28,29-Dihydroxyfriedelan-3-one, a Friedelane with Two Oxygenated Methyl Groups, from *Elaeodendron balae* (Celastraceae) [1]

By **Gamini Weeratunga, Vijaya Kumar,*** and **M. Uvais S. Sultanbawa,** Department of Chemistry, University of Peradeniya, Peradeniya, Sri Lanka
Sinnathamby Balasubramaniam, Department of Botany, University of Peradeniya, Peradeniya, Sri Lanka

A new friedelane with two oxygenated methyl groups, isolated from *Elaeodendron balae* Kosterm. (Celastraceae), has been shown to be 28,29-dihydroxyfriedelan-3-one by spectroscopic and chemical data.

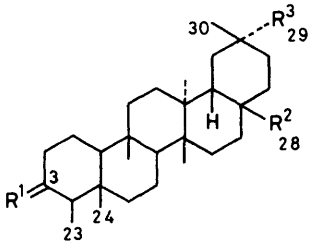
ELAEODENDRON BALAE Kosterm.[2] (Celastraceae) is an evergreen tree growing in southeast Sri Lanka and is similar to the only *Elaeodendron* species previously studied, *E. glaucum*.[3,4] The seeds of *E. glaucum* contain a cardiac glycoside with a doubly linked sugar substituent [3] while a similar glycoside, five friedelanes, and two norfriedelanes were isolated from the bark.[4] We report herein the isolation of 28,29-dihydroxyfriedelan-3-one (1) from *E. balae*. The only friedelane with two oxygenated methyl groups previously reported is salaspermic acid, the hemiacetal of 24-hydroxy-3-oxofriedelan-29-oic acid, isolated from *Salacia macrosperma*.[5]

RESULTS AND DISCUSSION

The benzene extract of the dried, powdered bark of *E. balae*, collected at Tellula in the Moneragala district of Sri Lanka, contained 28,29-dihydroxyfriedelan-3-one (1) ($\nu_{max.}$ 3 500—3 200 and 1 704 cm^{-1}). Its ^1H n.m.r. spectrum, showing the presence of a secondary methyl doublet, only five tertiary methyl singlets, and two CH_2 singlets (Table), together with its mass-spectral fragmentation pattern, was strongly suggestive of a friedelanone structure with two methyl groups oxygenated as CH_2OH moieties. The strong peak at *m/z* 273 in its mass spectrum indicated that the carbonyl group resides on one of the rings A, B, or C, and that no oxygenated methyl groups are present in those rings.[6] This leaves only C-28, C-29, and C-30 as possible locations for the two oxygenated methyl groups.

Oxidation of the diol (1) with chromium trioxide–pyridine at 0 °C gave a dialdehyde (2) (δ 9.55 and 9.50) and a monoaldehyde (3) [$\nu_{max.}$ 3 540 and 1 710 cm^{-1}; δ 3.28 (2 H, s, CH_2OH) and 9.50]. Huang Minlon reduction of the monoaldehyde (3) gave a friedelanol (4) [δ 3.28 (2 H, s, CH_2OH)] which was shown to be friedelan-29-ol, identical with an authentic sample prepared from 29-hydroxyfriedelan-3-one (5),[7,†] thus confirming that one of the CH_2OH groups in the diol (1) is at C-29.

Treatment of the acetate (6) of the monoaldehyde (3) with ethylene glycol afforded, selectively, the 3,3-ethylenedioxy-derivative (7) [δ 3.74 (2 H, s, CH_2OAc) and 9.50] which, on Huang Minlon reduction, gave an acetal (8), identical with 3,3-ethylenedioxyfriedelan-29-ol prepared from 3-oxofriedelan-29-yl acetate (9). This confirms the presence of a carbonyl group at C-3 and provides further evidence for the presence of the CH_2OH group at C-29.



