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NEW SESQUITERPENE LACTONES FROM *ARTEMISIA HERBA ALBA*

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Key Word Index—*Artemisia herba alba;* Compositae; herbolides A, B and C; structure elucidation; sesquiterpene lactones; germacranolides.

Abstract—The structures of herbolides A, B and C, new sesquiterpene lactones isolated from *Artemisia herba alba*, were determined by chemical and spectroscopic methods.

INTRODUCTION

Artemisia herba alsa is a dwarf shrub which grows wild in various areas of North Africa and the Middle East. This plant is used in folk medicine as an anthelmintic and lately, Khafagy *et al.* [1], isolated santonin from the flowering branches. The essential oils of this plant have been thoroughly investigated [2] and the isolation of a new flavonoid has been reported [3].

Since sesquiterpene lactones are widely distributed among *Artemisia* species [4], it seemed reasonable to undertake a thorough investigation of *Artemisia herba alba* for these compounds.

We now wish to report the isolation and identification of three new sesquiterpene lactones, designated herbolide A, B and C, and to which structures **1**, **5** and **9** were assigned.

RESULTS AND DISCUSSION

The chloroform extract of the flowers, small stems and leaves yielded on column chromatography two crystalline fractions. The less polar fraction yielded on crystallization pure herbolide A(**1**), mp 162°, $[\alpha]_D^{25} = +84$ ($CHCl_3$).

Work up of the more polar fraction yielded two sesquiterpene lactones, herbolide B (**5**), mp 209° (dec.), $[\alpha]_D^{25} = +23$ ($CHCl_3$), and herbolide C (**9**), mp 197–198°, $[\alpha]_D^{25} = -26$ (EtOH). Herbolide B was by far the more abundant of the two (the quantitative ratio was about 20:1). They are isomers whose empirical formula $C_{17}H_{24}O_5$ was confirmed by elemental analysis and MS (M^+ 308).

In the IR region the three herbolides showed bands for lactone groups (*ca* 1760 cm^{-1}), ester functions (1720–1740 cm^{-1}) and for double bonds (1665 cm^{-1}). These data along with the MS peaks at $M^+ - 42$ and $M^+ - 60$, obtained for all three herbolides, indicated that they were sesquiterpene lactone monoacetates. Since apart from the lactone and ester bands there was no spectral evidence for either another carbonyl function or a hydroxyl group, the fifth oxygen atom in herbolides B and C had to be present as an ether. The epoxide nature of these ether functions as well as the interrelationship of the three herbolides was shown by epoxidation of herbolide A. Addition of an equimolar amount of *m*-chloroperbenzoic acid to herbolide A yielded two monoepoxides identical with herbolides B and C (the quantitative ratio was approximately that found in nature). Furthermore, epoxidation of all three substances with excess reagent yielded a common product, the diepoxide **10**, mp 215–16°, $[\alpha]_D^{25} = -38$ ($CHCl_3$).

The germacranolide structure was assigned to herbolide A (**1**), on the basis of the following data. Its NMR spectrum showed a three proton singlet at δ1.69 (C-4 methyl) and a narrow three proton doublet at δ1·46 (J = 1.4 Hz, C-10 methyl) attributed to olefinic methyl groups. A three proton doublet centered at δ 1.27 (J = 6.8 Hz) was indicative of the presence of a C-11 methyl group. At low field (δ 4.46 to 5.36 ppm) signals for four protons were observed and were assigned to two olefinic protons and to two protons α to an oxygen function. (All NMR data are summarized in Table 1. They are in accordance with the proposed structures and were confirmed by double irradiation). The germacranolide structure of herbolide A, with the typical *trans* 1,5-diene system was in accordance with the CD couplet which was positive at higher wave lengths (λ = 214 nm, $\Delta\varepsilon = +33.34$) and strongly negative at lower wavelengths [5–7].

