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THE C-2,C-3-GLYCOL DERIVATIVES OF GLYCYRRHETIC ACID

M. H. A. ELGAMAL and B. A. H. EL-TAWIL
National Research Centre, Dokki, Cairo, Egypt

and

M. B. E. FAYEZ*
College of Pharmacy and Pharmacal Sciences, Howard University, Washington, D.C. 20001

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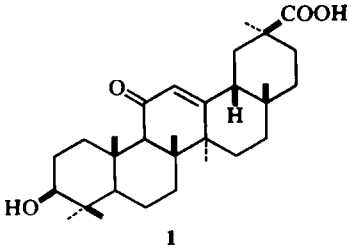
Abstract—The synthesis of the 2β,3β-, 2α,3α- and 2β,3α-glycol derivatives of 18β-olean-12-en-11-oxo-30-oic (glycyrrhetic) acid is described. During the study, the 2-keto,3β-acetoxy, 2α-hydroxy,3-keto, ring-A diosphenol (of the 2,3-diketo), and 2-keto,3β-hydroxy derivatives have been obtained, *inter alia*.

All the hitherto known[1,2] C-30- and C-29-carboxylated oleanane diols (glycyrrhetic acid and liquiritic acid derivatives) encountered in nature (principally in liquorice (*Glycyrrhiza glabra* L.) root) carry the additional OH group on one of the angular methyls, on C-18 or on C-21. Since the occurrence of 1,2-glycol systems in ring A is common in many other types of natural triterpenoids and steroids, the synthesis of such derivatives in the glycyrrhetic acid (**1**) series was attempted; their natural occurrence being not unlikely. The preparation of the 2α,3β-diol (**2**) has previously been reported,[2] and the remaining three possible isomers, as well as some related products are now described in this communication.

Methyl 3-ketoglycyrrhetate (**3**) was the starting material for the synthesis of the 2β,3β-diol (**4**), as it was for the 2α,3β isomer[2] (**2**), since it contained a potential for generation of the sterically more favorable 3β (equatorial) OH group. Reaction of **3** with lead tetraacetate in boiling benzene gave an acetoxyketone—different from that (2α-acetoxy-3-ketone, **5**) obtained[2] with the same reagent in hot acetic acid—which was shown to be methyl 3β-acetoxy-18β-olean-12-ene-2,11-dioxo-30-oate (**6**). It was obtained along with the previously known[3] methyl 18α-oleana-1,12-diene-3,11-dioxo-30-oate (**7**). Most likely, the reaction generates initially the 2α-acylation product (**5**) which subsequently rearranges rapidly to **6** *via* a cyclic intermediate.[4] Monitoring of the reaction course on the chromatoplates revealed that **7** was the first product to be formed, presumably by dehydrogenation of **3** or elimination of acetic acid from **5** with concomitant epimerization at C-18. The conversion of **5** to **6** has been realized experimentally by treatment of **5** with basic alumina. Spectral (UV, IR and NMR) data are in full accord with structure **6**. These include NMR signals at δ4·96 (singlet) for the C-3α proton and at δ5·68 (singlet) for the vinylic C-12 proton (the latter providing an indication that the C-18β stereochemistry is retained). The CD shows the expected negative Cotton effect for the αβ-unsaturated ketone chromophore and positive effect for the ring A saturated ketone group. Reaction of compound **6** with sodium borohydride in



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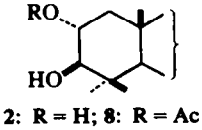
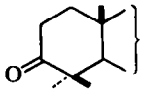


2: R = H; 8: R = Ac



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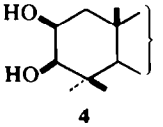

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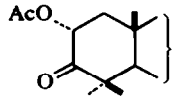

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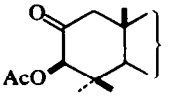

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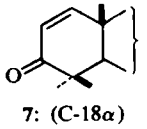
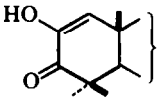


7: (C-18α)

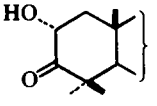
boiling solvent* (conditions known[5] not to affect the C-30 carboxymethyl group or the unsaturated system in ring C) afforded the desired 2β,3β-diol (**4**), which gave a diacetate and an acetonide.