(1) $R^1 = O, R^2 = R^3 = CH_2OH$
(2) $R^1 = O, R^2 = R^3 = CHO$
(3) $R^1 = O, R^2 = CHO, R^3 = CH_2OH$
(4) $R^1 = H_2, R^2 = Me, R^3 = CH_2OH$
(5) $R^1 = O, R^2 = Me, R^3 = CH_2OH$
(6) $R^1 = O, R^2 = CHO, R^3 = CH_2OAc$
(7) $R^1 = O[CH_2]_2O, R^2 = CHO, R^3 = CH_2OAc$
(8) $R^1 = O[CH_2]_2O, R^2 = Me, R^3 = CH_2OH$
(9) $R^1 = O, R^2 = Me, R^3 = CH_2OAc$
(10) $R^1 = O[CH_2]_2O, R^2 = Me, R^3 = CH_2OAc$
(11) $R^1 = O, R^2 = CO_2H, R^3 = CHO$
(12) $R^1 = H_2, R^2 = CO_2H, R^3 = Me$
(13) $R^1 = O, R^2 = CH_2OH, R^3 = Me$
(14) $R^1 = H_2, R^2 = CH_2OH, R^3 = Me$

CrO_3–pyridine oxidation of the diol (1) at 27 °C gave, as the major product, an aldehydo-acid (11) [$\nu_{max.}$ 3 500—3 100, 2 680, 1 720, and 1 710 cm^{-1}; δ 9.37]. Huang Minlon reduction of the acid (11) afforded friedelan-28-oic acid (12) which was identified by comparison with an authentic sample prepared from 28-hydroxyfriedelan-3-one (13) (see Experimental section). This confirms that the other CH_2OH group in the diol (1) must be at C-28 and the diol (1) must therefore be 28,29-dihydroxyfriedelan-3-one. Analytical and spectral data were in agreement with the above structural assignments.

EXPERIMENTAL

M.p.s were recorded on a Kofler hot-stage apparatus. I.r. spectra were determined for KBr discs on a Perkin-Elmer 257 spectrophotometer, whilst ^1H n.m.r. spectra

† The C-20 α-substituent in these compounds has been assigned the number 30 by Betancor *et al.*[7] but we have followed the more common convention of using number 29 to indicate this centre.

were measured on a Varian T 60 spectrometer in $CDCl_3$ or $(CD_3)_2CO$ solution using $SiMe_4$ as internal standard (see Table). Optical rotations were measured in $CHCl_3$ solution at 25 °C on a Perkin-Elmer 141 polarimeter. Microanalyses and mass-spectral studies were carried out at Ciba-Geigy Ltd., Basle and at Tokushima Research Institute, Otsuka Pharmaceutical Co. Ltd., Tokyo. Preparative layer chromatography (p.l.c.) was carried out on Merck Silica Gel $PF_{254+366}$.

(*b*) 29-Hydroxyfriedelan-3-one (5) [7] (100 mg) was reduced under Huang Minlon conditions with ethylene glycol (8 ml), hydrazine hydrate (1 g), and KOH (160 mg). The usual work-up gave the alcohol (4) (43 mg), m.p. 275—277 °C; $[\alpha]_D$ +21° (*c*, 1.0), and identical with a sample prepared by method (*a*) (mixed m.p., i.r.).

3,28-*Dioxofriedelan*-29-*yl Acetate* (6).—The alcohol (3) (35 mg) was stirred with acetic anhydride–pyridine (1 : 1) (3 ml) for 18 h at 27 °C. The usual work-up, followed by purification by p.l.c. ($CHCl_3$ as developer), gave 3,28-*dioxofriedelan*-29-*yl acetate* (6) (32 mg) as plates from $CHCl_3$–MeOH, m.p. 176—178 °C; $[\alpha]_D$ −19° (*c*, 1.0) (Found: M^+, 498.3717. $C_{30}H_{50}O_4$ requires *M*, 498.3709); $\nu_{max.}$ 1 720, 1 710, and 1 250 cm^{-1}; *m/z* 498 (M^+, 13%), 469 (76), 409 (81), 273 (75), and 135 (100).

