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D:A-Friedooleananes from *Elaeodendron glaucum**

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Abstract

Two new trioxygenated *D:A*-friedooleananes from the stem bark of *Elaeodendron glaucum* have been shown to be the angular methyl dioxygenated 25,28-dihydroxy-*D:A*-friedooleanan-3-one (2) and 25-hydroxy-3-oxo-*D:A*-friedooleanan-28-al (3).

Introduction

Elaeodendron glaucum Pers (Celastraceae) is a tree growing in northern Sri Lanka. Constituents previously reported in extracts of its stem bark include a cardiac glycoside with a doubly linked sugar substituent,[1] six *D:A*-friedooleananes, two *D:A*-friedonoroleananes,[2] *D:A*-friedooleanan-3α-ol, two betulin derivatives, two sitosterol derivatives and octacosan-1-ol.[3]

Discussion

Investigation of the benzene extract of *E. glaucum* bark led to the isolation of 29-hydroxy-*D:A*-friedooleanan-3-one (1)†[4] and the highly polar components 25,28-dihydroxy-*D:A*-friedooleanan-3-one (2) and 25-hydroxy-3-oxo-*D:A*-friedooleanan-28-al (3). In addition, six *D:A*-friedooleananes and the *D:A*-friedo-28-noroleanane, elaeodendrol, previously reported[2] were found to be present but we were unable to isolate octacosan-1-ol and the betulin and sitosterol derivatives reported.[3]

* Part LXVII, in the series 'Chemical Investigation of Ceylonese Plants' (Part LXVI, Wijeratne, D. B. T., Kumar, V., Sultanbawa, M. U. S., and Balasubramaniam, S., *Phytochemistry*, 1982, in press). Part of this work was reported in a preliminary communication, *Tetrahedron Lett.*, 1982, **23**, 2031.

† The 20α-carbon substituent in this compound has been assigned the number 30 by Betancor *et al.*[4] but we have followed the more common convention of using number 29 to indicate this centre.

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

[2] Anjaneyulu, A. S. R., and Rao, M. N., *Phytochemistry*, 1980, **19**, 1163.

[3] Joshi, K. C., Bansal, R. K., and Patni, R., *J. Indian Chem. Soc.*, 1980, **57**, 1042.

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

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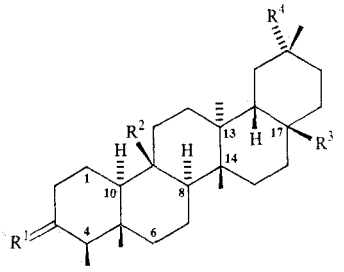
Spectroscopic evidence suggested that the diol (2) is a *D:A*-friedooleanane containing an oxo and two hydroxymethylene groups. The i.r. spectrum showed hydroxy (3000–3100 cm^{-1}) and carbonyl (1700 cm^{-1}) absorptions while the ^1H n.m.r. spectrum showed two hydroxymethylene CH_2 signals (δ 3·66, 3·92). The mass spectrum showed a low intensity molecular ion at *m/z* 458; loss of CH_2OH gave the base peak at *m/z* 429. The i.r. spectrum of the aldehyde (3) showed hydroxyl (3500–3240 cm^{-1}), aldehyde (1710, 2660 cm^{-1}) and carbonyl (1700 cm^{-1}) absorptions. Its ^1H n.m.r. spectrum showed a hydroxymethylene CH_2 signal (δ 3·92) and an aldehyde singlet (δ 9·50) while its mass spectrum showed a low-intensity M peak at *m/z* 456, a base peak at *m/z* 427 (M − CHO) and an abundant peak at *m/z* 425 (M − CH_2OH). The two compounds were shown to be interrelated as sodium borohydride reduction of both gave the same triol (4) with two CH_2OH groups (δ 3·63 and 3·94) and a CHOH group (δ 3·73). This suggests that the aldehyde group in compound (3) was in the same position as the additional hydroxymethylene group in the diol (2).