The allylic position of the lactone ring closure was confirmed by comparing chemical shifts of the NMR signals in the low field regions of compound **1** and of compounds **2**, **3** and **4** obtained by basic hydrolysis and catalytic hydrogenation of **1** (Table 1).

The signal at δ 4.55 ppm in **1** and 4.47 in **2** which is assigned to the proton adjacent to the lactone function shifted to higher field (δ 4.15 ppm) after saturation of the double bonds showing its original allylic character. The lactone ring closure is consequently at C-6. The signal at δ *ca* 5.15 ppm in **1** which moved to δ 4.03 ppm after hydrolysis to **2**, was attributed to the proton adjacent to the acetate function. It was shown that by reacetylation of **2** only herbolide A was obtained.

Assignment of herbolide B as the 1,10 epoxide and of herbolide C as the 4,5 epoxide was established from their NMR spectra. The allylic character of H-6 in herbolide B was shown by comparison of its signal in the NMR spectrum with those of its hydrogenation and hydrolysis products (compounds **7**, **8** and **6**). On hydrogenation an

Table 1. NMR chemical shifts (δ, ppm) of herbolides A, B and C, and of their derivatives*

Cmpd	C-11 methyl	C-4 methyl	C-10 methyl	H-1	H-5	H-6	H-9	COMe
1	1.27 (*d*, 6.8)	1.69 (*s*)	1.46 (*d*, 1.4)	5.15†		5.55‡	5.15†	2.03(*s*)
2	1.25 (*d*, 7)	1.69 (*s*)	1.43 (*d*, 1.4)	4.95 (*m*)		4.47‡	4.03 (*dd*, 10,3)	—
3	1.24 (*d*, 6)	Two doublets at *ca* 0.95§		—	—	4.15 (*brd*)	5.15 (*brd*)	1.95 (*s*)
4	1.28 (*d*, 6)	Two doublets at *ca* 1.0§		—	—	4.15†	4.15†	—
5	1.24 (*d*, 6)	1.78 (*d*, 1.4)	1.21 (*s*)	2.79 (*dd*, 12,3)‖	5.06 (*dd*, 10, 1.4)	4.50 (*dd*, 8, 10)	4.19 (*t*)¶	2.02 (*s*)
6	1.25 (*d*, 6.5)	1.85 (*d*, 1.4)	1.18 (*s*)	2.87 (*dd*, 12, 3)‖	5.13 (*dd*, 10, 1.4)	4.59 (*dd*, 8, 10)	3.13 (*br*)¶	—
7	1.31 (*d*, 7)	1.09 (*d*, 4)	1.40 (*s*)	3.12 (*br*)	—	4.26†	—	2.06(*s*)
8	1.29 (*d*, 7)	0.99 (*d*, 4)	1.39 (*s*)	3.17†	—	4.36 (*brd*)	3.17†	—
9	1.34 (*d*, 6.0)	1.34 (*s*)	1.75 (*brd s*)	5.41 (*dd*, 4, 11)	2.62 (*d*, 10)	3.81 (*t*, 9)	5.05 (*m*)	2.05(*s*)
10	1.30 (*d*, 7)	1.40 (*s*) 1.38 (*s*)§		2.97† (*dd*)	2.79 (*d*, 11)	3.88 (*t*, 10)	4.20 (*dd*, 6.5, 3)	2.08 (*s*)

* Spectra were determined as specified in the Experimental section with coupling constants shown in parentheses (Hz); *s* = singlet, *d* = doublet, *dd* = double doublet, *m* = multiplet, *t* = triplet, *br* = broad and *brd* = broadened signal. † The exact chemical shift and coupling constants cannot be determined because of overlap of the signals. ‡ H_5 and H_6 have the same chemical shifts. H_5 thus appears as a singlet and H_6 as a doublet. (Fig. 1). § The exact assignments could not be made. ‖ Double doublet typical for a proton having an axial (J = 10 Hz) and an equatorial (J = *ca* 3 Hz) neighbour. ¶ The unusually high chemical shift can be explained by the anisotropic effect of the epoxide ring.

