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EUDESMANOLIDES DERIVED FROM HERBOLIDE B

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Abstract—The reaction of acidic reagents with the germacranolide-herbolide B (**2**) and its derivatives was investigated. Cyclisation products of the eudesmanolide series were isolated in all cases. The chemical and physical data of these new compounds are described.

We recently[1] reported the isolation and characterisation of the germacranolides herbolides A1 and B2 from *Artemisia herba alba* Asso.

Germacradienolides are well known for the facility by which they yield acid catalysed trans annular cyclisation products.[2] No such products could be obtained however from herbolide A **1** which has an allylic acetoxy group at position 9. Several acidic reagents like boron trifluoretherate, hydrochloric acid, and thionyl chloride were used with no success. Under mild conditions no reaction took place, while with more drastic methods, only decomposition products were obtained. In contrast, herbolide B **2**,[3] the 1,10-epoxide of herbolide A, was readily converted into cyclisation products.

We wish to describe a series of eudesmanolides which were derived from herbolide B, with the aid of various acidic reagents.

Treatment of **2** with acetic anhydride in the presence of *p*-toluenesulphonic acid yielded the three derivatives **3**, **4** and **5**, acetyl α, β and γ cycloherbolide B respectively. These products were analogous to those obtained from pyrethrosin under the same reaction conditions.[4]

The structures of compounds **3**, **4** and **5** were derived from their empirical formula, $C_{19}H_{26}O_6$ (elementary analysis and mass spectra) and spectroscopic results. The NMR data which are summarised in Table 1 are in accordance with the proposed structures. The decalin system was deduced from the pattern of the Me signals. Besides the C-11 doublet, a sharp three proton singlet was observed for all three compounds. This signal was readily assigned to the angular Me group at C-10. A signal for a third Me group which appeared as a broad singlet in compounds **3** and **5**, and which was replaced by two methylene singlets in compound **4**, was attributed to the C-14 protons. Furthermore, the C-6 proton, adjacent to the lactone oxygen, appeared as triplet with J = 10 Hz, showing the trans diaxial disposition of H-5, H-6 and H-7, which is in accordance with the α-orientation of H-5. The signals of H-1 and H-9 which appeared superimposed could not be differentiated even after addition of Eu(fod)$_3$.

Acetyl-β-cycloherbolide -B (**4**) was ozonised to the nor ketone **6** whose structure was confirmed by its spectral data. (IR, MS and NMR). Compound **6** exhibited a remarkable large negative Cotton effect ($\Delta\epsilon = -5$ at 293 nm) as compared with the one exhibited by the analogous compound **7** published by Doskotsch *et al.* ($\Delta\epsilon = -1.3$).[2c]

†This acid reagent was introduced by Doskotsch *et al.*[2c] for cyclisation of germacranolides.

Cyclisation with the aid of thionyl chloride† yielded only two pure cyclisation products **8** and **9**, α and β cycloherbolide B. The parent peaks of both compounds (M$^+$ 308) showed that isomerisation had occurred. An OH group was indicated in the IR region (3570 cm^{-1}) and was confirmed by the presence of one deuterium exchangeable proton in the NMR spectra. All the NMR data which are summarised in Table 1 are in accordance with the proposed structures. They were further confirmed by acetylation of **8** and **9** to compounds **3** and **4** respectively. α-Cycloherbolide -B **8** could be oxidised to the ketone **10** which exhibited in the IR spectrum besides the lactone and the acetate bands a further CO band due to the C-1 keto group. Compound **10** gave a negative Cotton effect ($\Delta\epsilon = -1$ at 300 nm).

Very good models for confirming the stereochemistry at C-1 and of the A/B trans ring annulation were compounds **11**, **12** and **13**. These were obtained by acetic anhydride and thionyl chloride cyclisation of the ketone **14** which had been prepared by CrO_3 oxidation of deacetyl herbolide B **15**. In the NMR spectra well resolved signals for H-1 were observed. This proton appeared in compound **11** as a triplet, J ~ 8 Hz and in compounds **12** and **13** as double doublets, J 4, 11 Hz, (Table 1). Both patterns are typical for an axial proton with one axial and one equatorial neighbouring proton.[5] Consequently the substituent at C-1 is equatorial.

