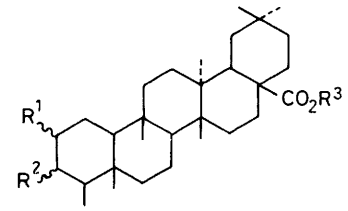
New D:A-Friedooleananes from *Euonymus revolutus* (Celastraceae)

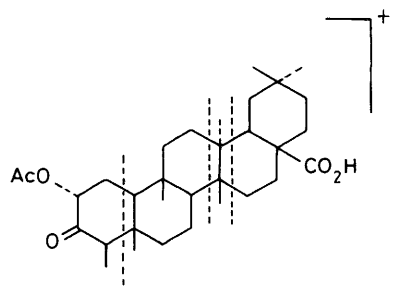
N. Savitri Kumar* and P. Mangala Muthukuda
Department of Chemistry, University of Peradeniya, Peradeniya, Sri Lanka
John K. MacLeod
Research School of Chemistry, The Australian National University, A.C.T. 2601, Canberra, Australia

Three new D:A-friedooleananes isolated from the stem bark of *Euonymus revolutus* Wight (Celastraceae) were established to be 2α-hydroxy-3-oxo-D:A-friedooleanan-28-oic acid, 3α-hydroxy-2-oxo-D:A-friedooleanan-28-oic acid, and 29-hydroxy-3-oxo-D:A-friedooleanan-28-oic acid on the basis of spectroscopic data and chemical interconversions.

Euonymus revolutus Wight (Celastraceae) is a tree of moderate size found in the upper montane forests of Sri Lanka.[1] Compounds previously isolated from this genus include cardioactive glycosides,[2] three D:A-friedooleanane derivatives,[3–7] 1α,3β-dihydroxyolean-12-en-28-oic acid,[8] taraxaren-3β-ol,[4] α-amyrin,[7] and three tingenone derivatives.[9–11] In this paper we report the isolation of three new oxygenated friedelane derivatives, 2α-hydroxy-3-oxo-D:A-friedooleanan-28-oic acid (**1**), 3α-hydroxy-2-oxo-D:A-friedooleanan-28-oic acid (**2**) and 29-hydroxy-3-oxo-D:A-friedooleanan-28-oic acid (**3**). The friedelanes (**1**) and (**2**) are oxygenated on vicinal carbon atoms. Only one other friedelane derivative with vicinal oxygenation, a D:A-friedooleanane-2,3-diol,[12] has thus far been isolated from the family Celastraceae. Oxygenation of two angular methyl groups as in the friedelane (**3**) has been reported in friedelanes isolated from four other plants belonging to the Celastraceae, *i.e. Salacia macrosperma*,[13] *S. prinoides*,[14] *Elaeodendron glaucum*,[15] and *E. balae*.[16]



(**1**) R^1 = α-OH, β-H; R^2 = O; R^3 = H
(**2**) R^1 = O; R^2 = α-OH, β-H; R^3 = H
(**4**) R^1 = α-OAc, β-H; R^2 = O; R^3 = H
(**5**) R^1 = α-OAc, β-H; R^2 = O; R^3 = Me
(**6**) R^1 = R^2 = α-OH, β-H; R^3 = H
(**7**) R^1 = R^2 = α-OAc, β-H; R^3 = H
(**8**) R^1 = R^3 = H; R^2 = O
(**9**) R^1 = H; R^2 = O; R^3 = Me
(**15**) R^1 = R^3 = H; R^2 = α-OAc, β-H



m/z 514
($C_{32}H_{50}O_5$)

Figure 1.

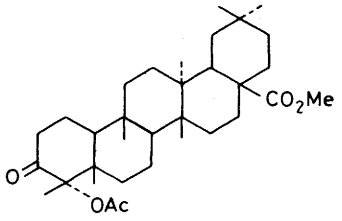
Discussion

Dried stem bark of *Euonymus revolutus* was collected at Hakgala in the Nuwara Eliya district of Sri Lanka. Combined column chromatography and preparative layer chromatography of the dichloromethane extract from the stem bark of *Euonymus revolutus* yielded two polar fractions. Both fractions were found to consist of two triterpenes each. The two triterpenes (**1**) and (**2**) in the less polar fraction were separated by p.l.c. Both triterpenes were found to be friedelane derivatives with similar spectroscopic properties (see Experimental section). A pure sample of the more polar D:A-friedooleanane (**1**) on treatment with either sodium hydroxide or acetic acid yielded a mixture of compounds (**1**) and (**2**), while a pure sample of the D:A-friedooleanane (**2**) gave a mixture of the D:A-friedooleananes (**1**) and (**2**) on standing. Hence, the friedooleananes (**1**) and (**2**) are probably α-hydroxy ketones.

The i.r. spectrum of the triterpene (**1**) ($C_{30}H_{48}O_4$) showed it to be a carboxylic acid ($\nu_{max.}$ 3 550—3 100, 1 690 cm^{-1}), with a hydroxy group ($\nu_{max.}$ 3 440 cm^{-1}) and an α-hydroxy carbonyl group ($\nu_{max.}$ 1 725 cm^{-1}). Treatment of the acid (**1**) with acetic anhydride–pyridine yielded a monoacetate (**4**) which reacted with diazomethane forming the methyl ester (**5**). The ^1H n.m.r. spectrum of compound (**4**) showed the presence of seven methyl groups, and a secondary acetoxy group [δ 4.89 (m)]. The half-height width of this signal ($w_{\frac{1}{2}}$ 5 Hz) indicated that the acetoxy group was axial. High resolution mass spectroscopy gave a molecular formula $C_{32}H_{50}O_5$. The fragment at *m/z* 331 ($C_{21}H_{31}O_3$) suggested that the carbonyl group and the acetoxy group were both attached to one of the rings A, B, or C (see Figure 1), while the fragments at *m/z* 372($C_{25}H_{40}O_2$) and 235($C_{15}H_{23}O_2$) indicated that the carboxy group was in either ring D or E.[17]