upfield shift of approximately 0.24 ppm was observed, while basic hydrolysis did not affect its chemical shift (see Table 1). Furthermore the signal of the proton attached to the epoxide ring-carbon (2.79 ppm) was a double doublet and hence must be on C-1. In herbolide C on the other hand, the proton attached to the epoxide ring carbon (2.62 ppm) appeared as a sharp doublet which collapsed to a singlet when the proton at C-6 (δ 3.81 ppm) was irradiated.

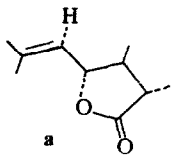
As the three herbolides are structurally related the stereochemical assignment at all the assymetric centers and the position of the acetate function must be identical for all of them.

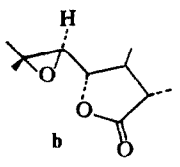
The stereochemical assignment at C-4, C-5, C-6 and C-7 could be derived from the NMR spectra of herbolide B (**5**) and deacetylherbolide B (**6**). The signals for H-5 (5.06 and 5.13 ppm resp., *dd*, J = 10,1.4 Hz) and for H-6 (4.50 and 4.59 ppm resp., *dd*, J = 8, 10 Hz) showed the typical pattern of a C-6 *trans*-γ-lactone with the 4,5-*trans* double bond. The AB pattern for H-5 and H-6 was further indicated by double irradiation experiments performed on compound **6**.

Similar coupling constants were observed in other 4,5-*trans* germacranolides, viz. the tulipinolides [8, 9] lanuginolide [10], lipiferolide [11], having the 1,10-*trans*, 4,5-*trans* double bond or epoxide equivalents, and for the melampolides [12] which have the 1,10-*cis*, 4,5-*trans* configuration.

In the NMR spectra overlapping chemical shifts obscure the structure of several resonances which are essential for solving the structure of the new compounds. The spectrum of compound **2** was markedly simplified by sequential addition of small amounts of $Eu(fod)_3$ to a solution of this compound in $CDCl_3$.

An almost first order spectrum was obtained for a molar ratio of 0.3 $Eu(fod)_3$ to **2**. This technique coupled with double irradiation experiments enabled us to reach several conclusions with regard to the structure of the herbolides. The signals for H-1, H-5, H-6 and H-11 as well as for the three methyl resonances could be unequivocally assigned. (Fig. 1 shows how these signals are shifted). The coupling between the protons at C-11 and C-7 (J = 11 Hz) indicated the pseudoaxial position of the C-11 proton. Since from biogenetic considerations H-7 is assumed to be below the plane of the ring [13] the absolute configuration at positions 4, 5, 6, 7 and 11 is thus established as shown in partial structure **a** for herbolides A and B, and partial structure **b** for herbolide C.





The assignment of the acetate group to C-9 as well as its orientation were established in the following way. The signal of the proton on the same carbon as the acetate function appeared as a broad doublet (J = 10 Hz)