Compound **13** exhibited bands in the IR at 3615 cm^{-1} and at 3370 cm^{-1}. Since the appearance of the latter band was independent of concentration, an intramolecular C=O $\cdots$ H-O must be present, and this is compatible only with trans ring annulation in the hydroxy ketone **13**.

The aromatic solvent-induced shifts (ASIS) in benzene were determined for the C-10 and C-11 Me groups in various cycloherbolides (Table 2). In the non-ketonic compounds **3**, **4**, **8** and **9**, the angular C-10 Me group undergoes an upfield shift of approximately 0.2 ppm, due to the OH and acetate substituents. However, in the corresponding ketones **11**, **12**, **13** and **10** the shifts were 0.36 ± 0.03 ppm. Since the ASIS are additive[6] the contribution due to the ketones must be at least +0.20 ppm in all cases. This value is in accordance with the shift expected for an axial Me α to a CO function.[7]

The ASIS which the C-11 Me groups underwent was 0.27 ± 0.05 ppm in most cases. This is in accordance with its pseudo-equatorial orientation[8] as was established for herbolide B.[1]

Further examination of the NMR data of the cycloherbolides B showed that while the chemical shifts of the Me groups at C-4 and C-11 remained practically unchanged, the chemical shift of the Me group at C-10 was

Table 1. The NMR data of the cyclic derivatives of herbolide B[e]

Compound No.	Solvent	C-11 methyl	C-10 methyl	C-4 methyl or methylene	H-1	H-3	H-5	H-6	H-9	$COCH_3$
2	$CDCl_3$	1.24 [d,6]	1.21 [s]	1.78 [d,1.4]	2.79 [dd, 12,3]		5.06 [dd,10, 1.4]	4.50 [dd,8, 10]	4.19 [t]	2.02 [s]
	C_6D_6	1.20	1.02	1.32	2.34		4.62	4.1	(f)	1.69
3(g)	$CDCl_3$	1.20 [d,8]	1.18 [s]	1.84 [br]	5.0 [f]	5.38 [br.s]		3.95 [t,10]	5.0 (f)	2.04[s] 1.99[s]
	C_6D_6	0.88	0.94	1.8	4.7 - 5.2 (f)			3.15	5.0 (f)	1.70[s] 1.68[s]
4(g)	$CDCl_3$	1.20 [d,9]	1.09 [s]	5.0[br.s] 4.82[br.s]	4.9 (f)			3.95 [t,10]	4.9 (f)	1.99[s] 1.96[s]
	C_6D_6	0.97	0.93	4.84 (f)				3.33	4.84 (f)	1.70[s] 1.68[s]
5(g)	$CDCl_3$	1.16 [d,7]	1.20 [s]	1.84 [br]	4.75 (f)			4.75 (f)		2.00 [s]
6	$CDCl_3$	1.20 [d,7]	1.10 [s]	-	5.2 (f)			4.13 [t,10]	5.2 [br]	2.01[s] 2.05[s]
	C_6D_6	0.91	0.91		4.85 [m] (h)			3.88	5.15 [m] [h]	1.63[s] 1.66[s]
8	$CDCl_3$	1.23 [d,7]	1.10 [s]	1.83 [d,2.5]	3.80 (f)	5.36 [br.s]		3.80 (f)	5.05 [m]	2.08 [s]
	C_6D_6	0.96	0.88	1.58 [br]						
9	$CDCl_3$	1.22 [d,7]	1.00 [s]	5.03[br.s] 4.88[br.s]	3.85 (f)			3.85 (f)	5.0 (f)	2.06 [s]
	C_6D_6	1.00	0.89	4.85 [br] (f)	3.35 (f)			3.35 (f)	4.85 (f)	1.6 [s]
10	$CDCl_3$	1.17	1.32	1.74	-	5.36 [br.s]		4.3 [t,11]	5.0 [m]	2.01 [s]
	C_6H_6	0.79 [d,7]	0.91 [s]	1.82 [br.s]						
11	$CDCl_3$	1.24 [d,7]	1.34 [s]	1.89 [br]	5.35 (f)			4.44 [t,10]	-	2.01 [s]
	C_6D_6	0.84	0.96	1.33 [br]	5.44 [t,8]	5.08 [br.s]		3.61	-	1.82 [s]
12	$CDCl_3$	1.22 [d,7]	1.25 [s]	5.01[s] 5.17[s]	5.26 (f)			4.46 [t,10]	-	2.01 [s]
	C_6D_6	0.91	0.87	4.89[s] 4.92[s]	5.34 [dd, 11,4]			3.84	-	1.81
13	$CDCl_3$	1.22 [d,6]	1.16 [s]	5.12[br] 4.96[br]	4.08 [dd, 12,4]			4.45 [t,11]	-	-
	C_6D_6	0.82	0.82	4.85[br] 4.92[br]	3.85 (f)			3.64 (f)	-	-
14	$CDCl_3$	1.29 [d,7.5]	1.51 [s]	1.93 [d,2]	2.80 [dd, 3,9]		5.1 [dd, 10.2]	4.73 [t,10]	-	-
15	$CDCl_3$	1.25 [d,6.5]	1.18 [s]	1.85 [d,1.4]	2.85 [dd, 12,3]		5.13 [dd, 10, 1.4]	4.59 [dd, 8,10]	3.13	