The dialcohol **4** was also prepared by other routes from the ketone **3** *via* the diosphenol **9**. The latter compound (as the methyl ester, **9a**) was found to result from the previously reported[2] methyl 2α-hydroxy-18β-olean-12-ene-3,11-dioxo-30-oate (**10**) upon storage (in solution or even in the dry state) for long periods or by oxidation with bismuth trioxide[6] in hot acetic acid. It was also obtained directly from **3** by oxidation with atmospheric oxygen in t-butanol containing potassium t-butoxide,[7] in which case it resulted as the free acid (**9b**). The diosphenol (**9**) gave the expectable spectral (UV, IR, NMR and MS) data, which also confirmed that the original 18β stereochemistry is retained, and CD (showing a negative Cotton effect due to the αβ-unsaturated ketone system). The acetyl and methyl derivatives (**11** and **12**, respectively) were prepared and both show the expected UV hypsochromic shift in the absorption of the diosphenol system.[8] Controlled hydrogenation of the diosphenol (**9b**) affected only the double bond of ring A giving a product identified as 3β-hydroxy-18β-olean-12-ene-2,11-dioxo-30-oic acid (**13**), which possessed fitting spectral (UV, IR, NMR and MS, substantiating an 18β stereochemistry) and CD data. The formation of **13** may be rationalized as the outcome of rearrangement of the immediate hydrogenation product (presumably the 2β-hydroxy-3-ketone, **14**) due to steric factors.† Reduction of the diosphenol (**9b**) with sodium borohydride followed by methylation afforded the 2β,3β-glycol, as the methyl ester (**4**).

The remaining two C-2,C-3-glycols, comprising a 3α-OH group, were obtained utilizing methyl 18β-oleana-2,12-dien-11-oxo-30-oate (**15**), obtained[10] by dehydration of methyl glycyrrhetate with phosphorus oxychloride in pyridine, a reaction which gives also the 18α epimer (of **15**). Oxidation with osmium tetroxide in dioxane afforded both the *cis* isomers 2α,3α-diol (**16**) and 2β,3β-diol (**4**) which were separated chromatographically. This oxidant is also reported in the literature[11,12] to give a mixture of both *cis* glycols in the oleanolic acid series. The stereochemistry of **16** finds support in the spectral data which include the expected NMR signals for the protons on C-3 (doublet at δ3·45, $J_{2,3}$ = 2 Hz), C-2 (poorly resolved double triplet centered at δ4·10, about 14 Hz wide) and the equatorial one on C-1 (pair of doublets at δ2·86, $J_{1,1}$ = 12 Hz and $J_{1eq,2}$ = 4 Hz), in addition to the C-12 proton signal (singlet at δ5·68) and one (singlet at δ2·48) attributable to the C-9 proton. Hydrogen peroxide oxidation of **15** followed by treatment of the reaction product with sodium borohydride yielded the remaining isomer, namely methyl 2β,3α-dihydroxy-18β-olean-12-en-11-oxo-30-oate (**17**). The diacetates of both glycols (**16** and **17**) were also obtained. The NMR spectrum of the 2β,3α-glycol (**17**) showed that the C-2 and C-3 proton signals were unresolved and hidden beneath the OMe group signal, which is not entirely unexpected. Attempts to cause separation of the signals were made (Experimental) but gave no conclusive results. In contrast, however, the NMR spectrum determined for the 2α,3β-glycol (**2**) revealed a complete set of well resolved signals supporting the stereochemsitry which we assigned[2] earlier to this compound. These include a doublet for the C-3 proton (δ3·04, $J_{2,3}$ = 9·5 Hz), a triplet of doublets for the C-2 proton (δ3·79; $J_{2,ax}$ = 13 Hz, $J_{2,3}$ = 9·5 Hz, $J_{2,eq}$ = 4·5 Hz), a pair of doublets for the equatorial C-1 proton (δ3·18; $J_{1,1}$ = 13 Hz, $J_{1eq,2}$ = 4·5 Hz) and a triplet for the axial C-1 proton (δ1·60; $J_{1,1}$ = $J_{ax,2}$ =