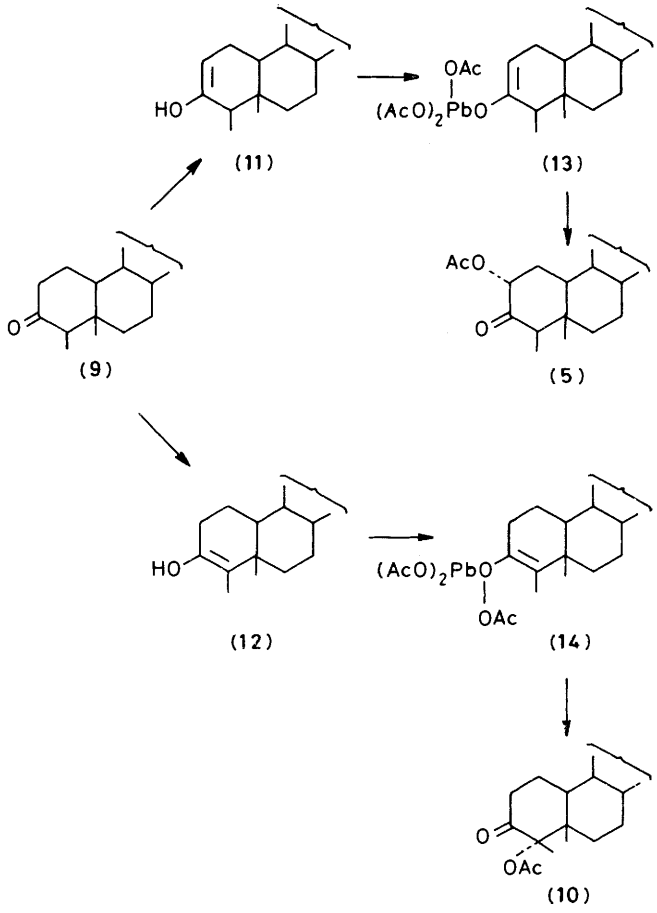
Reduction of the friedooleanane (**1**) with sodium borohydride yielded a diol (**6**); this underwent ready oxidation with periodic acid suggesting the presence of a vicinal diol system. The diol (**6**) on treatment with acetic anhydride—pyridine gave a diacetate (**7**). The half-height width of the two C*H*OAc proton signal which appeared as a multiplet ($w_{\frac{1}{2}}$ 12.0 Hz) suggested the presence of one axial and one equatorial acetoxy group in the diacetate (**7**).

The position of the carbonyl group and the carboxylic acid group in compound (**4**) and hence in (**1**) was established by deacetoxylation of the monoacetate (**4**) by reflux with zinc dust in acetic acid.[18] Deacetoxylation was found to be complete in one hour. Zinc dust in acetic acid is known to deacetoxylate axial acetoxy ketones rapidly, while equatorial isomers are deacetoxylated slowly under the same conditions.[19a] Hence the



(10)

ready deacetoxylation of the friedelane (**4**) also suggested the axial orientation of this acetoxy group. The product (**8**) obtained on deacetoxylation was established to be 3-oxo-D:A-friedooleanan-28-oic acid (**8**) by comparison with an authentic sample. Hence the carbonyl group and the carboxylic acid group in D:A-friedooleanane (**1**) were at C-3 and C-28 respectively. As the hydroxy group is vicinal to the carbonyl group, it must be located at either C-2 or C-4. Location at C-4 can be ruled out as spectroscopic evidence indicated the presence of a secondary hydroxy group. Hence the hydroxy group must be located at C-2 and should have the α-axial configuration. Therefore the D:A-friedooleanane (**1**) was assigned the structure 2α-hydroxy-3-oxo-D:A-friedooleanan-28-oic acid. This structure was confirmed by a partial synthesis of the D:A-friedooleanane (**5**) from methyl 3-oxocanophyllate (**9**) by treatment with lead tetra-acetate–glacial acetic acid in the presence of boron trifluoride–ether.[20] The monoacetate (**10**) ($C_{33}H_{52}O_5$) [δ 3.66 (3 H, s, $COCH_3$), 2.06 (3 H, s, O_2CCH_3), 1.83 (3 H, s, 23-CH_3)] was also formed during this reaction. This type of acetoxylation with lead tetra-acetate has been suggested to occur in the enol form by a radical mechanism. Enolisation of the carbonyl group in compound (**9**) could give rise to two enols. Acetoxylation would then occur at the less hindered α-face, thus giving rise to the monoacetates (**5**) and (**10**) (Scheme).[19b]

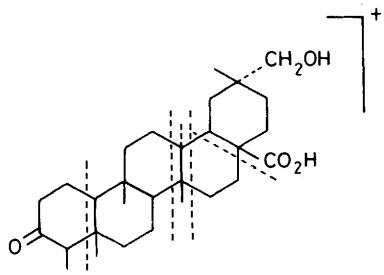


Scheme 1.