(e) The spectra were determined on a Varian HA-100D N.M.R. spectrometer, using TMS as internal standard. The chemical shifts are reported in δ (ppm) units.

(f) Because of the superposition of several signals, the exact chemical shifts cannot be assigned.

(g) Taken on a JEOL 60 M spectrometer.

(h) Exact assignment could not be made.

Figures in square brackets are the coupling constants (J, in Hz).

[s] = singlet, [d] = doublet, [dd] = double doublet, [m] = multiplet, [t] = triplet, (br) = broad, [brd] = broadened signal.

Table 2. The aromatic solvent-induced shifts (ASIS) of the methyl groups at C-10 and at C-11 in the cycloherbolides

Compound	C-10 methyl			C-11 methyl		
	δ $CDCl_3$	δ C_6D_6	Δ	δ $CDCl_3$	δ C_6D_6	Δ
3	1.18	0.94	0.24	1.20	0.88	0.32
4	1.09	0.93	0.16	1.20	0.97	0.23
6	1.10	0.91	0.19	1.20	0.91	0.29
8	1.10	0.88	0.22	1.23	0.96	0.27
9	1.00	0.89	0.11	1.22	1.00	0.22
10	1.32	0.91	0.39			
11	1.34	0.96	0.38	1.24	0.84	0.40
12	1.25	0.87	0.38	1.22	0.91	0.31
13	1.16	0.82	0.34	1.22	0.82	0.40

consistently influenced by exchanging the substituents at C-1 and C-9 (Table 1). The cycloherbolides proved to be excellent models for confirming the additive effect which α substituents exert on the chemical shift of angular Me groups.[9] Thus exchanging an acetate group at C-1 in both α- and β-cycloherbolides for an OH group always causes an upfield shift of 0.08–0.09 ppm (compare compounds **3** and **8**; **4** and **9**; **12** and **13** Table 1). Furthermore substitution of the C-9 acetate for a CO group gives rise to a constant downfield shift of 0.16 ppm. (Compare compounds **3** with **11**; **4** with **12**; **9** with **3**.) Moreover, the influence which a particular substituent has on the C-10 Me signal is almost identical when it is positioned at C-1 or C-9. Thus the chemical shift in the 1-oxo-9-acetoxy-derivative **10** is lower by only 0.02 ppm than in the 1-acetoxy-9-oxo derivative **11**, (δ, 1.32 and 1.34 ppm respectively). These observations seem to point to the Me group at C-10 as being placed equally between the two oxygen functions, although the lactone ring is annelated to ring B.