9a: C-30 $COOCH_3$
9b: C-30 COOH



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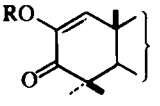
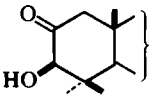
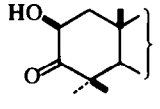


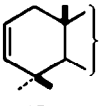
11: R = Ac (C-30 COOH)
12: R = CH_3 ($COOCH_3$)



13: C-30 COOH



14: C-30 COOH



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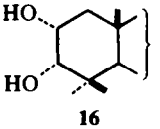

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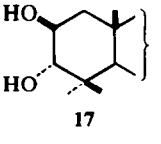


17

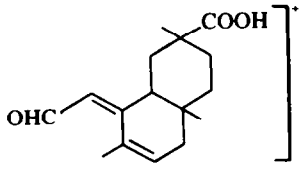
*Under similar reaction conditions, the isomeric 2α-acetoxy-3-ketone (**5**) gives[2] the 2α,3β-glycol (**2**) whereas methyl 2α-acetoxy-3β-hydroxy-18β-olean-12-en-11-on-30-oate (**8**) resulted when the reaction was carried out at room temperature and allowed only 5 min. Oxidation of **8** with Jones' reagent gave back the 2α-acetoxy-3-ketone (**6**).

†An attractive explanation is that the 2β-hydroxy-3-ketone (**14**), formed initially as a result of a rear attack) has a strained ring A—due to multiple 1,3-diaxial interaction of the axial groups on C-2, C-4, and C-10—in which the strain[9] is released by enolization of the carbonyl group leading to the more stable 2-keto-3β(equatorial)-hydroxy derivative (**13**).

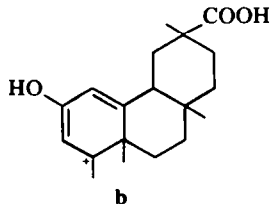
13 Hz) in addition to a singlet for the vinylic proton on C-12 (δ5·68) and one attributed to the C-9 proton (δ2·39).

A comparison of the OH group absorptions in the 3μ region of the IR spectra, determined in highly diluted solutions, revealed additional information. As might be expected, the two *cis* diols (**4** and **16**) give lengths of the hydrogen bond ($d_{H\cdots O}$, found* 1·68 and 2·01 Å, respectively) which are decreased[11] (by comparison with the length calculated[11] on the basis of an undistorted (ideal) chair conformation of ring A), as a result of flattening of the ring due to steric interaction of the axially-bound Me groups on C-4, C-8 and C-10. However, the decrease for the 2β,3β-diol (**4**) is markedly greater, presumably due to the additional interaction imposed by the axial OH group on C-2. The $d_{H\cdots O}$ value found (2·29 Å) for the 2β-3α-diol (**17**) is in reasonable agreement with that (2·25 Å) reported[11] for the analogous glycol in the oleanolic acid series. The value found (2·45 Å) for the 2α,3β-diol (**2**), and reported[2] earlier, shows an increase which is also a result of flattening of ring A.

Finally, it may be stated that in all the compounds described above (with the exception of **7**) the C-18β stereochemistry was prevailing as evidenced in several cases by spectral data. C-18β configuration is distinguished by ring-C $\alpha\beta$-unsaturated ketone UV absorption at 248–250 nm (as opposed to 242–244 nm for the C-18α series[14]), NMR sharp C-12 vinylic proton signal (as opposed to a doublet in the C-18α series[15]), and—in the mass spectra of some cases—by an appreciably strong *m/e* 262 ion (species **a**, resulting[16] by retro-Diels-Alder fragmentation across ring C) relative to the *m/e* 303 ion (species **b**, formed by collapse of ring β in a cleavage involving a McLafferty rearrangement[16]) (the latter ion is by far the stronger one in the 18α-olean-12-en-11-one derivatives[16]).



a



b

EXPERIMENTAL

M.ps are uncorrected. Optical rotations were measured in chloroform. UV spectra were determined in ethanol unless otherwise stated. NMR spectra: in $CDCl_3$ with TMS as a standard using Varian 100 and 300 MHz instruments. CD measurements were made with a Roussel-Jouan dichrograph in dioxane at 20°, 2 cm path length. Mass spectra were taken on an Associated Electrical Industries MS9 instrument. R_f data were obtained on silica gel G chromatoplates developed with toluene-ethyl acetate-acetic acid (12:4:0·5) and the spots visualized by spraying with the chlorosulfonic acid-acetic acid (1:3) reagent.