The i.r. spectrum of the thermodynamically less stable isomer (**2**) showed the presence of a carboxylic acid group and an α-hydroxy carbonyl system ($\nu_{max.}$ 1 710 cm^{-1}). The lower frequency of this absorption when compared with that of the friedelane (**1**) may be ascribed to intramolecular hydrogen bonding. The ^1H n.m.r. spectrum of compound (**2**) showed a doublet at δ 3.85 (*J* 12 Hz). The splitting of this signal indicated the presence of an axial proton and therefore an equatorial hydroxy group. As the D:A-friedooleananes (**1**) and (**2**) are isomeric α-hydroxy ketones, the hydroxy group in compound (**2**) must be at C-3. This conclusion is in agreement with the observed multiplicity of the carbinol methine proton which appeared as a doublet split by the single proton at C-4. Hence the structure of the friedelane (**2**) was established to be 3α-hydroxy-2-oxo-D:A-friedooleanan-28-oic acid. Attempts to prepare derivatives of the friedooleanane (**2**), for example by treatment with Ac_2O–pyridine, led to complete isomerisation and the formation of the monoacetate (**4**). The ready isomerisation of the hydroxy ketone (**2**) to the isomeric friedelane (**1**) may be attributed to the relative instability of compound (**2**) which is due to eclipsing of the carbonyl group at C-2 with the equatorial hydroxy group at C-3. Partial isomerisation of compound (**1**) is possible under more vigorous conditions (*e.g.* treatment with dilute acids and bases; see Experimental section) to give the $3\alpha_{eq}$-hydroxy isomer in *ca.* 30% yield. No $3\beta_{ax}$-hydroxy isomer is formed during this isomerisation. There is a possibility that equilibration of the hydroxy ketones (**1**) and (**2**) may have occurred during chromatography and isolation, leading to a higher proportion of compound (**1**) than in the natural state. However the possibility that the hydroxy ketone (**2**) is the natural product and that compound (**1**) is an artefact formed during the isolation procedures cannot entirely be discounted.

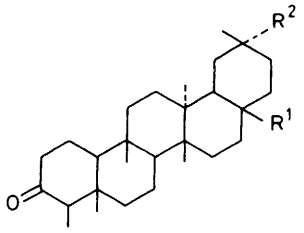
The more polar fraction was separated by p.l.c. to give two triterpenes, an acid (**3**) and a diol (**11**). Acetylation of the diol (**11**) gave a diacetate (**12**) [δ_H 4.2 (2 H, dd, *J* 11.0 Hz), 3.72 (2 H, s), 2.05 (3 H, s) and 2.03 (3 H, s)]. The diol (**11**) was found to be identical with 28,29-dihydroxy-D:A-friedooleanan-3-one obtained from *Elaeodendron balae*.[16]

I.r. evidence indicated the presence of carboxylic acid and hydroxy groups ($\nu_{max.}$ 3 560—3 160, 3 360 and 1 690 cm^{-1}) in compound (**3**). High resolution mass spectroscopy gave a molecular formula $C_{30}H_{48}O_4$. Treatment of compound (**3**) with acetic anhydride–pyridine yielded a monoacetate (**13**) which reacted with diazomethane to give the methyl ester (**14**). ^1H N.m.r. data for the acetate (**13**) together with the mass spectral fragmentation patterns for the acid (**3**) suggested the presence of a D:A-friedooleanane derivative. The ^1H n.m.r. spectrum of compound (**13**) showed the presence of six methyl groups, a primary acetoxy group [δ 3.72 (2 H, br s) and 2.09 (3 H, s)] and a carboxylic acid group [δ 9.60 (1 H, br s, disappears with D_2O)]. The broad singlet at δ 3.72 indicated that the CH_2OAc group occupied a non-hindered position. Comparison of the chemical shift data of the acetoxy methylene protons with those reported for friedelane derivatives suggested that the most probable location for the CH_2OAc group was at C-29.[21] The intense fragment at *m/z* 441 ($C_{29}H_{45}O_3$, $M^+ - CH_2OH$) in the mass spectrum of the acid (**3**) confirmed the presence of a primary hydroxy group. The strong peak at *m/z* 273 indicated the absence of any oxygenation in the rings A, B, and C other than a carbonyl group which was probably at C-3, while the fragments



m/z 472
($C_{30}H_{48}O_4$)

Figure 2.



(**3**) $R^1 = CO_2H$, $R^2 = CH_2OH$
(**11**) $R^1 = R^2 = CH_2OH$
(**12**) $R^1 = R^2 = CH_2OAc$
(**13**) $R^1 = CO_2H$, $R^2 = CH_2OAc$
(**14**) $R^1 = CO_2Me$, $R^2 = CH_2OAc$
(**16**) $R^1 = CO_2H$, $R^2 = CHO$

at *m/z* 251 and 170 suggested that the CH_2OH and CO_2H groups were attached to ring E (see Figure 2).[17] The absence of a methyl signal further downfield than δ 1.09 in the ^1H n.m.r. spectrum of the acid (**3**) suggested that the 28-methyl group was oxygenated[22] and that the carboxylic acid group was not at the 20 position. The carboxylic acid group was therefore probably at the 17 position. This was confirmed by relating the acetate to the known D:A-friedooleanane derivative oxocanaphyllic acid (**8**). Reduction of the acetate (**13**) with lithium in ethylenediamine[23] gave a mixture of three products from which an alcohol was isolated and acetylated to give the monoacetate (**15**) [δ 4.64 (1 H, dt, *J* 10.5 and 4.0 Hz)]. The monoacetate (**15**) was shown to be identical with the monoacetate prepared from the lithium–ethylenediamine reduction product from oxocanaphyllic acid (**8**).