	R^1	R^2	R^3	R^4
(1)	O	Me	Me	CH_2OH
(2)	O	CH_2OH	CH_2OH	Me
(3)	O	CH_2OH	CHO	Me
(4)	αH,βOH	CH_2OH	CH_2OH	Me
(5)	H_2	CH_2OH	Me	Me
(6)	O	CH_2OH	Me	Me

	R^1	R^2	R^3	R^4
(8)	O	CO_2H	Me	Me
(9)	O	CO_2Me	Me	Me
(10)	—OCH_2O—	CO_2Me	Me	Me
(11)	O	CH_2OAc	Me	Me
(12)	αOH,βH	Me	Me	Me
(13)	O	CH_2OAc	CHO	Me
(14)	O	Me	CHO	Me

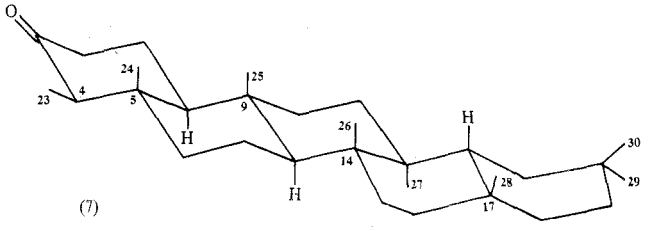
Huang Minlon reduction of the aldehyde (3) gave *D:A*-friedooleanan-25-ol (5) identical with that obtained by similar reductions of 25-hydroxy-*D:A*-friedooleanan-3-one (6),[2] which was present in the plant extract.

The *D:A*-friedooleanane skeleton is believed to assume a chair–chair–chair–twist boat–boat conformation (7)[5] in most derivatives and not the all-chair conformation previously proposed.[6] In either conformation, the 9β-angular methyl group with its 1,3-diaxial relationship with the 5β- and 14β-methyl groups is sterically hindered.

The report of Courtney *et al.*[7] that the 9β-hydroxymethylene group or aldehyde group could not be oxidized to a carboxylic acid is readily explained by the steric environment of these groups as seen in conformation (7). We found however that

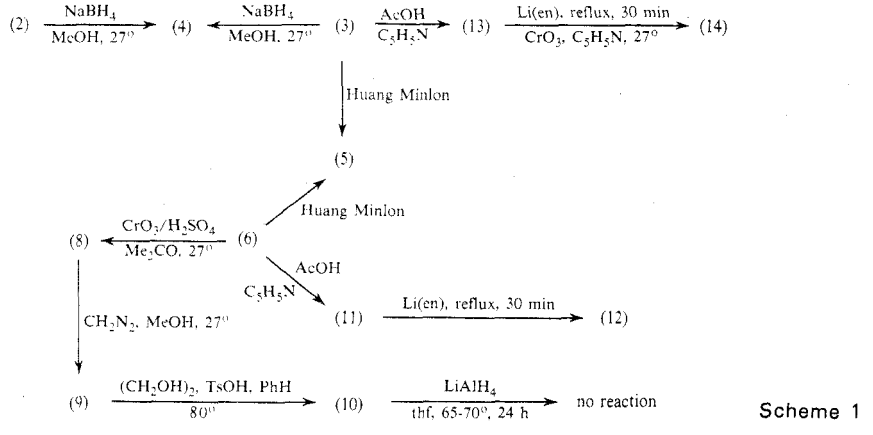
[5] Laing, M., Burke-Laing, M. E., Bartho, R., and Weeks, C. M., *Tetrahedron Lett.*, 1977, 3839.
[6] Corey, E. J., and Ursprung, J. J., *J. Am. Chem. Soc.*, 1956, **78**, 5041.
[7] Shannon, J. S., Macdonald, C. G., and Courtney, J. L., *Tetrahedron Lett.*, 1963, 173.