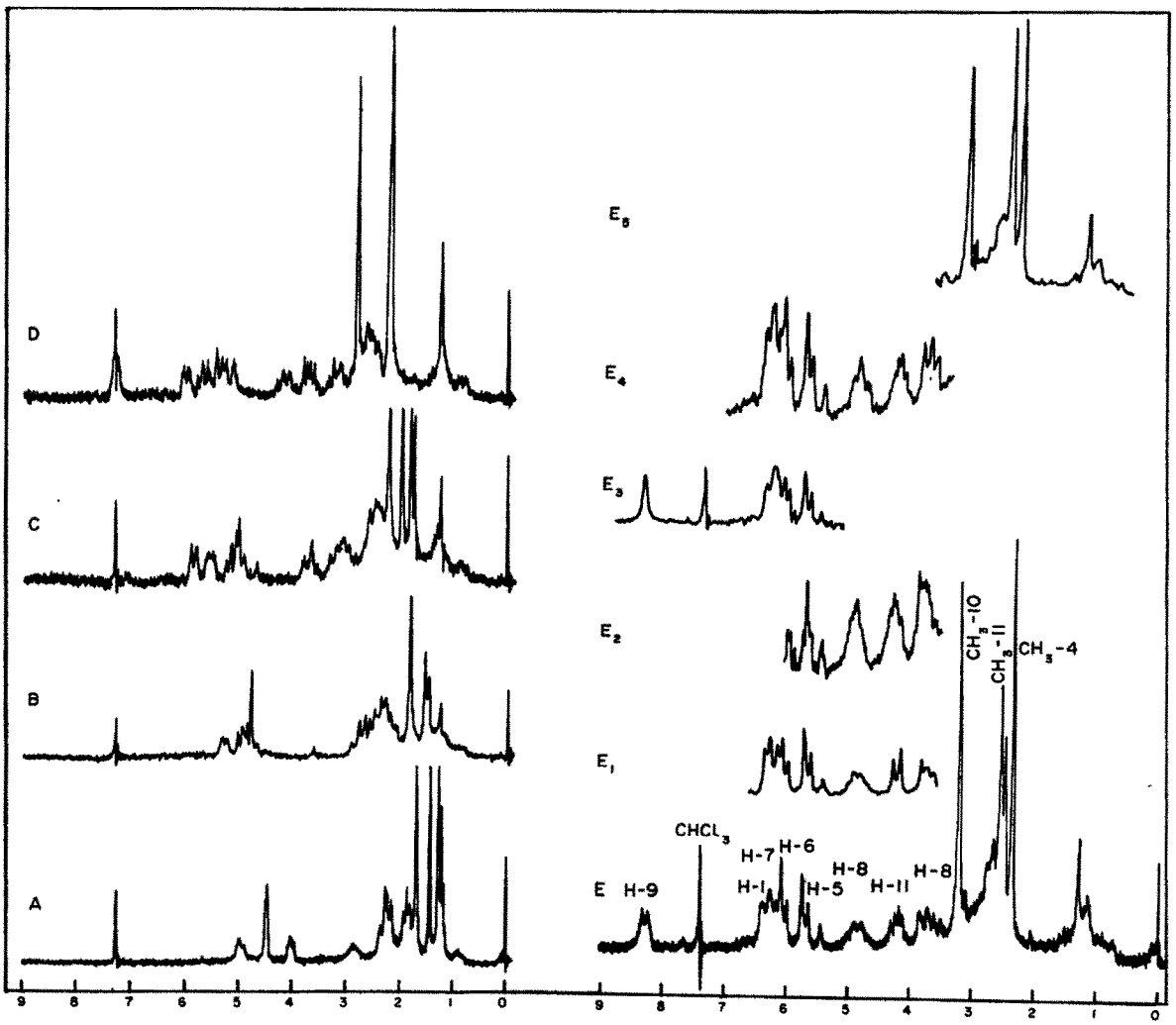


Fig. 1. 100 MHz NMR spectra of deacetylherbolide A (2), 0.56×10^{-3} mol in 0.3 ml of $CDCl_3$. A: Normal spectrum (for assignment see Table 1). B–E. Spectra after sequential addition of $Eu(fod)_3$. Mole Ratios [$Eu(fod)_3$/(2)] B = 0.1; C = 0.18; D = 0.27; E = 0.31. E_1–E_5. Decoupled spectra of **E** irriadiated at the frequencies of: E_1, Me 11; E_2, H–7; E_3, H-8; E_4, H–9; E_5, H—11. The signal at δ = 1.25 ppm, which is not affected by $Eu(fod)_3$ is attributed to an impurity.