The reduction of the acid (**3**) and the ester (**14**) with lithium aluminium hydride was attempted. In both instances reduction of the carboxy function did not take place, but the carbonyl group was reduced to a secondary hydroxy group. Oxidation of the acid (**3**) with CrO_3–pyridine at 27 °C gave an aldehyde acid (**16**) [$\nu_{max.}$ 3 460—3 250, 2 920, 1 710, and 1 690 cm^{-1}] which was shown to be identical (mixed m.p., co-t.l.c. and i.r.) with the aldehyde acid prepared from an authentic sample of 28,29-dihydroxy-D:A-friedooleanan-3-one (**11**),[16] thus establishing the position of the carbonyl, carboxy, and hydroxymethyl groups at C-3, C-28, and C-29 respectively. Hence the structure of the friedelane derivative (**3**) was established to be 29-hydroxy-3-oxo-D:A-friedooleanan-28-oic acid. Analytical and spectroscopic data were in agreement with this structure.

Experimental

M.p.s. were determined on a Kofler hot stage apparatus and are uncorrected. The identities of compounds were established by mixed melting point, co-t.l.c. and ^1H n.m.r. comparison. Light petroleum refers to the fraction having boiling range 60—80 °C. P.l.c. was carried out on Merck Kieselgel 60 $PF_{254+365}$. Optical rotations were measured at 27 °C in $CHCl_3$ on a Perkin-Elmer 141 polarimeter. I.r. spectra were determined for KBr discs on a Perkin-Elmer 257 spectrophotometer. ^1H N.m.r. spectra were recorded unless otherwise stated on a Varian T 60 spectrometer in $CDCl_3$ at 60 MHz with $SiMe_4$ as internal standard. Low resolution electron impact (E.I.) mass spectra were recorded at 70 eV on a VG 7070F instrument using the direct insertion probe. High resolution (*ca.* 10 000) accurate mass measurements were carried out on a MS-902 instrument under the same operating conditions. Usual work-up refers to dilution with ice cold water, acidification with dil. HCl, extraction with ether, drying of the ether layer ($MgSO_4$), and evaporation to dryness. Ether refers to diethyl ether.

Extraction of E. revolutus.—Dried and powdered stem bark (5 kg) was extracted with cold CH_2Cl_2. The CH_2Cl_2 extract was evaporated to dryness (111 g) and re-extracted with hot MeOH to remove gutta-percha. The dried MeOH extract (70 g) was chromatographed on silica gel (C_6H_6–EtOAc–MeOH).

Isolation of Compounds (**1**) *and* (**2**).—Elution of the column with EtOAC and 5% MeOH afforded a gummy solid which was crystallised with EtOAc to give a white solid. P.l.c. (CH_2Cl_2–5% MeOH) of the solid gave two compounds. The more polar compound on crystallisation from MeOH gave 2α-*hydroxy*-3-*oxo*-D:A-*friedooleanan*-28-*oic acid* (**1**) (114 mg), m.p. 258—260 °C (Found: M^+, 472.3546. $C_{30}H_{48}O_4$ requires *M*, 472.3552); $\nu_{max.}$ 3 550—3 100, 3 440, 1 725, and 1 690 cm^{-1}; δ_H (100 MHz), 4.14 (1 H, m, $w_{\frac{1}{2}}$ 7 Hz, 2β-H), and 1.05—0.70 (7 × CH_3); *m/z* 472 (M^+, 12%), 454(47), 439(87), 426(51), 411(25), 386(13), 317(24), 303(10), 289(67), 271(16), 263(19), 247(42), 235(27), 205(43), 191(85), 189(78), 175(29), and 163(72). The less polar compound on crystallisation from MeOH yielded 3α-*hydroxy*-2-*oxo*-D:A-*friedooleanan*-28-*oic acid* (**2**) (30 mg), m.p. 288—290 °C; $\nu_{max.}$ 3 600—3 100, 3 430, 1 710, and 1 685 cm^{-1}; δ_H (100 MHz), 3.85 (1 H, d, *J* 12 Hz, 3β-H), and 1.08—0.72 (7 × CH_3).

Isolation of Compounds (**3**) *and* (**11**).—Further elution of the column with EtOAc and 5% MeOH yielded a yellow gummy solid which on p.l.c. (CH_2Cl_2–10% MeOH) gave 29-*hydroxy*-3-*oxo*-D:A-*friedooleanan*-28-*oic acid* (**3**) (100 mg) as colourless needles, m.p. 288—290 °C obtained on crystallisation from $CHCl_3$–MeOH [Found: $(M - H_2O)^+$, 454.344 33; $(M - CH_2OH)^+$, 441.343 08; $(M - CO_2H - H)^+$, 426.350 13; $(M - C_5H_9O)^+$, 387.293 18; $(M - C_{11}H_{19}O_3)^+$, 273.220 49; $(M - C_{15}H_{25}O)^+$, 251.165 89; $(M - C_{16}H_{26}O_3)^+$, 206.166 85; $(M - C_{16}H_{27}O_3)^+$, 205.158 98; $(M - C_{21}H_{34}O)^+$, 170.096 08. Calc. for $C_{30}H_{48}O_4$: $(M - H_2O)$, 454.344 70; $(M - CH_2OH)$, 441.336 87; $(M - CO_2H - H)$, 426.349 78; $(M - C_5H_9O)$, 387.289 92; $(M - C_{11}H_{19}O_3)$, 273.221 84; $(M - C_{15}H_{25}O)$, 251.164 72; $(M - C_{16}H_{26}O_3)$, 206.167 06; $(M - C_{16}H_{27}O_3)$, 205.159 24; $(M - C_{21}H_{34}O)$, 170.094 29)]; $\nu_{max.}$ 3 560—3 160, 3 360, 1 710, and 1 690 cm^{-1}; *m/z* 472 (M^+, 16%), 454 (14), 441(26), 439(17), 426(12), 387(14), 273(51), 251(6), 206(12), 205(22), and 170(3); and 28,29-dihydroxy-D:A-friedooleanan-3-one (**11**) (50 mg), colourless needles from $CHCl_3$–MeOH; m.p. 286—288 °C (lit.,[16] m.p. 286—288 °C); $\nu_{max.}$ 3 450, 1 710 cm^{-1}.