25-hydroxy-*D*:*A*-friedooleanan-3-one (6) could be oxidized slowly to 3-oxo-*D*:*A*-friedooleanan-25-oic acid (8) with Jones reagent[8] in 60% yield, although attempts to reduce a 9β-methoxycarbonyl group proved less successful. The acid (8) was esterified with diazomethane to give the methyl ester (9) which was converted into the cyclic ethylene acetal (10). Heating the acetal (10) under reflux with lithium aluminium hydride in tetrahydrofuran for 24 h gave only starting material. The resistance of a hydroxymethylene group to oxidation or a methoxycarbonyl group to reduction has not been reported for any other ring junction substituent in the *D*:*A*-friedooleanane series and this suggests that the 9β-position is one of the most hindered positions in the skeleton.



(7)

Ethylenediamine/lithium deoxygenation[9] has been used to remove sterically hindered primary alcohol groups[10] and the sterically hindered 25-acetoxy group appears to be eminently suitable for removal by this method. Ethylenediamine/lithium deoxygenation of 3-oxo-*D*:*A*-friedooleanan-25α-yl acetate (11) gave *D*:*A*-friedooleanan-3α-ol (12) in 65% yield. The aldehyde (3) was acetylated with acetic anhydride/pyridine and the acetate (13) was heated under reflux with lithium and ethylenediamine. Workup gave a mixture of products which on oxidation with chromium trioxide/pyridine gave canophyllal (3-oxo-*D*:*A*-friedooleanan-28-al)[2] (14) in 48% yield; this confirms that the keto group is at the 3-position and the aldehyde



Scheme 1

[8] Bowden, K., Heilbron, I. M., Jones, E. R. H., and Weedon, B. C. L., *J. Chem. Soc.*, 1946, 39.
[9] Boar, R. B., Joukhadar, L., McGhie, J. F., Misra, S. C., Barrett, A. G. M., Barton, D. H. R., and Prokopiou, P. A., *Chem. Commun.*, 1978, 68.
[10] Gunatilaka, A. A. L., Nanayakkara, N. P. D., and Sultanbawa, M. U. S., *Tetrahedron Lett.*, 1981, **22**, 1425.

group at the 17β-position in the *D*:*A*-friedooleanane ring system. The aldehyde (3) is therefore 25-hydroxy-3-oxo-*D*:*A*-friedooleanan-28-al and the diol (2) 25,28-dihydroxy-*D*:*A*-friedooleanan-3-one. Scheme 1 summarizes the relations between the various derivatives.

Experimental

Melting points were recorded on a Kofler hot-stage apparatus and are uncorrected. I.r. spectra were determined for KBr discs on a Perkin–Elmer 257 spectrophotometer; ^{1}H n.m.r. spectra were measured on a Varian T 60 spectrophotometer for $CDCl_3$ and $CDCl_3+CD_3OD$ solutions, tetramethylsilane being the internal reference. Optical rotations were measured in $CHCl_3$ solution at 25°, on a Perkin–Elmer 141 polarimeter, and mass spectral studies were carried out at Ciba-Geigy Ltd., Basel and at Kanazawa University, Japan. Thin-layer chromatography (p.l.c.) was carried out on silica gel (Merck $PF_{254+366}$).

Isolation of the Terpenoids

The stem bark of *Elaeodendron glaucum* (11·4 kg) collected in Mankulam in the Jaffna district of Sri Lanka* was dried, ground and extracted with benzene; 16 g of extract were obtained. The material was crystallized from MeOH/$CHCl_3$ and the crude crystalline mixture (10·0 g) was chromatographed over silica gel (250 g) in light petroleum (40–60°). The column was eluted successively with light petroleum, light petroleum/$CHCl_3$, $CHCl_3$ and $CHCl_3$/MeOH. The compounds eluted were *D*:*A*-friedooleanan-3-one (0·73 g), m.p. 262–264°, $[\alpha]_D$ −22°, 3-oxo-*D*:*A*-friedooleanan-28-al (0·85 g), m.p. 262–263°, $[\alpha]_D$ −16°, 3-oxo-*D*:*A*-friedooleanan-25-al (0·57 g), m.p. 298–300°, $[\alpha]_D$ −59°, *D*:*A*-friedooleanan-3β-ol (0·60 g), m.p. 283–284°, $[\alpha]_D$ +15°, 17β-hydroxy-*D*:*A*-friedooleanan-3-one (elaeodendrol) (0·03 g), m.p. 228–229°, $[\alpha]_D$ −26°, 28-hydroxy-*D*:*A*-friedooleanan-3-one, m.p. 280–282°, $[\alpha]_D$ −21°, 25-hydroxy-*D*:*A*-friedooleanan-3-one (2·0 g), m.p. 295–296°, $[\alpha]_D$ −19°, previously isolated from *E. glaucum*[2] and 29-hydroxy-*D*:*A*-friedooleanan-3-one (1) (1·6 g), m.p. 270–273° ($CHCl_3$/MeOH), $[\alpha]_D$ −22° (*c*, 2·0) (lit.[5] 270–272°, $[\alpha]_D$ −24°).