The effect which substituents have on the chemical shift of the C-10 protons can thus be derived by comparing our data with those reported for α- and β-cyclocostunolide (**16** and **17** resp.). The increments (in ppm) due to β-acetoxy, β-hydroxy and keto functions at positions C-1 or C-9 were calculated accordingly and are summarised in Table 3. The similarity in the values derived from the α- and β-cycloherbolides show that in the eudesmanolide series introduction of a double bond at $\Delta^{4(14)}$ instead of at Δ^{1}, does not cause alterations in the observed increments.

The cycloherbolides described in this paper are derivatives of compounds having a firmly established structure. Since till now no eudesmanolides with substituents at position 9 were isolated they may prove to be valuable reference compounds in the future.

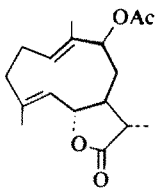
EXPERIMENTAL

M.ps were determined on a Fisher–Jones m.p. apparatus. Infrared spectra were recorded with Perkin Elmer Models 577 or 457 recording spectrophotometers. Optical rotations were determined on a Perkin Elmer 141 M polarimeter. The CD values were determined on a Cary 60 spectrophotometer at room temp. Mass spectra were obtained on a Varian Model CH5 DF instrument

Table 3. The effect of substituents on the chemical shift of the C-10 methyl protons

Compound	Substituent at C-1	Substituent at C-9	Chemical Shift	Increment Calculated* Function	ppm
α-cyclocostunolide (16)	-	-	0.92[9]		
3	β-OAc	β-OAc	1.18	β-OAc	0.13
8	β-OH	β-OAc	1.10	β-OH	0.05
10	oxo	β-OAc	1.32	oxo	0.27
11	β-OAc	oxo	1.34	oxo	0.29
β-cyclocostunolide (17)	-	-	0.86[9]		
4	β-OAc	β-OAc	1.09	β-OAc	0.115
9	β-OH	β-OAc	1.00	β-OH	0.035
12	β-OAc	oxo	1.25	oxo	0.275
13	oxo	β-OH	1.16	oxo	0.265

* Calculated by using cyclocustunolide as reference.



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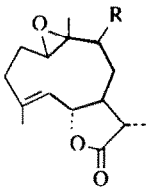
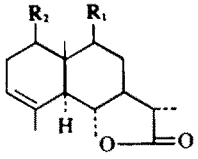
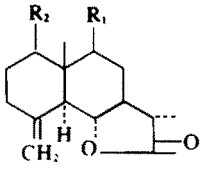


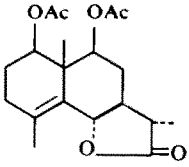
2: R = OAc
14: R = O
15: R = OH



3: $R_1 = R_2 = OAc$
8: $R_1 = OAc$; $R_2 = OH$
10: $R_1 = OAc$; $R_2 = O$
11: $R_1 = O$; $R_2 = OAc$
16: $R_1 = R_2 = H$



4: $R_1 = R_2 = OAc$
9: $R_1 = OAc$; $R_2 = OH$
12: $R_1 = O$; $R_2 = OAc$
13: $R_1 = O$; $R_2 = OH$
17: $R_1 = R_2 = H$



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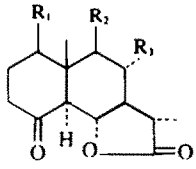

6: $R_1 = R_2 = OAc$; $R_3 = H$
7: $R_1 = R_2 = H$; $R_3 = OAc$

using direct inlet system (relative intensities are noted in parentheses). Analytical TLC was carried out on Silica gel G(Merck) plates and developed by spraying with a soln containing 5 ml phosphomolibdic acid (5% in MeOH), anisaldehyde (2.1 ml), glacial HOAc (45 ml), conc. H_2SO_4 (22.5 ml) and MeOH (430 ml). The plates were heated to 100° after spraying. Silica gel 60 (Merck) or Silica gel M.F.G. (Hopkin and Williams) was used for column chromatography. Silica gel impregnated with $AgNO_3$ was prepared in the following way: a suspension of 40 g silica gel (Hopkin–Williams) in 80 ml of aq. $AgNO_3$ (50%) was stirred for 30 min. over a steam bath. After filtration, the silica gel was dried overnight at 120° and stored in the dark.