Isomerisation of Compound (**1**).—(*a*) Compound (**1**) (10 mg) was dissolved in ether (5 ml) and stirred with 2N-NaOH (1.0 ml) for 5 min. The aqueous layer was separated, acidified with 1M-hydrochloric acid and extracted twice with ether. The ether extract was dried ($MgSO_4$) and evaporated. T.l.c. of the reaction mixture showed the presence of two compounds, corresponding to the friedooleananes (**1**) and (**2**) in the approximate ratio 2:1. P.l.c. (CH_2Cl_2–5% MeOH) of the mixture gave friedooleanane

(**1**) (5.5 mg) and friedooleanane (**2**) (2.5 mg). The identities of these two compounds were established by co-t.l.c., mixed m.p. and i.r. comparison.

(*b*) Compound (**1**) (8 mg) was dissolved in ether (5 ml) and shaken with 1M-acetic acid (1.0 ml) for 20 min. The ether layer was separated, dried and evaporated. Separation of the reaction mixture by p.l.c. (CH_2Cl_2–5% MeOH) gave the friedooleananes (**1**) (4.5 mg) and (**2**) (2 mg).

Isomerisation of Compound (**2**).—(*a*) A solution of compound (**2**) (2 mg) in dichloromethane (5 ml) was left at room temperature for 72 h. T.l.c. of the reaction mixture showed the presence of compounds (**1**) and (**2**) in the approximate ratio 2:1 respectively.

(*b*) A solution of compound (**2**) (1 mg) was dissolved in ether (2 ml), 2N-NaOH (0.5 ml) was added, and the solution was stirred for 2 min. The aqueous layer was separated, acidified with 1M-hydrochloric acid and extracted with ether. The ether extract was dried. T.l.c. of the reaction mixture showed the presence of compounds (**1**) and (**2**) in the approximate ratio 2:1 respectively.

(*c*) A solution of compound (**2**) (1 mg) was dissolved in ether (2 ml) and shaken with 1M-acetic acid (0.5 ml) for 5 min. T.l.c. of the ether layer showed the presence of compounds (**1**) and (**2**) in the approximate ratio 2:1 respectively.

Acetylation of Compound (**1**).—Compound (**1**) (50 mg) was treated with Ac_2O–pyridine (1:1) (5 ml) at 27 °C for 24 h. Usual work-up afforded a brown semisolid which on p.l.c. ($CHCl_3$) gave a white solid. Crystallisation of this solid from $CHCl_3$–MeOH yielded colourless needles of 2α-*acetoxy*-3-*oxo*-D:A-*friedooleanan*-28-*oic acid* (**4**) (48 mg), m.p. 275 °C, $[\alpha]_D$ − 41.4° (*c*, 1.0) [Found: M^+, 514.358 89; $(M - CO_2H)^+$, 469.373 93; $(M - CH_3CO_2H)^+$, 454.343 51; $(M - C_7H_{10}O_3)^+$, 372.296 63; $(M - C_{11}H_{19}O_2)^+$, 331.222 29; $(M - C_{17}H_{27}O_3)^+$, 235.171 51. $C_{32}H_{50}O_5$: *M*, 514.365 83; $(M - CO_2H)$, 469.368 17; $(M - CH_3CO_2H)$, 454.344 70; $(M - C_7H_{10}O_3)$, 372.302 83; $(M - C_{11}H_{19}O_2)$, 331.227 32; $(M - C_{17}H_{27}O_3)$, 235.169 80]; $\nu_{max.}$ 3 530—3 100, 1 745, 1 725, and 1 685 cm^{-1}; δ_H 4.89 (1 H, m, $w_{\frac{1}{2}}$ 5 Hz, 2-H), 2.09 (3 H, s, CH_3CO), and 1.03—0.69 (7 × CH_3); *m/z* 514 (M^+, 24%), 496(10), 481(17), 468(12), 454(37), 271(31), 235(19), 190(37), and 108(16).

Methylation of Compound (**4**).—Compound (**4**) (10 mg) was suspended in MeOH (0.5 ml) and CH_2N_2–Et_2O added dropwise until a yellow colour persisted. Evaporation of the solvent followed by crystallisation from MeOH yielded methyl 2α-acetoxy-3-oxo-D:A-friedooleanan-28-oate (**5**) (10 mg), m.p. 260 °C, $[\alpha]_D$ − 31.5° (*c*, 1.0) (Found: C, 73.5; H, 9.9%; M^+ 528.3848. Calc. for $C_{33}H_{52}O_5 \cdot \frac{1}{2}H_2O$: C, 73.69; H, 9.93%; *M*, 528.3815); $\nu_{max.}$ 1 745, 1 725, and 1 230 cm^{-1}; δ_H 4.95 (1 H, m, $w_{\frac{1}{2}}$ 7 Hz, 2-H), 3.66 (3 H, s, OCH_3), 2.12 (3 H, s, CH_3CO), and 1.03—0.69 (7 × CH_3); *m/z* 528 (M^+, 3%), 510(41), 495(71), 481(100), 271(39), 249(24), 217(33), 205(50), and 189(91).