Methyl 3β-acetoxy-18β-olean-12-ene-2,11-dioxo-30-oate (**6**). A soln of **3** (1 g) in dry benzene (70 ml) containing lead tetraacetate (5·5 g) was refluxed for 7 hr; complete reaction was revealed by TLC follow-up which also revealed that **7** was the first product to be formed. After the usual work-up, the crude mixture was resolved on an alumina column from which **7** (150 mg, R_f 0·66) was initially removed by elution with benzene; it was obtained as plates (chloroform-methanol), m.p. 267–270°, $[\alpha]_D$ + 150° (reported[3] m.p. 261°, $[\alpha]_D$ + 160°. (UV: one max at 250 nm, ϵ 12,700; IR (Nujol) bands near 1750, 1675, 1625, 1225 and 1175 cm^{-1}.). (Found: C, 77·51; H, 9·56. $C_{31}H_{44}O_4$ requires: C, 77·46; H, 9·23%).

Further elution of the column with benzene removed the main product (**6**, total yield 255 mg, R_f 0·34) which was obtained as needles (chloroform-methanol), m.p. 340–342°, $[\alpha]_D$ + 186°. (UV: one max at 250 nm, ϵ 16,000; IR (Nujol) bands at 1755, 1735, 1665, 1625, 1230 and 1190 cm^{-1}; CD (λ, $\Delta\epsilon$): 382 (+0·06), 364 (+0·06), 354 (−0·12), 340 (−0·15), 327 (−0·06), 312 (+0·88), 304 (+1·44), 296 (+1·41). NMR signals at δ0·82, 0·87, 1·13, 1·33, 1·41 (Me groups C-28, C-23, C-24, C-27, C-26, respectively), 5·68 (sharp singlet, vinyl proton), 4·96 (proton on C-3), 2·17 (acetate CH_3), and 3·70 (OMe), (Found: C, 73·52: H, 9·18. $C_{33}H_{48}O_6$ requires: C, 73·30; H, 8·95%).

Treatment of methyl 2α-acetoxy-18β-olean-12-en-3,11-dioxo-30-oate (**5**) *with alumina.* A soln of **5** (200 mg) in benzene was added to a column of basic alumina (50 g) and allowed to stand for 3 hr. Elution with ether removed 120 mg of **6** (R_f 0·34) which was obtained as needles (chloroform-methanol), m.p. and mixed m.p. 340–343° (identical IR spectra).

Methyl 2β,3β-dihydroxy-18β-olean-12-en-11-oxo-30-oate (**4**). A soln of **6** (75 mg) in a mixture of methanol, dioxane and water (2:2:1, 15 ml) containing sodium borohydride (75 mg) was refluxed for 5 hr (complete reaction revealed by TLC follow-up). The product (R_f 0·25) was isolated, after acidification with HCl, and obtained as fine needles (55 mg), m.p. 208–210°, $[\alpha]_D$ + 138°. (UV: one max at 250 nm, ϵ 12,000; IR bands near 3450, 1730, 1660 and 1620 cm^{-1}). By acetylation (acetic anhydride-pyridine), the diacetate derivative (R_f 0·54) was obtained as plates, m.p. 193–194°, $[\alpha]_D$ + 127·5°. (UV: one max at 248 nm, ϵ 12,500. IR (KBr) bands near 1750, 1675 1620, 1260 and 1160 cm^{-1}.). (Found: C, 71·50; H, 9·19. $C_{35}H_{52}O_7$ requires: C, 71·88; H, 8·96%). Treatment of **4** (30 mg) in dry acetone (20 ml) soln with anhydrous copper sulfate (room temp for 7 days), followed by work-up, gave the acetonide derivative (R_f 0·67, 24 mg) as plates (chloroform-methanol), m.p. 233–235°. (Found: C, 75·23, H, 9·97. $C_{34}H_{52}O_5$ requires: C, 75·51; H, 9·69%).

