Phytochemistry, Vol. 23, No. 11, pp. 2601–2603, 1984
Printed in Great Britain

0031-9422/84 $3.00+0.00

TRITERPENES AND NEOFLAVONOIDS OF *CALOPHYLLUM LANKAENSIS* AND *CALOPHYLLUM THWAITESII*

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(*Received* 6 *February* 1984)

Key Word Index—*Calophyllum thwaitesii*; *Calophyllum lankaensis*; leaves; D:A-friedo-oleanan-3-one; 28-hydroxy-D:A-friedo-oleanan-3-one; canophyllol; calozeylanic acid; thwaitesic acid; calozeylanolactone; thwaitesi lactone; 28-oxo-D:A-friedo-oleanan-3-one; canophyllal; apetalactone.

Abstract—The petrol extracts of the leaves of *Calophyllum lankaensis* and *C. thwaitesii* yielded D:A-friedo-oleanan-3-one, 28-hydroxy-D:A-friedo-oleanan-3-one (canophyllol), 28-oxo-D:A-friedo-oleanan-3-one (canophyllal), calozeylanic acid, thwaitesic acid, isothwaitesic acid and apetalactone. Thwaitesic acid and iso-thwaitesic acid are two novel neoflavonoids.

INTRODUCTION

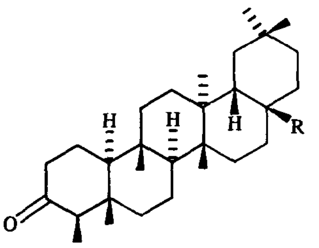
We reported [1] the constituents of the bark acids of seven *Calophyllum* species including those of *C. thwaitesii* and *C. lankaensis*. The leaf extracts of the latter two *Calophyllum* species have now been investigated and the results are reported in this paper.

RESULTS AND DISCUSSION

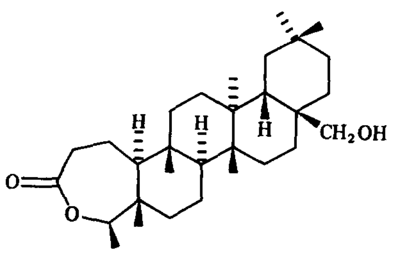
The petrol extract of the leaves of *C. lankaensis* when separated on a silica gel column gave D:A-friedo-oleanan-3-one (**1**), 28-oxo-D:A-friedo-oleanan-3-one (canophyllal) (**2**) and 28-hydroxy-D:A-friedo-oleanan-3-one (canophyllol) (**3**) in that order when eluted with petrol–ethyl acetate. Canophyllal on reduction with lithium aluminium hydride gave canophyllol which was identical with **3**.

Elution of the silica gel column with further amounts of petrol–ethyl acetate gave an acid mixture which was extremely difficult to separate. Treatment of this acid mixture with *p*-toluene sulphonic acid gave three lactones which were separated by preparative TLC. The major product, mp 125°, $[\alpha]_D^{27}$ +123.7°, was found to be calozeylanolactone (**4**) which was identical with the *p*-toluene sulphonic acid cyclised product of calozeylanic acid (**5**) isolated [1] from the bark of *C. lankaensis* in an earlier investigation. The second lactone (ν_{max} 1735 cm^{-1}), mp 208°, $[\alpha]_D^{27}$ −5.4°, had a molecular formula of $C_{20}H_{20}O_4$ (MW 324.1173). The ^{1}H NMR spectrum showed the presence of (a) five aromatic protons as a multiplet at δ7.17 and another aromatic proton at 6.36 as a singlet, (b) a two-proton doublet at 3.0 (J = 5 Hz) coupled to a one-proton triplet at 4.5 (J = 5 Hz), (c) two three-proton singlets at 1.07 and 1.30 and (d) two coupled two-proton triplets at 2.60 and 1.70 (J = 7 Hz). This lactone, unlike calozeylanolactone showed the absence of a chelated hydroxyl group(s). The ^{1}H NMR spectral data in the upfield region are in keeping with the presence of a 2,2-dimethylchromanyl system in the lactone. Comparison of the δ values for calozeylanolactone and the second lactone (Fig. 1) shows that the latter has structure **6**. The third lactone (**7**) which was a minor product had δ values very similar to those of **6** except that the two three-proton singlets for two methyl groups appeared at δ1.29 and 1.27 (Fig. 1). The chemical similarity of these 2,2-dimethyl chromanyl protons is due to the stereochemical arrangement of the phenyl group in this lactone **7** as opposed to in the lactone **6**.