$NaBH_4$ *Reduction of Compound* (**1**) *and Acetylation.*—Compound (**1**) (20 mg) was reduced with $NaBH_4$ (100 mg) in MeOH (5 ml) at 27 °C for 8 h. Evaporation of the solvent under reduced pressure followed by usual work-up yielded a white solid which was crystallised from EtOAc–light petroleum to give the diol (**6**) (18 mg). Part of the diol (**6**) (10 mg) was treated with Ac_2O–pyridine at 27 °C for 24 h. Usual work-up followed by crystallisation from MeOH yielded 2α,3α-*bis*(*acetoxy*)-D:A-*friedooleanan*-28-*oic acid* (**7**) (8 mg), m.p. 300 °C, $[\alpha]_D$ − 11.4° (*c*, 0.8) (Found: M^+ 558.3862·$C_{34}H_{54}O_6$ requires *M*, 558.3921); $\nu_{max.}$ 3 500—3 020, 1 745, 1 695 cm^{-1}; δ_H 4.83 (2 H, m, $w_{\frac{1}{2}}$ 12 Hz, 2β-H and 3β-H), 2.03 (3 H, s, CH_3CO), 2.06 (3 H, s, CH_3CO), and 1.03—0.80 (7 × CH_3); *m/z* 558 (M^+, 0.3%), 512(3), 499(3), 452(3), 289(6), and 273(10).

Periodate Oxidation of the Diol (**6**).—The diol (**6**) (3 mg) was dissolved in tetrahydrofuran (1 ml) and a saturated solution of periodic acid (0.5 ml) was added dropwise. T.l.c. of the reaction mixture after 45 min showed the absence of starting material and the formation of a single less polar product. The reaction product was not isolated.

Deacetoxylation of Compound (**4**).—Compound (**4**) (40 mg) was refluxed with Zn in HOAc for 1 h. The mixture was filtered, diluted with cold water, and extracted with ether (× 3). The combined ether extracts were dried ($MgSO_4$), filtered and evaporated to dryness. The white solid was then crystallised with $CHCl_3$–MeOH to yield 3-oxo-D:A-friedooleanan-28-oic acid (**8**) (30 mg), m.p. 310 °C (lit.,[24] m.p. 310 °C); $\nu_{max.}$ 3 560—3 040, 1 710, and 1 680 cm^{-1}; δ_H 1.04—0.69 (7 × CH_3).

Methylation of 3-*Oxo*-D:A-*friedooleanan*-28-*oic Acid* (**8**).—3-Oxo-D:A-friedooleanan-28-oic acid (**8**) (100 mg) was suspended in MeOH, and CH_2N_2 in ether was added dropwise until a yellow colour persisted. Evaporation of the solvent followed by crystallisation from MeOH yielded colourless needles of methyl-3-oxo-D:A-friedooleanan-28-oate (**9**), m.p. 248–249 °C, $[\alpha]_D$ −31.0° (*c*, 1.0) (lit.,[24] m.p. 247—249 °C, $[\alpha]_D$ − 27°).

Partial Synthesis of Compound (**5**).—Compound (**8**) (100 mg) was treated with $Pb(OAc)_4$ (100 mg) in glacial HOAc (25 ml) and BF_3–ether (2 ml) at 27 °C for 2 h in the dark. Dilution of the reaction mixture with H_2O followed by extraction with ether gave a dark brown solid which was chromatographed on silica gel. Elution with benzene yielded two compounds. The less polar compound was crystallised from MeOH to yield *methyl* 2α-*acetoxy*-3-*oxo*-D:A-*friedooleanan*-28-*oate* (**5**) (30 mg), m.p. 260 °C, $[\alpha]_D$ − 31.5° (*c*, 1.0); $\nu_{max.}$ 1 745, 1 720, 1 235 cm^{-1}; δ_H 4.95 (1 H, m, $w_{\frac{1}{2}}$ 7 Hz, 2β-H), 3.66 (3 H, s, CH_3O), 2.12 (3 H, s, CH_3CO), and 1.03—0.69 (7 × CH_3). The more polar compound, on crystallisation from $CHCl_3$–MeOH, gave *methyl* 4α-*acetoxy*-3-*oxo*-D:A-*friedooleanan*-28-*oate* (**10**) (60 mg), m.p. 330 °C, $[\alpha]_D$ + 4.8° (*c*, 1.0) (Found: M^+ 528.3823. $C_{33}H_{52}O_5$ requires *M*, 528.3815); $\nu_{max.}$ 1 755, 1 725, and 1 235 cm^{-1}; δ_H 3.66 (3 H, s, CH_3O) 2.06 (3 H, s, CH_3CO), 1.83 (3 H, s, 23-CH_3), and 1.06—0.72 (6 × CH_3); *m/z* 528 (M^+, 47%), 486(70), 468(18), 450(6), 436(7), 426(29), 203(44), 189(100), and 175(23).

Attempted Acetylation of Compound (**2**).—Compound (**2**) (10 mg) was treated with pyridine–Ac_2O (1:1) (1 ml) for 12 h at 27 °C. T.l.c. showed the presence of only one product. The usual work-up followed by crystallisation from $CHCl_3$–MeOH yielded 2α-acetoxy-3-oxo-D:A-friedooleanan-28-oic acid (**4**) (6 mg), m.p. 275 °C (mixed m.p. co-t.l.c.) identical with the acetate (**4**) prepared from compound (**1**).