Methyl 2α-acetoxy-3β-hydroxy-18β-olean-12-en-11-

*Calculated from the observed $\Delta\nu$ (for the ν values of the free and bonded hydroxyl groups) according to the formula of Kuhn[13].

oxo-30-*oate* (**8**). A soln of 5[2] (50 mg) in MeOH (4 ml) containing sodium borohydride (150 mg) was allowed to stand at room temp for 5 min (shown by TLC to be sufficient for complete reaction). After the usual workup, the product (R_f 0·25, 20 mg) was crystallized from aqueous EtOH to give plates, m.p. 178°, $[\alpha]_D$ + 50·6°. (UV: one max at 254 nm, ϵ 8200; IR ($CHCl_3$) bands near 3400, 1745, 1675 and 1190 cm^{-1}.). (Found: C, 72·61; H, 9·32. $C_{33}H_{50}O_6$ requires: C, 73·03; H, 9·29%).

Oxidation of **8** (40 mg) in acetone (20 ml) soln with Jones' reagent (4 ml) during a period of 7 min afforded **5** (R_f 0·50, 28 mg) which was obtained as needles (MeOH), m.p. and mixed m.p. 220–222°, $[\alpha]_D$ + 139·5° (reported[2] m.p. 218–221°, $[\alpha]_D$ + 148·6°).

2-*Hydroxy*-18β-*oleana*-1, 12-*dien*-3, 11-*dioxo*-*oic acid* (**9b**). A stream of air was passed for 4 hr through a soln of **3** (8 g) in t-BuOH (350 ml) containing t-BuOK (from 5·33 g K in 133 ml t-BuOH) maintained at 35–40°. After acidification and work-up, the product (R_f 0·43) was isolated to give fine needles (5·1 g, from EtOH-benzene), m.p. 320–323°, $[\alpha]_D$ + 163°, which gave an olive-green color reaction with alcoholic ferric chloride. (UV: max at 255 and 260 nm, ϵ 16,300 and 16,600, respectively; in ethanolic alkali soln: max at 255 and 310 nm, ϵ 7700 and 5800, respectively; IR ($CHCl_3$) bands at 3333, 1745, 1710 and 1660 cm^{-1}; CD (λ, $\Delta\epsilon$): 380 (+0·07), 350 (−1·25), 340 (−2·11), 329 (−2·36). NMR signals at δ1·47, 1·38, 1·22, 1·17, 1·14, 0·86 (7 Me groups), 5·78 and 7·13 (vinyl protons on C-12 and C-1, respectively) and 7·33 (diosphenol OH group). (Found: C, 75·12; H, 8·99; mol. wt. 484 (by MS). $C_{30}H_{42}O_5$ requires: C, 74·86; H, 8·71%). The mass spectrum showed M^+ at *m/e* 482 (100%) and ions resulting therefrom by losses of Me (*m/e* 467), CO (*m/e* 454), CO + H_2O *m/e* 436), 2 CO (*m/e* 426) and CH_3 + CO + H_2O *m/e* 421). The nuclear fragmentations expectable[16] for glycyrrhetic acid type of compounds give ions at *m/e* 303 (species *b*) and 262 (species *a*); the latter giving satellite ions at *m/e* 247, 218 and 203 (due to losses of CH_3, CO_2 and CH_3 + CO_2, respectively. The relative intensities of the *m/e* 303 and 262 ions are as expected[16] for an $\alpha\beta$-stereochemistry. Other strong ions occur at *m/e* 301, 299, 219 and 175.

The crystallization mother liquors gave, upon concentration, 1·2 g of 3-ketoglycyrrhetic acid, m.p. 309–312°, $[\alpha]_D$ + 156·5°. (Found: C, 76·69; H, 9·42. $C_{30}H_{44}O_4$ requires: C, 76·92; H, 9·40%).