Acetyl α-, β- and γ-cycloherbolides B (**3**, **4** *and* **5**)

A soln of **2** 430 mg in Ac_2O (15 ml) and a catalytic amount of *p*-toluenesulphonic acid was refluxed for 90 min. The acid was neutralised ($NaHCO_3$, 5% in H_2O) and extracted with $CHCl_3$. The $CHCl_3$ extract was dried ($MgSO_4$). Evaporation of the solvent yielded 470 mg of a mixture which was applied to a column of 6 g silica gel (treated with $AgNO_3$) and eluted with petroleum ether, isopropanol 24:1.

The first fraction (TLC-monitored) yielded the α-isomer **3** (140 mg) crystallised from acetone–petroleum ether; m.p. 173°; $[\alpha]_D^{25}$ + 54.7° (*c* 0.6, $CHCl_3$); ν_{max} ($CHCl_3$), 1770, 1760, 1740, 1430, 1375, 1275 and 1240 cm^{-1}; (*m/e*) 290 (M^+-60) (98), 248, (6), 230 (100) and 275 (77). (Found: C, 64.99; H, 7.50. $C_{19}H_{26}O_6$ requires: C, 65.14; H, 7.43%).

Next, the γ-isomer **5** was eluted, crystallised from ether (33 mg); m.p. 145°C $[\alpha]_D^{25}$ − 33° (*c*, 0.03, $CHCl_3$); ν_{max} ($CHCl_3$), 1780, 1740, 1735, 1455, 1260 and 1240 cm^{-1}; (*m/e*) 290 (M^+-60) (100), 248 (80), 230 (100), 215 (60) and 204 (60). $C_{19}H_{26}O_6$ requires: (M^+-60) 290.

The third fraction yielded the β-isomer **4** which was further purified on silica gel column eluent: petroleum ether–acetone 10:1 m.p. 165°C; $[\alpha]_D^{25}$ + 62° (*c*, 0.2, $CHCl_3$); ν_{max} ($CHCl_3$) 1775, 1745, 1735, 1650, 1475, 1260 and 915 cm^{-1} (*m/e*) 317 (M^+-60) (100), 262 (8), 248 (40) and 230 (80). $C_{19}H_{26}O_6$ required (M-60) 290.

14-*Nor*-4-*oxo*-*acetyl β-cycloherbolide B* (**6**). A soln of B **4** (24 mg) in glacial AcOH (3 ml) was treated at 0° with a stream of O_2 containing 3% O_3 for 30 min. The mixture was then shaken for 30 min at ambient temp. with 150 mg of Zn dust and filtered. The residue remaining after evaporation of the solvent was purified by column chromatography eluent: $CHCl_3$, MeOH 100:0.5 Crystallization from ether yielded pure **6** (5 mg); m.p. 95–96°; $[\alpha]_D^{25}$ + 11° (*c*, 0.22, $CHCl_3$); CD λ_{max} 293 nm, $\Delta\epsilon$ = −5.1 (*c*, 0.11, $CHCl_3$) ν_{max} ($CHCl_3$) 1780, 1740, 1735, 1720, 1600, 1460, 1370, 1250 and 1020 cm^{-1}. (*m/e*) 352(M^+) (1), 326 (6), 309 (4.2), 292 (100), 250 (24) and 232 (22). $C_{18}H_{24}O_7$ requires: M^+ 352.