Acetylation of compound (**11**).—Compound (**11**) (40 mg) was treated with pyridine–Ac_2O (1:1) (2 ml) at room temperature for 24 h. Usual work-up afforded a solid which on p.l.c. ($CHCl_3$–MeOH) followed by crystallisation gave 28,29-diacetoxy-D:A-friedooleanan-3-one (**12**) (38 mg); m.p. 119—122 °C (lit.,[25] m.p. 119—120 °C); $\nu_{max.}$ 2 930, 1 730, 1 710, and 1 230 cm^{-1}; δ_H 4.20 (2 H, dd, *J* 11.0 Hz, 28-CH_2OAc), 3.72 (2 H, s, 29-CH_2OAc), 2.05 (3 H, s, CH_3CO), 2.03 (3 H, s, CH_3CO), and 1.09—0.69 (6 × CH_3).

Acetylation of Compound (**3**).—Compound (**3**) (70 mg) was treated with pyridine–Ac_2O at 27 °C for 24 h. Usual work-up yielded colourless needles of 29-*acetoxy*-3-*oxo*-D:A-*friedooleanan*-28-*oic acid* (**13**) (68 mg), m.p. 270—271 °C, $[\alpha]_D$ − 25° (*c*, 1.0) (Found: M^+, 514.3683. $C_{32}H_{50}O_5$ requires *M*, 514.3658); $\nu_{max.}$ 3 500—3 040, 2 920, 1 735, 1 710, 1 690, and 1 240 cm^{-1}; δ_H 9.60 (1 H, br s, 28-CO_2H, disappears with D_2O), 3.72 (2 H, s, 29-CH_2OAc), 2.09 (3 H, s, O_2CCH_3), and 1.09—0.73 (6 × CH_3);

m/z 514 (M^+, 22%), 499(11), 481(13), 468(10), 453(9), 429(22), 408(14), 308(16), 301(11), 273(50), 259(10), 247(20), 233(36), 189(41), and 175(30).

Methylation of Compound (**13**).—Compound (**13**) (20 mg) was dissolved in ether and CH_2N_2 in ether was added dropwise until the yellow colour persisted. Crystallisation from $CHCl_3$–MeOH afforded colourless crystals of *methyl 29-acetoxy-3-oxo-*D:A*-friedooleanan-28-oate* (**14**) (20 mg), m.p. 185—187 °C, $[\alpha]_D$ − 30° (*c*, 1.0) (Found: C, 75.2; H, 9.8. $C_{33}H_{52}O_5$ requires C, 74.96; H, 9.91%); $\nu_{max.}$ 2 940, 1 735, 1 710, and 1 220 cm^{-1}; $\delta_H(CCl_4)$, 3.66 (5 H, br. s, CH_3O and 29-CH_2OAc), 2.00 (3 H, s, CH_3CO), and 1.26—0.69 (6 × CH_3).

Lithium–Ethylenediamine Reduction of Compound (**13**).—Compound (**13**) (50 mg) was refluxed with lithium (100 mg) in ethylenediamine (8 ml) until a blue colour appeared. The mixture was kept at this temperature for another 20 min. Excess of lithium was destroyed by the addition of t-butyl alcohol. The usual work-up yielded a yellow solid which was treated with pyridine–Ac_2O (1:1) (2 ml) at 27 °C for 24 h. The usual work-up gave a solid which on crystallisation from $CHCl_3$–MeOH afforded 3α-*acetoxy*-D:A-*friedooleanan*-28-*oic acid* (**15**) (20 mg), m.p. 309—310 °C; $\nu_{max.}$ 3 610—3 050, 1 725, 1 715, 1690, and 1 260 cm^{-1}; δ_H(100 MHz), 4.64 (1 H, dt, $J_{ax,ax}$ 10.5 Hz, $J_{ax,eq}$ 4.0 Hz, 3β-H), 2.02 (3 H, s, $COCH_3$), and 1.04—0.74 (7 × CH_3).

Lithium–Ethylenediamine Reduction of 3-*Oxocanophyllic Acid* (**8**).—Compound (**8**) (30 mg) was reduced with lithium (60 mg) in ethylenediamine following the procedure described above. The yellow solid obtained after work-up on acetylation with pyridine–Ac_2O afforded a monoacetate which was found to be identical with 3α-*acetoxy*-D:A-*friedooleanan*-28-*oic acid* (**15**) (15 mg), m.p. 309—310 °C; $\nu_{max.}$ 3 610—3 050, 1 725, 1 715, 1 690, and 1 260 cm^{-1}; δ_H(100 MHz) 4.64 (1 H, dt, $J_{ax,ax}$ 10.5 Hz, $J_{ax,eq}$ 4.0 Hz, 3β-H), 2.02 (3 H, s, $COCH_3$), and 1.04—0.74 (7 × CH_3).

Oxidation of Compound (**3**).—Compound (**3**) (30 mg) was treated with pyridine–CrO_3 (40 mg) at 27 °C for 5 h. The usual work-up yielded a dark brown solid which was purified by p.l.c. (CH_2Cl_2–10% MeOH). Crystallisation from $CHCl_3$–MeOH afforded 3,29-dioxo-D:A-friedooleanan-28-oic acid (**16**) (10 mg), m.p. 219—221 °C (lit.,[16] m.p. 220—222 °C), $[\alpha]_D$ − 10.0° (*c*, 0.5) {lit.,[16] $[\alpha]_D$ − 12.0° (*c*, 1.0)}; $\nu_{max.}$ 3 460—3 250, 1 710, 1 690, and 1 685 cm^{-1}.