Acetylation of **9b** with acetic anhydride-pyridine gave **11** as needles (chloroform-methanol), m.p. 186–187°, $[\alpha]_D$ + 193·5°. (UV: max at 250 and 255 nm, ϵ 14,900 and 14,800 respectively; IR (CCl_4) bands near 3900 (broad), 1820, 1780, 1750, 1700, 1680, 1630 and 1208 cm^{-1}). Methylation of **9b** with diazomethane in chloroform afforded **12** as needles (chloroform-methanol), m.p. 215–217°, $[\alpha]_D$ + 176°. (UV: max at 248 nm, ϵ 15,200; IR (CCl_4) bands near 1770, 1740, 1700, 1670, 1625, 1220 and 1175 cm^{-1}). (Found: C, 74·92; H, 9·11. $C_{32}H_{46}O_5$ requires: C, 75·26; H, 9·08%).

Methyl 2-*hydroxy*-18β-*oleana*-1,12-*dien*-3,11-*dioxo*-30-*oate* (**9a**). A soln of **10**[2] (60 mg) in AcOH (5 ml) was heated at 100° with bismuth trioxide (25 mg) for 30 min, after which period more of the oxidant (25 mg) was added and heating continued for a further 30 min. After work-up the product (R_f 0·60, 33 mg) was obtained as matted needles (benzene-ethanol), m.p. 250–253°, giving olive-green coloration with alcoholic ferric chloride. Methylation of this material (with MeI in acetone containing anhyd K_2CO_3) gave **12** described above, m.p. and mixed m.p. 215–217° (identical IR spectra).

Transformation of the diosphenol (**9b**) *to the* 2β,3β-*glycol* (**4**). A soln of **9b** (150 mg) in MeOH (200 ml) was treated with $NaBH_4$ (500 mg) at room temp for 1 hr (complete reaction revealed by TLC monitoring). The product was isolated in the usual manner and directly methylated (MeI in acetone containing anhyd Na_2CO_3) to give **4**, described above, as needles, m.p. and mixed m.p. 207–209° (identical UV and IR spectra).

3β-*Hydroxy*-18β-*olean*-12-*ene*-2,11-*dioxo*-30-*oic acid* (**13**). A soln of **9b** (300 mg) in EtOAc (100 ml) containing Pd-C (5%, 30 mg) was shaken with H_2 at room temp for 5 hr. The product (R_f 0·32,200 mg) was isolated in the usual manner and obtained as needles, m.p. 250–253°, $[\alpha]_D$ + 181°. (UV: one max at 250 nm, ϵ 12,000; IR (KBr) bands near 3375, 1725 and 1625 cm^{-1}; CD (λ, $\Delta\epsilon$): 380 (+0·05), 366 (−0·08), 350 (−0·41), 338 (0·59), 330 (−0·48), 290 (+1·36). NMR signals at δ 1·41), 1·23, 1·14, 0·86 (7 Me groups), 4·97 (C-3 proton) and 5·92 (sharp singlet, vinyl proton on C-12). Mol. wt. (by MS) 484 ($C_{30}H_{44}O_5$). The mass spectrum showed M^+ at *m/e* 484 (100%) and ions resulting therefrom by losses of CH_3, CO, CH_3 + CO and CO + H_2O (*m/e* 469, 456, 441 and 438, respectively). Ions resulting from breakdown of the nucleus exist at *m/e* 303 (species *b*) and 262 (species *a*) with the latter having higher intensity. Another strong ion occurs at *m/e* 411.