25,28-Dihydroxy-D:A-*friedooleanan-3-one* (2) (0·8 g), m.p. 238–240° (MeOH/$CHCl_3$), $[\alpha]_D$ −31° (*c*, 0·5) (Found: $M^{+\cdot}$, 458·3779. $C_{30}H_{50}O_3$ requires $M^{+\cdot}$, 458·3760). I.r. ν_{max} 3600–3100, 1700 cm^{-1}; ^{1}H n.m.r. δ ($CDCl_3$, MeOD) 0·70, 0·93, 0·95, 1·01, 1·10, each s, 5Me; 0·88, d, *J* 7 Hz, 4β-Me; 3·6, s, 17β-CH_2OH; 3·93, m, $W_{h/2}$ 2 Hz, 9β-CH_2OH; *m*/*z* 458 (M, 46%), 440 (25), 427 (100), 409 (50), 289 (38) and *25-hydroxy-3-oxo*-D:A-*friedooleanan-28-al* (3) (0·1 g), m.p. 293–295° (MeOH/$CHCl_3$), $[\alpha]_D$ −6·7° (*c*, 0·5) (Found: C, 77·3; H, 10·7. $C_{30}H_{48}O_3$,$\frac{1}{2}H_2O$ requires C, 77·4; H, 10·5%). I.r. ν_{max} 3500, 2660, 1710, 1700 cm^{-1}; ^{1}H n.m.r. δ ($CDCl_3$) 0·66, 0·96×2, 1·01, 1·1, each s, 5Me; 3·92, m, $W_{h/2}$ 2 Hz, 9β-CH_2OH; 9·5, s, 17β-CHO; *m*/*z* 456 (M, 4%), 427 (100), 425 (32), 409 (12), 289 (33), 259 (15).

D:A-*Friedooleanane-3β,25,28-triol* (*4*)

(A) The diol (2) (20 mg) in methanol (5 ml) was treated with sodium borohydride (10 mg) at 27° for 0·25 h with stirring. Dilution with water and extraction with ether gave a crude product which was subjected to preparative t.l.c. ($CHCl_3$/MeOH 47/3). Recrystallization of this product from MeOH/$CHCl_3$ gave D:A-*friedooleanane-3β,25,28-triol* (4) (15 mg) as colourless needles, m.p. 308–310°, $[\alpha]_D$ +23·2° (*c*, 0·5) (Found: 442·3795 ($M^{+\cdot}-H_2O$, 2·5%). $C_{30}H_{52}O_3$ requires $M^{+\cdot}-H_2O$, 442·3811). I.r. ν_{max} 3600–3150; ^{1}H n.m.r. δ ($CDCl_3$+MeOD) 0·9, 0·98×2, 1·06, 1·11, each s, 5Me; 0·88, d, *J* 7 Hz, 4β-Me; 3·63, s, 17β-CH_2OH; 3·73, m, $W_{h/2}$ 3 Hz, 3-CHOH; 3·91, m, $W_{h/2}$ 2 Hz, 9β-CH_2OH; *m*/*z* 460 (M, 4%), 442 (M−18, 0·5), 429 (100), 411 (37), 291 (25).