The lactones **4**, **6** and **7** were not present in the mixture



1 R = Me
2 R = CHO
3 R = CH_2OH



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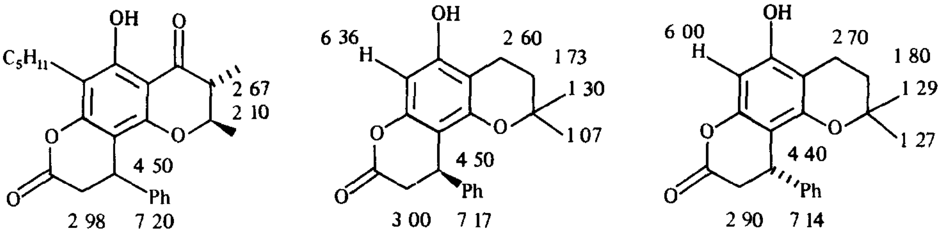


4 **6** **7**

Fig 1 Chemical shifts (δ) of compounds **4**, **6** and **7**

before it was treated with *p*-toluene sulphonic acid Hence, since lactone **4** was earlier [1] obtained from **5** isolated from the bark of *C lankaensis* and since the major acid of the bark and the leaf extractives were identical (co-TLC), calozeylanic acid (**5**) is also the major component of the leaf acids of *C lankaensis* Lactones **6** and **7** could be derived from the acids named thwaitesic acid (**8**) and isothwaitesic acid (**9**), respectively The ^{1}H NMR spectrum of the leaf acid mixture had a singlet at δ6 10 for an aromatic proton indicating the presence of **8** and **9** in the acid mixture

After separation of the acid mixture, the silica gel column was eluted with methanol Preparative TLC separation of the residue obtained on evaporation of the methanol gave a product, mp 335°, $[\alpha]_D^{27} = +33°$ It had a molecular formula $C_{30}H_{50}O_3$ (high resolution MS) The product was identical with apetalactone (**10**) isolated [2] from *Calophyllum apetalum*

The petrol extract of the leaves of *C thwaitesii* on separation by a silica gel column gave D A-friedo-oleanan-3-one (**1**) and 28-hydroxy-D A-friedo-oleanan-3-one (**3**) The leaf acid mixture obtained on washing the petrol extract with aq sodium carbonate was shown to contain calozeylanic acid (**5**), thwaitesic acid (**8**) and isothwaitesic acid (**9**) as in the case of the leaf acid mixture of *C lankaensis*

Thwaitesic acid (**8**) and iso-thwaitesic acid (**9**) are two new neoflavonoids Moreover, this is the first isolation of acids from the leaves of *Calophyllum* species The presence of the same acid in the leaves as well as in the bark of the same plant is of biogenetic significance

EXPERIMENTAL

The leaves of *C lankaensis* were collected at Madugoda, Sri Lanka Whilst the leaves of *C thwaitesii* were collected from Kanneliya forest, Sri Lanka The sun-dried leaves of *C lankaensis* (3 0 kg) and *C thwaitesii* (4 0 kg) were milled and then extracted with petrol to yield 0 4 kg and 0 196 kg, respectively, of extract

D A-friedo-oleanan-3-one (**1**) The petrol extract was chromatographed over silica gel Elution with petrol–EtOAc (9 1) gave **1** as white needles ($CHCl_3$–MeOH), mp 264–265°, $[\alpha]_D^{27} = -22 5°$ ($CHCl_3$) lit [3] mp 263°, $[\alpha]_D = -22 5°$ ($CHCl_3$)

28-oxo-D A-friedo-oleanan-3-one (*canophyllal*) (**2**) Continued elution of the silica gel column gave white needles ($CHCl_3$–MeOH) of **2**, mp 260–262°, $[\alpha]_D = -16 0°$ ($CHCl_3$), lit [3] mp 263–265°, $[\alpha]_D = -16 0°$ ($CHCl_3$)

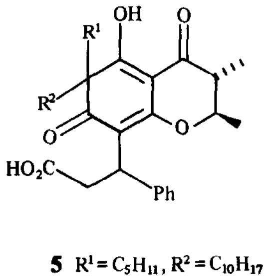
28-Hydroxy-D A-friedo-oleanan-3-one (*canophyllol*) (**3**) Elution with petrol–EtOAc (1 4) gave **3** as white needles ($CHCl_3$–MeOH), mp 282°, $[\alpha]_D^{27}$ $-21 0°$ ($CHCl_3$), lit [3] mp 280–282°, $[\alpha]_D$ $-21 22°$

Acid mixture Continued elution of the column with petrol–EtOAc (1 4) gave a waxy solid This was separated into the acid mixture of **5**, **8** and **9** by washing with 5% Na_2CO_3 soln

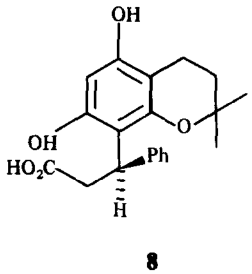
Apetalactone (**10**) Elution of the column with MeOH gave a solid which was washed with 5% Na_2CO_3 soln The neutral fraction was purified by preparative TLC to give **10** as white needles (MeOH–$CHCl_3$), mp 335–336°, $[\alpha]_D^{27}$ $+33°$ ($CHCl_3$), lit [2] mp 336°, $[\alpha]_D$ $+37 5°$ ($CHCl_3$), ^{1}H NMR ($CDCl_3$) δ4 21 (1H, *br m*, H-4), 3 60 (2H, *s*, H-28), 2 57 (2H, *m*, H-2), 1 53–0 6 (CH_2-envelope), 1 06 (3H, *s*, Me), 0 98 (6H, *s*, 2 × Me), 0 90 (6H, *s*, 2 × Me), 0 83 (3H, *s*, Me), 1 10 (3H, *d*, *J* = 8 Hz, Me), MS *m/z* (rel int) 458 $[M]^+$ (0 1), 443 (0 1), 440 (0 5), 427 (3), 383 (11), 291 (13), 289 (35), 245 (50), 259 (7), 273 (6), 227 (12), 203 (17), 191 (20), 177 (22), 163 (25), 149 (45), 137 (100), 123 (50)