Oxidation of methyl oleana-2,12-*dien*-11-*oxo*-30-*oate* (**15**) *with osmium tetroxide.* A soln of **15**[10] (m.p. 236–239°, 500 mg) in dioxane (15 ml) was treated with osmium tetroxide (1 g) and the mixture allowed to stand at room temp for 14 days. After evaporation, the residue was refluxed with aqueous-ethanolic Na_2SO_3 soln for 2 hr followed by the usual work-up. The product was fractionated on alumina (deactivated with AcOH soln) to give, upon elution with benzene-ether (3:1), 50 mg of 2α,3α-**16**, (R_f 0·26) as needles (chloroform-methanol), m.p. 258–260°, $[\alpha]_D$ + 83°. (UV: one max at 248 nm, ϵ 11,900; IR (KBr) bands near 3360, 1730, 1670, 1625, 1225 and 1160 cm^{-1}). NMR (100 MHz instrument) signals at δ0·78, 0·86, 1·03, 1·10, 1·13, 1·17 and 1·36 (Me groups), 2·48 (sharp singlet, C-9 proton), 2·86 (double doublet, equatorial C-1 proton), 3·45 (doublet, C-3 proton), 3·68 (OCH_3), 4·10 (broadened double triplet, 14 Hz wide, C-2 proton) and 5·68 (vinylic proton on C-12). Acetylation (acetic anhydride-pyridine) gave the diacetyl derivative (R_f 0·68) obtained as plates (chloroform-methanol), m.p. 243–245°, $[\alpha]_D$ + 159°. (UV: one max at 250 nm, ϵ 11,100; IR (KBr) bands near 1740, 1665, 1618 and 1260 cm^{-1}). (Found: C, 71·44; H, 8·96. $C_{35}H_{52}O_7$ requires: C, 71·88; H, 8·96%).

Further elution of the chromatographic column with the same solvent afforded 30 mg of **4**, m.p. and mixed m.p. 208–210° (identical IR spectra).

Methyl 2β,3α-*dihydroxy*-18β-*olean*-12-*en*-11-*oxo*-30-*oate* (**17**). A soln of **15** (200 mg) in AcOH (10 ml) was treated with 0·2 ml of H_2O_2 at 95° for 2 hr. The crude product, obtained after the usual work-up, was subsequently treated with $NaBH_4$ (250 mg) in a methanol-dioxane-water (5:5:2) mixture (40 ml) at reflux temp for 30 min. The product (R_f 0·12, 170 mg crude) was isolated by working up in the usual manner and obtained as needles (aqueous EtOH), m.p. 280–283°, $[\alpha]_D$ + 168°. (UV: one max at 250 nm, ϵ 11,900; IR (KBr) bands near 3490, 1730, 1650, 1618, 1220 and 1160 cm^{-1}). NMR (300 MHz instrument) signals at δ0·84, 0·97, 1·09, 1·13, 1·18, 1·34 and 1·40 (Me groups), 2·58 (sharp singlet, C-9 proton), 5·75 (vinylic proton on C-12) and 3·74 (superimposed OCH_3 and signals from the C-2 and C-3 protons). Addition* of

50% C_6D_6 to the $CDCl_3$ solvent caused very little effect in the region of the latter signal although it shifted the rest of the protons appreciably. Addition* of Eu- $(Fod)_3$, a shift reagent, caused the C-2 and C-3 proton signals to move out from under the OCH_3 signal (δ3·32) and show up, unresolved, as a broadened signal at δ3·72. (Found: C, 73·96; H, 9·60. $C_{31}H_{48}O_5$ requires: C, 74·36; H, 9·66%). Acetylation (acetic anhydride-pyridine) gave the diacetyl derivative (R_f 0·52) obtained as plates (chloroform-methanol), m.p. 193–195°, $[\alpha]+104°$. (UV: one max at 250 nm, ϵ 11,000; IR (KBr) bands near 1733, 1665, 1618 and 1250 cm^{-1}). (Found: C, 72·13; H, 9·09. $C_{35}H_{52}O_7$ requires: C, 71·88; H, 8·96%).

Methyl 2α,3β-dihydroxy-18β-olean-12-en-11-oxo-30-oate (2). The preparation of this compound has been described earlier.[2] NMR (300 MHz instrument) signals at δ0·80, 0·85, 1·04, 1·10, 1·14, 1·20 and 1·36 (Me groups), 1·60 (triplet, axial C-1 proton), 2·39 (sharp singlet, C-9 proton; signal unaffected upon addition of D_2O), 3·04 (doublet, C-3 proton), 3·18 (pair of doublets, equatorial C-1 proton), 3·69 (OCH_3), 3·79 (triplet of doublets, C-2 proton), and 5·68 (sharp singlet, vinylic proton on C-12).

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