(B) 25-Hydroxy-3-oxo-*D*:*A*-friedooleanan-28-al (3) (25 mg) was reduced with sodium borohydride for 0·25 h as described above. Purification of the product by preparative t.l.c. gave the triol (20 mg) as colourless needles, m.p. 309–310° ($CHCl_3$/MeOH), $[\alpha]_D$ +23·3° (*c*, 0·5) identical with the above triol (4) (mixed m.p. and i.r.).

* A voucher specimen of the plant has been deposited with the University herbarium.

D:A-*Friedooleanan-25-ol* (*5*)

(A) 25-Hydroxy-3-oxo-*D:A*-friedooleanan-28-al (3) (40 mg) was reduced under Huang Minlon conditions by heating, under reflux with diethylene glycol (5 ml), hydrazine hydrate (1 g) and potassium hydroxide (80 mg) for 3 h, distilling to 200° and then refluxing for a further 3 h. Workup followed by preparative t.l.c. ($CHCl_3$/MeOH 49/1) gave *D:A*-friedooleanan-25-ol (5) (21 mg) as colourless needles, m.p. 219–221° ($CHCl_3$/MeOH), $[\alpha]_D$ +23° (*c*, 0·5) (lit.[11] m.p. 223–226°, $[\alpha]_D$ +23°) (Found: $M^{+\cdot}$, 428·3987. Calc. for $C_{30}H_{52}O$: $M^{+\cdot}$, 428·4018).

(B) 25-Hydroxy-*D:A*-friedooleanan-3-one (6) (50 mg) was reduced as above with diethylene glycol (5 ml), hydrazine hydrate (1 g) and potassium hydroxide (100 mg). Workup gave an alcohol (27 mg), m.p. 218–221° ($CHCl_3$/MeOH), $[\alpha]_D$ +23·1° (*c*, 0·5) identical with the alcohol (5) (mixed m.p. and i.r.).

3-Oxo-D:A-*friedooleanan-25-yl Acetate* (*11*)

The alcohol (6) (80 mg) gave with pyridine/acetic anhydride (2:1, 3 ml at 27° for 18 h), after workup, 3-oxo-*D:A*-friedooleanan-25-yl acetate (11) (75 mg) as colourless needles, m.p. 170–172° ($CHCl_3$/MeOH), $[\alpha]_D$ −23° (*c*, 1) (lit.[2] m.p. 171–173°, $[\alpha]_D$ −23°).

D:A-*Friedooleanan-3α-ol* (*12*)

3-Oxo-*D:A*-friedooleanan-25-yl acetate (11) (70 mg), dry ethylenediamine (10 ml) and lithium (100 mg) were refluxed under anhydrous conditions till a blue colour appeared and the reaction mixture was kept at this temperature for 0·3 h. It was then cooled and excess lithium was destroyed by the addition of t-butyl alcohol. Workup gave a mixture of two products. Preparative t.l.c. ($CHCl_3$) gave the less polar major product *D:A*-friedooleanan-3α-ol (12) as colourless needles, m.p. 293–295° ($CHCl_3$/MeOH), $[\alpha]_D$ +16·1° (lit.[12] m.p. 292–301°, $[\alpha]_D$ +18·0°) identical with an authentic sample (mixed m.p. and i.r.).

3,28-Dioxo-D:A-*friedooleanan-25-yl Acetate* (*13*)

25-Hydroxy-3-oxo-*D:A*-friedooleanan-28-al (3) (40 mg) gave with pyridine/acetic anhydride (2 : 1, 1·5 ml at 27° for 18 h) after workup and purification by preparative t.l.c. ($CHCl_3$/MeOH 99 : 1) *3,28-dioxo*-D:A-*friedooleanan-25-yl acetate* (13) (35 mg) as colourless needles, m.p. 150–153° ($CHCl_3$/MeOH), $[\alpha]_D$ −17° (*c*, 1·0) (Found: $M^{+\cdot}$ 498·3724. $C_{32}H_{50}O_4$ requires $M^{+\cdot}$, 498·3709). I.r. ν_{max} 2700, 1740, 1710, 1700, 1240 cm^{-1}; ^1H n.m.r. δ ($CDCl_3$) 0·71, 0·80, 0·97 × 2, 1·10, each s, 5Me; 0·86, d, *J* 7 Hz, 4β-Me; 4·37, AB dd, *J* 13 Hz, 9β-CH_2OAc; 2·03, s, 25-OAc; 9·5, s, 17β-CHO; *m/z* 498 (M, 1%), 469 (33), 331 (10), 259 (5), 137 (100).

