+$ peaks (*m/z* 327) were the base peaks due to formation of the stable benzopyrilium ion.

On the basis of the data presented, the skeleton of the cordatolides can be represented as either **11** or **12**. The $C_5H_{10}O$ part of structures **11** or **12** should be MeCH–CH–CH–OH since cordatolide A has two three-proton doublets for two methyl groups [δ1.43 (J = 3.5 Hz) and 1.11 (J = 6.2 Hz)] and the presence of the –CHOH group was shown earlier. Examination of molecular models for the acetate of cordatolide B having skeletons **11** and **12** showed that if cordatolide B had structure **6**, then the acetate group would have no effect on the chemical shifts of the gem-dimethyl group in the ^1H NMR spectrum of cordatolide B acetate. The observed data confirm that cordatolide B has structure **6**.

The stereochemical differences of cordatolides A and B have still to be elucidated. The coupling constants of H-6 and H-7 were found to be $J \sim 8$ Hz and $J \sim 10$ Hz for cordatolides A and B, respectively, indicating a *trans*-diaxial relationship in each case. The coupling constant for H-7 and H-8 for cordatolide A was found to be J = 7 Hz and the data are in agreement with the configuration shown by **5** for cordatolide A. The coupling constant for H-7 and H-8 for cordatolide B was found to be J = 3 Hz indicating an axial–equatorial geometry for these protons and, hence, cordatolide B has the relative stereochemistry shown in **6**. Thus, cordatolide B is 8-hydroxy-2,2,6,7-tetramethyl-7,8-dihydro-2H,6H,10H-benzo(1,2-*b*:3,4-*b*′:5,6-*b*″)tripyran-10-one (**6**) and cordatolide A is 8-hydroxy-2,2,6,7-tetramethyl-7,8-dihydro-2H, 6H, 10H-benzo (1,2-*b*:3,4-*b*′:5,6-*b*″) tripyran-10-one (**5**).

The third coumarin, oblongulide (**7**), was found to be a new dipyranone and is probably biogenetically related to the cordatolides. It was identified as 5-methoxy-2,2,10-trimethyl-6-(2-methyl-1-oxobut-2-enyl)-2H, 8H-benzo-(1,2-*b*:3,4-*b*′)dipyran-8-one (**7**) from the following data. High resolution mass spectral analysis gave $C_{21}H_{22}O_5$ as the formula for oblongulide. The mass fragmentations of oblongulide and of the cordatolides were typical of compounds having the 2,2-dimethylchromene system in that the $[M-15]^+$ peaks were base peaks due to the formation of the stable benzopyrilium ions. The IR spectrum of the oblongulide showed the presence of two types of carbonyl groups at IR ν_{max} cm^{-1}: 1735 (coumarin carbonyl) and 1665 (conjugated carbonyl). The UV of oblongulide was similar to those reported for a number of 5,7-dioxygenated coumarins. However, its IR spectrum showed the absence of hydroxyl group(s) unlike in the cordatolides (**5** and **6**). The ^1H NMR spectrum of oblongulide confirmed the presence of the following groups: 2 × Me (δ1.38), Me [δ1.86 (J_3 = 6.98 Hz, J_4 = 1.03 Hz)], Me [δ1.96 (J_4 = 1.33 Hz, J_5 = 1.03 Hz)], Me [δ2.56 (J_4 = 1.20 Hz)], –OMe (δ3.80), =CH [δ5.72 (J_3 = 10.06 Hz)], =CH [δ6.00 (J_4 = 1.20 Hz)], =CH [δ6.56 (J_3 = 10.06 Hz)], and =CH [δ6.46 (J_3 = 6.98 Hz, J_4 = 1.33 Hz)].

The ^{13}C NMR spectrum of oblongulide (see Fig. 1) showed that it has: (a) two carbonyl groups, (b) five methyl carbons (c) six aromatic carbons which are fully substituted, (d) six olefinic carbons, (e) one fully substituted aliphatic carbon and (f) one methoxyl carbon. Out of the olefinic carbons, two (at δ151.92 and 139.43) were found to be fully substituted whilst the others were found to be the =CH types from the undecoupled ^{13}C NMR spectrum of oblongulide.