which collapsed to a broad singlet (J = 3–4 Hz) on irradiation of H-8 (Fig. 1, E_3). These data are in full agreement with the presence of an axial proton split by both one axial and one equatorial vicinal proton. Inspection of Dreiding models showed that if the established conformation of 1,5-*trans,trans* germacranolides is considered i.e. both methyl groups being *syn* and pointing upwards [4], these data are compatible with either a 3β or a 9β oxygen function. However the large shift observed for the C-10 methyl protons on exposure of compound **2** to $Eu(fod)_3$ as compared to the shifts of the C-11 and especially that of the C-4 methyl protons (fig. 2) is compatible only with the hydroxyl group in the 9β position. (From fig. 2 it can be seen that the lactone carbonyl begins to coordinate competitively with Eu only at a molar ratio of about 0.1). From all these data we may conclude that herbolide A should be represented as shown in formula **1**.

Sesquiterpene lactones possessing the *trans, trans* cyclodeca-1,5 diene system are known to give acid catalysed transannular ring closure to eudesmanolides [8, 14–16]. No analogous cyclization products could be obtained from herbolide A. Under mild conditions no reaction took place. With more drastic methods, however, decomposition products only were obtained. This unusual behaviour may be due to the presence of the acetate function at C-9.

The interrelationship of the three herbolides was shown by epoxidation of herbolide A. Since epoxidation of herbolide A yields exclusively herbolides B and C, it must be assumed that the stereospecific epoxidation occurs at a definite conformation of the starting material. The attack on the double bonds should take place from the less hindered side. Thus herbolides B and C must be represented as shown in formulae **5** and **9**.

Final proof of the proposed structures was afforded by the X-ray crystallography of herbolide B (Dr. O. Kennard, unpublished results).

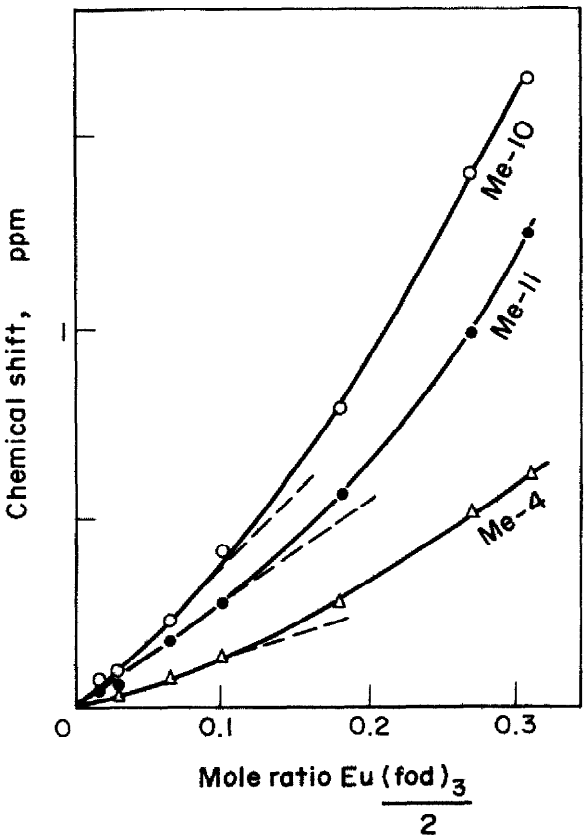
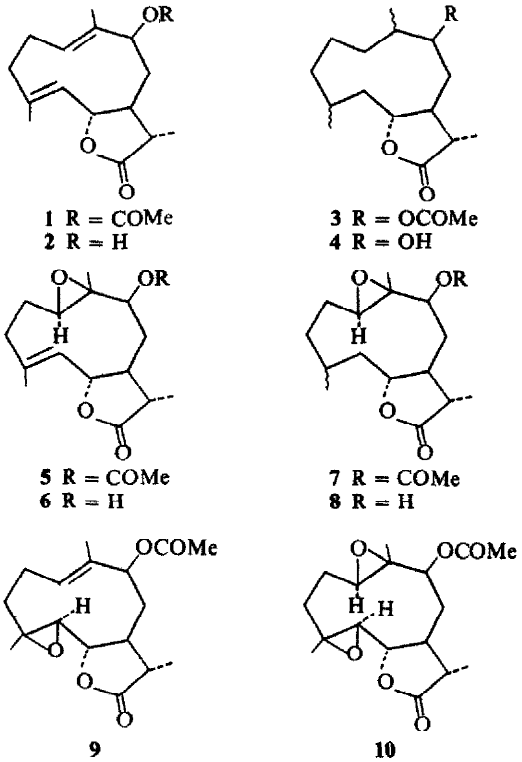