3-Oxo-D:A-*friedooleanan-28-al* (*14*)

The acetate (13) (35 mg), dry ethylenediamine and lithium (70 mg) were refluxed under anhydrous conditions as described earlier. Workup gave a mixture of two products (30 mg) which was taken up in pyridine (2 ml) and stirred with CrO_3 (20 mg) for 12 h at 27°. Workup and purification by preparative t.l.c. yielded a major product (14) (15 mg) as colourless needles, m.p. 262–264°, $[\alpha]_D$ −15·5° (*c*, 1·0) (lit.[2] m.p. 263–265°, $[\alpha]_D$ −16°) which was found to be identical with an authentic sample of 3-oxo-*D:A*-friedooleanan-28-al (canophyllal) (mixed m.p. and i.r.).

3-Oxo-D:A-*friedooleanan-25-oic Acid* (*8*)

The alcohol (6) (100 mg) in acetone was stirred with Jones reagent[8] at 0° for 0·5 h and then kept at 27° for 18 h. The reaction mixture was decanted into water and extracted with chloroform. Workup yielded 3-oxo-*D:A*-friedooleanan-25-oic acid (8) as needles (60 mg), m.p. 338–339° (MeOH/$CHCl_3$), $[\alpha]_D$ −22° (*c*, 1·0) (lit.[7] m.p. 340°). I.r. ν_{max} 3500–2500, 1710 cm^{-1}; ^1H n.m.r. δ ($CDCl_3$) 0·67, 0·76, 0·96 × 2, 1·06, 1·18, each s, 6Me; 0·83, d, *J* 7 Hz, 4β-Me; *m/z* 456 (M, 2%), 440 (12), 411 (16), 260 (100), 205 (72).

[11] Courtney, J. L., and Stern, W., *Tetrahedron Lett.*, 1965, 1607.
[12] Shoppee, C. W., Howden, M. E. H., and Johnston, G. A. R., *J. Chem. Soc.*, 1962, 498.

Methyl 3-Oxo-D:A-*friedooleanan-25-oate* (*9*)

The acid (8) (50 mg) in methanol (3 ml) was stirred with an excess of ethereal diazomethane at 27°. The product was recrystallized from MeOH/$CHCl_3$ to yield methyl 3-oxo-*D:A*-friedooleanan-25-oate (9) (35 mg) as silky needles, m.p. 173–175°, $[\alpha]_D$ −38·5° (*c*, 0·5) (lit.[7] m.p. 173–174°).

Methyl 3,3-Ethylenedioxy-D:A-*friedooleanan-25-oate* (*10*)

The methyl ester (9) (30 mg) was refluxed with toluene-*p*-sulfonic acid (5 mg) and ethylene glycol (0·5 ml) in dry benzene (30 ml) for 2 h, a Dean–Stark water separator being used. Workup followed by purification with preparative t.l.c. gave methyl 3,3-ethylenedioxy-*D:A*-friedooleanan-25-oate (10) (22 mg) as colourless needles, m.p. 197–199° ($CHCl_3$/MeOH), $[\alpha]_D$ +2·5° (*c*, 0·8) (lit.[7] m.p. 196–198°).

Attempted Reduction of Methyl 3,3-Ethylenedioxy-D:A-*friedooleanan-25-oate* (*10*)

The acetal (10) (20 mg) was stirred with $LiAlH_4$ (40 mg) in tetrahydrofuran (2 ml) for 2 h and then refluxed on a water bath for 24 h. The product was separated and found to be identical with starting material (10) (mixed m.p. and i.r.).

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