Comparison of the ^1H NMR chemical shifts of cordatolide (Table 1) with the data for oblongulide showed that the latter also probably has the same pyranocoumarin skeleton (**11**). This accounts for 15 carbon atoms in oblongulide. Out of the remaining six carbon atoms, five are probably present in a C_5 chain and one as a methoxyl group (δ3.80). The side chain has a conjugated carbonyl group (δ193.48), two methyl groups of the type

Me–C= (δ1.86 and 1.96) and a =CH group (δ6.46). It is attached to the aromatic carbon as indicated in **7** since oblongulide (**7**) co-occurred with **5** and **6** to which it is possibly biogenetically related. The stereochemistry around the olefinic carbon atoms is as indicated in **7** and was derived from the coupling constants of the Me–H (J_4 = 1.33 Hz) and also from the relatively upfield ^{13}C NMR chemical shift of the terminal methyl group (δ10.54). Similar coumarins have been isolated previously from *Calophyllum* sp. The resins of *C. costatum* gave [2] a 4-propylcoumarin, costatolide (**13**). 4-Phenylcoumarins are more commonly found in *Calophyllum* sp. The bark extracts of *C. soulattri* gave [3] soulattrolide (**14**). The nuts of *C. inophyllum* had [4] inophylloide (**15**) and calophylloide (**16**), whereas the leaves of the same species gave [5, 6] **15** and two other 4-phenylcoumarins, inophyllums A (**17**) and B (**18**). However, this is the first report of the occurrence of 4-methyl coumarins, **5** and **6**, co-occurring with the *O*-methyl derivative of their probable biogenetic precursor, **7**, in the leaf extracts of a *Calophyllum* sp. This finding is of biogenetic significance.

EXPERIMENTAL

^1H NMR: 360 MHz, $CDCl_3$, TMS as int standard; ^{13}C NMR: 360 MHz, $CDCl_3$, TMS as int. standard.

Leaves of *C. cordato-oblongum* were collected at Kanneliya forest in the south of Sri Lanka. Silica gel CC of the hot petrol extract and elution with petrol–EtOAc gave the following compounds.

D:A-Friedo-oleanan-3-one. Mp 264–265°, $[\alpha]_D^{27}$ −22.5° ($CHCl_3$). Lit. [7] mp 263°, $[\alpha]_D$ −22.5° ($CHCl_3$).

28-Hydroxy-D A-friedo-oleanan-3-one (canophyllol). Mp 282°, $[\alpha]_D^{27}$ −21.0° ($CHCl_3$). Lit [7] mp 280–282°, $[\alpha]_D$ −21.22°.

Cordatolide A (**5**). Mp 85°, $[\alpha]_D$ +54.8° ($CHCl_3$). MS: $[M]^+$ 342.1461, calc for $C_{20}H_{22}O_5$ 342.1467; *m/z* (rel. int.): 342 (32), 327 (100), 309 (10), 271 (55), 243 (10), 149 (18) and 115 (10); IR ν_{max}^{KBr} cm^{-1}: 3420, 2850–2950, 1738, 1590, 1390, 1200, 1110, 1130, 1150, 900, 850, 755 and 665; UV λ_{max}^{EtOH} nm (log ε): 230 (4.32), 275 sh, 283 (4.37), 289 sh, 307 sh and 326 (4.11); ^1H NMR: Table 1; ^{13}C NMR. Fig. 1

Cordatolide B (**6**). Mp 178°, $[\alpha]_D$ −23.2° ($CHCl_3$); MS: $[M]^+$ 342.1461, calc. for $C_{20}H_{22}O_5$ 342.1467; *m/z* (rel int.): 342 (30), 327 (100), 309 (10), 271 (48), 243 (6), 149 (7) and 115 (40); IR ν_{max}^{KBr} cm^{-1}: 3460, 2860–3000, 1740, 1590, 1390, 1200, 1110, 900, 860, 755 and 665; UV λ_{max}^{EtOH} nm (log ε): 228 (4.32), 274 sh, 283 (4.37), 289 sh, 307 sh, and 326 (4.11); ^1H NMR: Table 1; ^{13}C NMR: Fig. 1.

Cordatolide B acetate Acetylation of **6** using Ac_2O–C_5H_5N, gave the acetate: $[\alpha]_D$ −25° ($CHCl_3$); MS $[M]^+$ 384.1572, calc for $C_{22}H_{24}O_6$ 384 1573; *m/z* (rel int.): 384 (3), 369 (10), 356 (3), 341 (4), 324 (38), 309 (100) and 255 (9); ^1H NMR ($CDCl_3$): δ6.61 (1H, *d*, *J* = 10 Hz), 6.34 (1H, *d*, *J* = 3.8 Hz), 5.9 (1H, *m*), 5.50 (1H, *d*, *J* = 10 Hz), 4.15 (1H, *m*, *J* = 7, 3.8 Hz), 2.51 (3H, *m*, *J* = 1.0 Hz), 2.08 (3H, *s*), 1.48 (2 × Me, *s*), 1.85 (1H, *m*) and 1.0–1.4 (6H, 2 × Me).