^1H n.m.r. data (δ-values) ($CDCl_3$, 60 MHz)

	Compound										
	(1)	(2)	(3)	(4)	(6)	(7)	(8)	(10)	(11) [a]	(12)	(14)
28-H	3.66	9.50	9.50	1.16	9.50	9.50	1.17	1.18	—	—	3.66
29-H	3.28	9.55	3.28	3.28	3.74	3.74	3.28	3.74	9.37	0.96	0.90
OAc	—	—	—	—	2.06	2.06	—	2.06	—	—	—
$O[CH_2]_2O$ [b]	—	—	—	—	—	3.90	3.90	3.90	—	—	—
23-H_3 [c]	0.87	0.87	0.87	0.86	0.87	0.85	0.85	0.85	0.85	0.86	0.86
Other methyls	1.13	1.13	1.10	1.10	1.06	1.06	1.10	1.04	1.13	1.04	1.08
	1.01	1.06	1.00	1.06	1.02	1.02	1.00	1.00	0.93	1.00	1.00
	0.96	0.92	0.93	0.93	0.93	0.90	0.93	0.90	0.90	1.00	1.00
	0.88	0.86	0.86	0.88	0.88	0.87	0.89	0.86	0.86	0.89	0.87
	0.73	0.71	0.70	0.76	0.71	0.66	0.71	0.73	0.73	0.76	0.76

[a] In $(CD_3)_2CO$. [b] Multiplet, $w_{\frac{1}{2}}$ 5 Hz. [c] Doublet, *J* 6—8 Hz.

Isolation of 28,29-*Dihydroxyfriedelan*-3-*one* (1).—The stem bark of *E. balae* (10 kg), collected at Tellula in the Moneragala district of Sri Lanka, was dried, pulverised, and extracted with benzene (20 l). Evaporation of the extract gave a residue (32 g), chromatography of which (21 g) on silica (550 g) gave, with $CHCl_3$–MeOH (49 : 1) as eluant, 28,29-*dihydroxyfriedelan*-3-*one* (1) (0.8 g) which was recrystallised from $CHCl_3$–MeOH as needles, m.p. 286—288 °C; $[\alpha]_D$ −18.5° (*c*, 1.0) (Found: C, 78.05; H, 10.45%; M^+, 458.3765. $C_{30}H_{50}O_3$ requires C, 78.55; H, 10.99%; *M*, 458.3760); $\nu_{max.}$ 3 500—3 200 and 1 704 cm^{-1}; *m/z* 458 (M^+, 14%), 440 (13), 427 (90), 409 (52), 397 (38), 301 (49), 273 (55) and 109 (100).

Oxidation of the Diol (1).—Chromium(VI) oxide (0.81 g) was added to a solution of the diol (1) (0.25 g) in pyridine (5 ml) and the mixture was stirred for 0.75 h at 0 °C and was then poured into dilute hydrochloric acid. Work-up gave a yellow residue which was separated into two components by p.l.c. [CH_2Cl_2–MeOH (99 : 1) as developer]. Thus obtained were the less polar 3-*oxofriedelane*-28,29-*dial* (2) (0.05 g) as needles from $CHCl_3$–MeOH, m.p. 187—190 °C; $[\alpha]_D$ −12.5° (*c*, 2.0) (Found: M^+, 454.3454. $C_{30}H_{46}O_3$ requires *M*, 454.3447); $\nu_{max.}$ 2 680, 1 720, and 1 715 cm^{-1}; *m/z* 454 (M^+, 16%), 435 (29), 425 (68), 407 (21), 397 (12), 273 (89), 231 (33), 205 (35) and 109 (100), and the more polar 29-*hydroxy*-3-*oxofriedelan*-28-*al* (3) (0.1 g) as needles from $CHCl_3$–MeOH, m.p. 235—237 °C; $[\alpha]_D$ −15° (*c*, 1.0); (Found: M^+, 356.3606. $C_{30}H_{48}O_3$ requires *M*, 456.3603); $\nu_{max.}$ 3 540, 2 680, and 1 710 cm^{-1}; *m/z* 456 (M^+, 30%), 438 (39), 427 (96), 409 (36), 273 (51), 161 (38) and 109 (100).