α- and β-Cycloherbolides B (**8** *and* **9**). **2**. (200 mg) dissolved in chloroform (12 ml) and $SOCl_2$ (0.7 ml) was left for 90 min at room temp. After evaporation of the solvent at room temp. the residue was chromatographed on 7 g silica gel treated with $AgNO_3$, eluent: petroleum ether, isopropanol 20:1.

The first fraction (70 mg) which was further purified by chromatography on silica gel eluent chloroform, MeOH 350:1, yielded 35 mg of tlc pure **8** as an oil; $[\alpha]_D^{25}$ + 23° (*c*, 0.6, $CHCl_3$); ν_{max} ($CHCl_3$), 3570, 1770, 1745, 1450, 1440, 1375 and 1250 cm^{-1}; (*m/e* 308 (M^+) (2), 290 (1.5), 266 (2), 248 (100), 230 (21) and 215 (28). $C_{17}H_{24}O_5$ requires: M^+ 308. β-cycloherbolide B (**9**) was eluted next (35 mg), further purification on a silica gel column, eluent: $CHCl_3$, MeOH 100:0.5, yielded 25 mg of tlc—pure **9** as an oil. $[\alpha]_D^{25}$ + 65° (*c*, 0.44, $CHCl_3$); ν_{max} ($CHCl_3$) 3500, 1765, 1720, 1650, 1440, 1365, 1240 and 905 cm^{-1}; (*m/e*) M^+ 308 (22), 290 (28), 266 (24), 248 (100), 230 (100) and 215 (67). $C_{17}H_{24}O_5$ requires: M^+ 308.

Dehydro-α-cycloherbolide B (**10**). **8** (20 mg) in 0.2 ml pyridine was oxidised with Cornforth reagent (60 mg CrO_3 in 0.06 ml H_2O and 0.6 ml pyridine). After standing for two days at room temp. EtOAc was added, and the insoluble chromium salts were filtered through a small column containing silica gel. The residue (17 mg), obtained after evaporation of the solvent, was purified on plc eluent: chloroform, MeOH, 120:2, 5 mg of the pure ketone 10 were obtained as an oil; $[\alpha]_D^{25}$ − 33° (*c*, 0.3 $CHCl_3$); CD λ_{max} 300 nm $\Delta\epsilon$ = −1 (*c*, 0.15, $CHCl_3$); ν_{max} ($CHCl_3$) 1760, 1735, 1710, 1450, 1370 and 1260 cm^{-1}; (*m/e*) 306 (M^+) (37.5), 265 (62), 247 (100) and 231 (29); $C_{17}H_{22}O_5$ requires M^+ 306.

1-*Acetyl α- and β-cyclodehydroherbolides B* (**11** *and* **12**). The ketone **14** (72 mg) and a catalytic amount of *p*-toluenesulfonic acid were dissolved in Ac_2O (1 ml) and refluxed for 20 min. Then chloroform was added and the soln was washed with $NaHCO_3$ until neutral. The mixture obtained after evaporation of the solvent was chromatographed on 7 g silica gel (treated with $AgNO_3$), eluent: petroleum ether, isopropanol 24:1.

The α-isomer (**11**) emerged first (20 mg) and was crystallised from ether m.p. 162°C; $[\alpha]_D^{25}$ − 40° (*c*, 0.10, $CHCl_3$); CD λ_{max} 303 nm, $\Delta\epsilon$ -3.1 (*c*, 0.06, $CHCl_3$); ν_{max} ($CHCl_3$) 1780, 1735, 1710, 1600, 1435, 1370 and 1230 cm^{-1}; (*m/e*) 246 (M^+-60) (100), 230 (3.3) and 202 (6.6); $C_{17}H_{22}O_5$ requires (M^+-60) 246.