Oxidation of cordatolide B. Oxidation of **6** using Cr_2O_3–C_5H_5N at 5° for 0.5 hr gave the oxidized product **8**: mp 165°, $[\alpha]_D$ −23.7° ($CHCl_3$); MS $[M]^+$ 340.1316, calc for $C_{20}H_{20}O_5$ 340.1311; *m/z* (rel. int.): 340 (35), 325 (100), 297 (6), 284 (14), 269 (83), 241 (17) and 149 (17); ^1H NMR ($CDCl_3$): δ6.63 (1H, *d*, *J* = 10 Hz), 5.97 (1H, *br s*), 5.58 (1H, *d*, *J* = 10 Hz), 4.39 (1H, *m*), 3.50 (1H, *m*), 2.53 (3H, *br s*), 2.28 (1H, *m*), 1.56 (Me, *d*, *J* = 4 Hz), 1.5 (2 × Me, *s*) and 1.21 (Me, *d*, *J* = 6 Hz); IR ν_{max}^{KBr} cm^{-1}: 3000, 2820, 1750, 1700, 1600, 1450, 1340, 1230, 1200, 1150, 1000, 830, 760 and 690.

Reduction of the oxidized product of cordatolide B. $NaBH_4$ (20 mg) was added to a soln of the oxidized product of cordatolide B (69 mg) in MeOH (2 ml). The mixture was stirred for 2 hr The usual work-up gave a mixture of products (52 mg), which was separated by prep TLC to give cordatolides A (mp 82°) and B (mp 176°).

Hydrogenation of cordatolide A. Cordatolide A (0.16 g) was treated with 5% Pd/C (75 mg) in abs. EtOH (20 ml) and H_2 was passed into the stirred soln for 48 hr. The usual work-up gave a mixture which was separated by prep. TLC to give deoxydihydrocordatolide (0.03 g) and deoxytetrahydrocordatolide (0.08 g). Their physical data are given below

Deoxydihydrocordatolide (**9**). Mp 247–249°, $[\alpha]_D$ +56.6° ($CHCl_3$); MS: $[M]^+$ 328.1681, calc. for $C_{20}H_{24}O_4$ 328.1674; *m/z* (rel. int.): 328 (89), 272 (100), 257 (16), 243 (18), 229 (13), 217 (44), 188 (23) and 83 (11); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3060–2900, 1730, 1600, 1440, 1210, 755; ^1H NMR ($CDCl_3$): δ5.85 (1H, *m*), 3.65 (1H, *m*), 2.7–2.5 (4H, *m*), 2.5 (3H, *br s*), 1.87 (3H, *m*), 1.38 (3H, *d*, *J* = 6 Hz), 1.33 (6H, *s*) and 1.06 (3H, *d*, *J* = 6 Hz); UV λ_{max}^{MeOH} nm (log ε): 250 (3.86) and 272 (3.71).

Deoxytetrahydrocordatolide (**10**). $[\alpha]_D$ +44.5°; MS: $[M]^+$ 330.1835, calc. for $C_{20}H_{26}O_4$ 330.1831; *m/z* (rel. int.): 330 (100), 315 (24), 275 (95), 259 (42), 246 (20), 233 (18), 219 (15), 217 (9), 203 (16), 190 (8), 177 (12), 144 (5) and 118 (11); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3000–2800, 1730, 1600, 1450, 1330, 1200, 1030, 960 and 680; ^1H NMR ($CDCl_3$): δ3.68 (1H, *m*), 2.2–2.6 (7H, *m*), 1.7 (3H, *m*), 1.29 (6H, *s*) and 1.0–1.4 (9H, 3 × Me); UV λ_{max}^{MeOH} nm (log ε): 221 (3.37), 258 (3.02) and 273 (2.92).

Oblongulide (**7**). Mp 126°, MS. $[M]^+$ 354.1467 ($C_{21}H_{22}O_5$); *m/z* (rel. int.): 354 (16), 339 (100), 309 (10), 299 (6), 281 (8), 253 (6), 241 (6), 213 (6), 185 (5), 128 (16), 115 (10), 91 (10), 83 (12), 77 (12), 55 (50) and 43 (27); IR ν_{max}^{KBr} cm^{-1}: 1735, 1665, 1650, 1620, 1582, 1575, 1350, 1115, 945, 905, 845 and 745; UV λ_{max}^{EtOH} nm (log ε): 226 (4.0), 283 (3.3) and 344 (2.8); ^1H NMR ($CDCl_3$): see Results and Discussion.

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