Friedelan-29-*ol* (4).—(*a*) Compound (3) (50 mg) was reduced under Huang Minlon conditions [ethylene glycol (5 ml), hydrazine hydrate (1 g), KOH (100 mg), reflux, 3 h] followed by distillation to 200 °C; the residue was then heated at this temperature for a further 3 h. The usual work-up, followed by p.l.c. [$CHCl_3$–MeOH (99 : 1) as developer], gave *friedelan*-29-*ol* (4) (26 mg) as plates from $CHCl_3$–MeOH, m.p. 276—277 °C; $[\alpha]_D$ +22° (*c*, 1.0) (Found: M^+, 428.4008. $C_{30}H_{52}O$ requires *M*, 428.4018); $\nu_{max.}$ 3 500—3 300 cm^{-1}; *m/z* 428 (M^+, 18%), 413 (16), 397 (3), 259 (33), 221 (6), 149 (100), and 141 (23).

3,3-*Ethylenedioxy*-28-*oxofriedelan*-29-*yl Acetate* (7).—The ketone (6) (30 mg) was refluxed with toluene-*p*-sulphonic acid (3 mg) and ethylene glycol (0.5 ml) in dry benzene (30 ml) for 2 h in a Dean–Stark apparatus. The usual work-up, followed by purification by p.l.c. [light petroleum–$CHCl_3$ (1 : 1) as developer] gave, as the major product, 3,3-ethylenedioxy-28-oxofriedelan-29-yl acetate (7) (15 mg) as needles from $CHCl_3$–MeOH, m.p. 291—233 °C; $[\alpha]_D$ −2° (*c*, 0.5); $\nu_{max.}$ 2 695, 1 735, 1 720, 1 240, and 1 070 cm^{-1}.

3,3-*Ethylenedioxyfriedelan*-29-*ol* (8).—(*a*) The acetate (7) (15 mg) was reduced under Huang Minlon conditions, as described earlier, with ethylene glycol (7 ml), hydrazine hydrate (1 g), and KOH (50 mg). The usual work-up gave 3,3-*ethylenedioxyfriedelan*-29-*ol* (8) (8 mg) as needles from $CHCl_3$–MeOH, m.p. 333—335 °C; $[\alpha]_{578}$ +6.7° (*c*, 0.3) (Found: M^+, 486.4092. $C_{32}H_{54}O_3$ requires *M*, 486.4073); $\nu_{max.}$ 3 500 and 1 070 cm^{-1}.

(*b*) 3-Oxofriedelan-29-yl acetate (9) [7] (80 mg) was refluxed with toluene-*p*-sulphonic acid (8 mg) and ethylene glycol (0.5 ml) in dry benzene (30 ml) in a Dean–Stark apparatus. The usual work-up gave, on crystallisation from $CHCl_3$–MeOH plates (50 mg) of 3,3-ethylenedioxyfriedelan-29-yl acetate (10), m.p. 282—283 °C; $[\alpha]_{578}$ −1° (*c*, 1.0); $\nu_{max.}$ 1 735, 1 240, and 1 070 cm^{-1}.

The acetate (10) (50 mg) was refluxed with KOH (100 mg) in MeOH (2 ml) for 3 h. Work-up gave a residue which was recrystallised from $CHCl_3$–MeOH to afford needles, m.p. 334—335 °C; $[\alpha]_{578}$ +6.7° (*c*, 0.3), identical with the acetal (8) (mixed m.p. and i.r.).

3,29-*Dioxofriedelan*-28-*oic Acid* (11).—Chromium(VI) oxide (0.5 g) was added to a solution of the diol (1) (0.4 g) in pyridine (2 ml) and the mixture was stirred for 0.5 h at 0 °C and then for 6 h at 27 °C to give, on work-up followed by separation by p.l.c. [$CHCl_3$–MeOH (24 : 1) as developer] and recrystallisation from $CHCl_3$–MeOH, 3,29-dioxofriede-

lan-28-oic acid (11) (15 mg) as plates, m.p. 220—222 °C; $[\alpha]_D$ −12° (*c*, 1.0); $\nu_{max.}$ 3 500—3 100, 2 680, 1 720, and 1 710 cm^{-1}; *m/z* 470 (M^+, 8%), 441 (27), 425 (16), 273 (20), 206 (68), and 147 (100).