The β-isomer (**12**) was eluted next from the column (20 mg), and was further purified by plc, $CHCl_3$, MeOH, 100:1.2 and crystallised from ether yielding 9 mg pure **12**, m.p. 164°C; $[\alpha]_D^{25}$ − 90° (*c*, 0.12, $CHCl_3$); CD λ_{max} 320 nm $\Delta\epsilon$ = −0.3 (*c*, 0.1, $CHCl_3$) ν_{max} ($CHCl_3$) 1780, 1735, 1720, 1655, 1600, 1450, 1435, 1370, 1230 and 910 cm^{-1}; (*m/e*) M^+ 306 (31), 264 (74), 246 (100) and 232 (86). $C_{17}H_{22}O_5$ requires M^+ 306.

β-Cyclo-deacetoxy-dehydroherbolide B (**13**). A soln of **14** (60 mg) in $CHCl_3$ (3 ml) containing 0.6 ml $SOCl_2$, was kept at room temp. for two days. After evaporation of the solvent at room temp. the residue was chromatographed on silica gel (treated with $AgNO_3$) and eluted with petroleum ether isopropanol, 24:1. Only the β-isomer could be obtained in pure form; crystallised from benzene petroleum ether, m.p. 78–80°C $[\alpha]_D^{25}$ + 25° (*c*, 0.8, $CHCl_3$); CD λ_{max} 296 nm, $\Delta\epsilon$ = −0.3 (*c*, 0.05, $CHCl_3$); ν_{max} ($CHCl_3$) 3550, 1770, 1700, 1450, 1380, 1270, 1250, 1000 and 900 cm^{-1}; (*m/e*) M^+ 264 (100), 250 (90), 247 (70), 231 (20) and 220 (30). $C_{15}H_{20}O_4$ requires M^+ 264

Compound **13** was acetylated and the product was shown to be identical with **12** (tlc, IR), and inversely, hydrolysis of **12** (in MeOH, aq K_2CO_3) yielded **13** (tlc, IR).

Dehydroherbolide B (**14**). **15** (230 mg), dissolved in pyridine

(2 ml), was oxidised with Cornforth reagent (600 mg CrO_3 in 0.6 ml H_2O and 6 ml pyridine). The mixture was left for 2 days at 40° and EtOAc was added. The insoluble chromium salts which separated were thoroughly extracted with EtOAc and filtered through a layer of silica gel. After evaporation of the solvent, the residue (160 mg) was purified on a column of silica gel. Elution with $CHCl_3$–MeOH, 100:1 yielded 72 mg of the ketone **14**, crystallised from benzene, m.p. 138–140°; $[\alpha]_D^{25}$ − 72° (*c*, 0.09 $CHCl_3$); ν_{max} (1775, 1705, 1655, 1590, 1505, 1450, 1420, 1375, 1290, 1255 and 1210 cm^{-1}; (*m/e*) M^- 264 (48), 220 (68) and 194 (100). $C_{15}H_{20}O_4$ requires M^+ 264; U.V. λ_{max} 282 nm, ϵ 18 (*c*, 0.01, ethanol).

Deacetylherbolide B (**15**). A soln of **2** (500 mg) in MeOH (5 ml) was hydrolysed with 11% K_2CO_3 aq (5 ml). The mixture was stirred overnight at room temp., then water (5 ml) was added and the mixture was carefully neutralized with 1% HCl. The MeOH (with some of the water) was evaporated under reduced pressure at 30°, and the remaining 3 or 4 ml aqueous soln was extracted with ether. The ether extract was washed with sat NaCl, dried ($MgSO_4$) and the solvent was evaporated. The residue (177 mg) was crystallised from ether, petroleum ether to yield pure **15**; m.p. 162°; $[\alpha]_D^{25}$ − 11.5° (*c*, 0.61, $CHCl_3$); ν_{max} ($CHCl_3$) 3550, 1765, 1575, 1190 and 990 cm^{-1}; (*m/e*), 266 (M^+) (36), 248 (100), 230 (3) and 175 (90). Found: C, 67.27; H, 8.28; $C_{15}H_{22}O_4$ requires: C, 67.67; H, 8.27%.

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