Acetate of **10** Compound **10** (0 4 g) was dissolved in dry pyridine (1 0 ml) and was treated with Ac_2O (0 50 ml) at room temp for 6 hr The usual work up gave the acetate of **10** as white needles, mp 231°, $[\alpha]_D^{27}$ $+22°$ ($CHCl_3$), lit [2] mp 231–232°, $[\alpha]_D$ $+22 1°$, ^{1}H NMR (CCl_4, 60 MHz) δ4 10 (2H, *dd*, *J* = 10, 22 Hz, H-28), 4 16 (1H, *br m*, H-4), 2 50 (2H, *m*, H-2), 2 01 (3H, *s*, OAc), 1 33–1 20 (CH_2-envelope), 1 13 (3H, *s*, Me), 1 06 (3H, *s*, Me), 0 98 (6H, *s*, 2 × Me), 0 90 (3H, *d*, *J* = 8 Hz, H-4), 0 87 (3H, *s*, Me), MS *m/z* (rel int) 500 $[M]^+$ (7), 485 (4), 456 (4), 440 (64), 427 (100), 396 (40), 383 (78), 290 (25), 245 (57), 217 (21), 203 (78), 189 (38), 177 (61)

Reduction of **2** Compound **2** (0 025 g) in 2 ml of dry THF was added slowly to a boiling soln of $LiAlH_4$ (0 05 g) in dry THF



5 R^1 = C_5H_{11}, R^2 = $C_{10}H_{17}$



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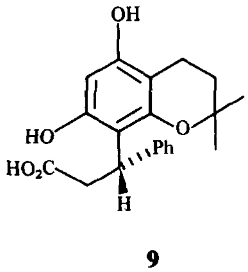

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(5 ml) The reaction mixture was maintained at 45° After 3 hr the usual work up gave pure 3 (0 019 g), mp 281–282°, $[\alpha]_D$ −22° ($CHCl_3$) lit [3] mp 280–282°, $[\alpha]_D$ −21 2°

Treatment of the acid mixture with p*-toluene sulphonic acid* The acid mixture (1 0 g) in dry benzene (10 ml) was treated with *p*-toluene sulphonic acid (1 0 g) at 80° for 8 hr The solvent was evaporated and the residue was extracted with Et_2O–H_2O The ethereal layer gave a crude product mixture (0 75 g) from which three lactones were isolated by preparative TLC using silica gel plates and they were characterised as calozeylanolactone (4), thwaitesic lactone (6) and isothwaitesic lactone (7) Their physical and spectroscopic data are given below

Calozeylanolactone (4) Mp 125°, $[\alpha]_D$ +123 7° ($CHCl_3$), lit [1] mp 125–126° $[\alpha]_D$ +123° It was identical with an authentic sample

Thwaitesic lactone (6) Pale pink crystals from petrol–$CHCl_3$ mp 208°, $[\alpha]_D^{27}$ −5 4° ($CHCl_3$), IR ν_{max}^{KBr} cm^{-1} 3410, 2800–3000, 1735, 1615, 1445, 1342, 1290, 1270, 1235, 1160, 1120, 1080, 980, 890, 820, 715 and 700, ^1H NMR ($CDCl_3$, 60 MHz), δ 7 17 (5H, *m*), 6 36 (1H, *s*), 4.50 (1H, *t*, $J = 5$ Hz), 3 00 (2H, *d*, $J = 5$ Hz), 2 60 (2H, *t*, $J = 7$ Hz), 1 70 (2H, *t*, $J = 7$ Hz), 1 30 (3H, *s*), 1 07 (3H, *s*), MS *m/z* (rel int.) 324 $[M]^+$ (17), 323 (72), 267 (100), 266 (4), 239 (12), 226 (14), 161 (12)

Isothwaitesic lactone (7) ^1H NMR (CCl_4, 60 MHz) δ 7 14 (5H, *m*), 6 00 (1H, *s*), 4 40 (1H, *t*, $J = 5$ Hz), 2 90 (2H, *d*, $J = 7$ Hz), 2 70 (2H, *t*, $J = 7$ Hz), 1 80 (2H, *t*, $J = 7$ Hz), 1 29 (3H, *s*), 1 27 (3H, *s*)

Acknowledgement—We thank the Natural Resources Energy and Science Authority of Sri Lanka for a grant

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