Friedelan-28-oic Acid (12).—(*a*) The acid (11) (15 mg) was reduced under Huang Minlon conditions with ethylene glycol (4 ml), hydrazine hydrate (1 g), and KOH (30 mg). The usual work-up, followed by p.l.c. [$CHCl_3$–MeOH (99 : 1) as developer], gave *friedelan-28-oic acid* (8 mg) as needles from $CHCl_3$–MeOH, m.p. 276—277 °C; $[\alpha]_D$ +8.4° (*c*, 1.0) (Found: M^+, 442.3803. $C_{30}H_{50}O_2$ requires *M*, 442.3811); $\nu_{max.}$ 3 500—3 200 and 1 695 cm^{-1}.

(*b*) 28-Hydroxyfriedelan-3-one (13) [8] (0.1 g) was reduced under Huang Minlon conditions with ethylene glycol (8 ml), hydrazine hydrate (1 g), and KOH (160 mg) to give *friedelan-28-ol* (14) (40 mg) as plates from $CHCl_3$–MeOH, m.p. 240—241 °C; $[\alpha]_D$ +18° (*c*, 1.0) (Found: C, 83.65; H, 12.5%; M^+, 428.4025. $C_{30}H_{52}O$ requires C, 84.04; H, 12.22%; *M*, 428.4018); $\nu_{max.}$ 3 400—3 200 cm^{-1}; *m/z* 428 (M^+, 10%), 397 (98), 259 (100), 221 (21), 149 (65), and 109 (100).

The alcohol (14) (40 mg), dissolved in acetone (10 ml), was oxidised with Jones reagent [9] (2 ml) to give, after work-up, needles, m.p. 276—277 °C; $[\alpha]_D$ +8.5° (*c*, 1.0), identical with a sample of the acid (12) (mixed m.p. and i.r.).

We thank Ciba–Geigy Ltd., Basle, for financial support, Drs. H. Fisher and J. P. Pachlatko for assistance in obtaining spectral and analytical data, Drs. S. Sonoda and M. Nishikawa of Otsuka Pharmaceutical Co. Ltd., Tokushima, for high-resolution mass spectra, and Mrs. S. C. Weerasekera for technical assistance.

[1/1995 *Received*, 30*th December*, 1981]

REFERENCES

[1] Part 45 in the series ' Chemical Investigation of Ceylonese Plants,' Part 44; D. B. T. Wijeratne, V. Kumar, and M. U. S. Sultanbawa, *J. Chem. Soc., Perkin Trans. 1*, 1981, 2724.

[2] A. J. Kostermans, personal communication.

[3] S. M. Kupchan, J. Uchida, K. Shimada, B. Yu Fei, D. M. Stevens, A. T. Sneden, R. W. Miller, and R. F. Bryan, *J. Chem. Soc., Chem. Commun.*, 1977, 255.

[4] A. S. R. Anjaneyulu and M. Narayana Rao, *Phytochemistry*, 1980, **19**, 1163; *Indian J. Chem., Sect. B*, 1980, **19**, 944.

[5] N. I. Viswanathan, *J. Chem. Soc., Perkin Trans. 1*, 1979, 349.

[6] H. Budzikiewicz, C. Djerassi, and D. H. Williams, ' Structure Elucidation of Natural Products by Mass Spectrometry,' Holden–Day, San Francisco and London, 1964, vol. II, p. 132.

[7] C. Betancor, R. Freire, A. G. Gonzalez, J. A. Salazar, C. Pascard, and T. Prange, *Phytochemistry*, 1980, **19**, 1989.

[8] T. R. Govindachari, N. Viswanathan, B. R. Pai, V. R. Rao, and M. Srinivasan, *Tetrahedron*, 1967, **23**, 1901.

[9] K. Bowden, I. M. Heilbron, E. R. H. Jones, and B. C. L. Weedon, *J. Chem. Soc.*, 1946, 39.