Oxidation of 28,29-*Dihydroxy*-D:A-*friedooleanan*-3-*one* (**11**).—CrO_3(50 mg) was added to a solution of the diol (**11**) (20 mg) in pyridine (2 ml) and the mixture was stirred at 0 °C for 0.5 h and then at 27 °C for 6 h. The usual work-up followed by p.l.c. (CH_2Cl_2–10% MeOH) and crystallisation from $CHCl_3$–MeOH gave 3,29-*dioxo*-D:A-*friedooleanan*-28-*oic acid* (**16**) (10 mg) m.p. 219—221 °C (lit.,[16] m.p. 220—222 °C); $[\alpha]_D$ − 10.0° (*c*, 1.0) {lit.,[16] $[\alpha]_D$ − 12.0° (*c*, 1.0)}; $\nu_{max.}$ 3 460—3 250, 1 710, 1 690, and 1 685 cm^{-1}.

Acknowledgements

We thank Professor S. Balasubramaniam, Department of Botany, University of Peradeniya, Sri Lanka for the collection and identification of the plant material; Dr. M. I. M. Wazeer, Department of Chemistry, University of Petroleum and Minerals, Saudi Arabia for the 100 MHz ^1H n.m.r. data; Mrs. S. C. Weerasekera for technical assistance; and the Natural Resources, Energy and Science Authority of Sri Lanka for a research grant.

References

1 B. A. Abeywickrama, *Ceylon J. Sci.* (*Bio. Sci.*), 1959, **2**, 187.
2 (*a*) O. S. Waleria, *Pr. Nank. Akad. Med. Wrolawain*, 1973, **7**, 41, (*b*) O. S. Waleria, *Diss. Pharm. Pharma.*, 1967, **19**, 91.
3 T. Mazaki and M. Aritomi, *J. Pharm. Soc. Jpn*, 1957, **77**, 1353.
4 H. K. Desai, D. H. Gawad, T. R. Govindachari, B. S. Joshi, V. N. Kamat, J. D. Modi, P. C. Parthasarathy, S. J. Patankar, A. R. Sidhaye, and N. Viswanathan, *Indian. J. Chem.*, 1971, **9**, 611.
5 A. Goncalves de Lima, I. L. D'Albueuerque, J. S. de Barros Coelho, D. G. Martins, A. Lacerda, and G. M. Maciel, *Rev. Inst. Antibiot.* (Recife), 1969, **9**, 17.
6 K. C. Joshi, R. K. Bansal, and R. Patni, *Planta Med.*, 1978, **34**(2), 211.
7 B. Pasich, D. W. Bishay, Z. Kowalewski, and H. Rompel, *Planta Med.* 1980, **39**(4), 391; *Herba Pol.*, 1980, **26**(2), 91.
8 A. Ulubelen and T. Baytop, *Phytochemistry*, 1973, **12**, 1824.
9 V. Krishnamoorthi, J. D. Ramanathan, and T. R. Seshadri, *Tetrahedron Lett.*, 1962, 1047.
10 K. Nakanishi, V. P. Gullo, I. Miura, T. R. Govindachari, and N. Viswanathan, *J. Am. Chem. Soc.*, 1973, **95**, 6473.
11 P. M. Brown, M. Moir, R. H. Thomson, T. King, V. Krishnamoorthi, and T. R. Seshadri, *J. Chem. Soc., Perkin Trans. 1*, 1973, 2721.
12 X. A. Domiquez, R. O. Franco, and G. Cano, *Rev. Latinoamer. Quim.*, 1978, **9**, 33.
13 N. Viswanathan, *J. Chem. Soc., Perkin Trans 1*, 1979, 349.
14 D. Roges, D. J. B. S. Williams, V. N. Kamat, and N. Viswanathan, *Tetrahedron Lett.*, 1974, 63.
15 G. Weeratunga, V. Kumar, and M. U. S. Sultanbawa, *Tetrahedron Lett.*, 1982, **23**, 2031.
16 G. Weeratunga, V. Kumar, M. U. S. Sultanbawa, and S. Balasubramaniam, *J. Chem. Soc., Perkin Trans. 1*, 1982, 2457.
17 J. L. Courtney and J. S. Shannon, *Tetrahedron Lett.*, 1963, 13.
18 R. S. Rosenfeld and T. F. Gallagher, *J. Am. Chem. Soc.*, 1955, **77**, 4367.
19 (*a*) D. N. Kirk and M. P. Hartshorne, 'Steroid Reaction Mechanisms,' Elsevier, Amsterdam, 1968, p. 56. (*b*) *ibid.*, p. 176.
20 H. B. Henbest, D. N. Jones, and G. P. Slater, *J. Chem. Soc.*, 1961, 4472.
21 (*a*) C. Betancor, R. Freire, A. G. Gonzalez, J. A. Salazar, C. Pascard, and T. Prange, *Phytochemistry*, 1980, **19**, 1989; (*b*) G. Weeratunga and V. Kumar, unpublished results.
22 A. S. R. Anjaneyulu and M. Narayana Rao, *Phytochemistry*, 1980, **19**, 1163.
23 A. A. L. Gunatilaka, N. P. D. Nanayakkara, and M. U. S. Sultanbawa, *Tetrahedron Lett.*, 1981, **22**, 1425.
24 T. R. Govindachari, N. Viswanathan, B. R. Pai, V. Ramadas Rao, and M. Srinivasan, *Tetrahedron*, 1967, **23**, 1901.
25 G. Weeratunga, Ph.D. Thesis (1984), Peradeniya, Sri Lanka.

Received 5th June 1984; *Paper* 4/913