Fig. 2. Variation of the chemical shifts of the three methyl groups in deacetylherbolide A (2) with increasing concentration of $Eu(fod)_3$, (0.56×10^{-3} mol 1l in 0.3 cc of $CDCl_3$).



EXPERIMENTAL

Mps were determined on a Fisher–Johns mp apparatus. Mmps were taken on a Thomas–Hoover capillary melting point apparatus. IR spectra were determined in $CHCl_3$. NMR spectra were measured in $CDCl_3$ at 60 or 100 MHz using TMS as internal standard. The chemical shifts are reported in δ (ppm) units. The CD values were determined with a Roussel–Jouan dichrographe model 185 at room temp. MS were obtained using a direct inlet system. Elemental analyses were determined by Mrs. Goldstein, the Hebrew University, Jerusalem. Analytical TLC was carried out on Si 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), MeOH (430 ml). The plates were heated to 100° after spraying. Si gel 60 (Merck) or Si gel M.F.G. (Hopkin and Williams) were used for column chromatography. Petrol refers to the fraction with bp 60–80°.

Isolation of herbolide A (1), *B* (5) *and C* (9). *Artemisia herba alba* Asso. was collected near Sde Boker (Negev desert). The dried flowers, leaves and small stems (1 kg) were crushed and extracted with petrol. The extract was discarded and the residue allowed to stand for several days covered with $CHCl_3$ or CH_2Cl_2. Evap. of the solvent yielded a thick tar (30 g). A portion of the crude product (15 g) was chromatographed on a column of 400 g Si gel. Elution with a soln of *iso*-PrOH (2%) in petrol, afforded crude herbolide *A* (1) (60 mg) which crystallized from Et_2O as needles. Recrystallization from EtOH yielded pure herbolide A (1); yield 0.012%, mp 162–163°; $[\alpha]_D^{25}$ + 84° (*c* 0.2; $CHCl_3$); CD $[\theta]_{214}^{20°} = +110{,}020$, and strongly negative at shorter wavelengths (*c* 0.00861 EtOH); IR ν_{max}^{KBr} cm^{-1}: 1760 (γ-lactone) 1710 (acetate), 1655 (C = C), 1235, 960, and 860. MS *m/e* (rel. int.): 292 (M^+, 5.7), 250 ($M^+ - 42$), 7.1) and 232 ($M^+ - 60$), 100). (Found: C, 70.08; H, 8.23. Calcd. for $C_{17}H_{24}O_4$; C, 69.86; H, 8.22%). Herbolides B and C were eluted from the column by raising the *iso*-PrOH concentration to 9%. A mixture of the crude herbolides B and C was obtained. Crystallization first from Et_2O and then from EtOH yielded pure herbolide B (6; yield 0.020%; mp 209° (decomp.); $[\alpha]_D^{25} = +23°$ (*c* 0.37; EtOH); IR ν_{max}^{KBr} cm^{-1}: 1755 (γ lactone), 1715 (acetate), 1665 (C = C), 1250, 1240, 960, 915 and 855; MS *m/e* (rel. int.): 308 (M^+, 6), 270 ($M^+ - 38$), 12), 266 ($M^+ - 42$), 100). 248 ($M^+ - 60$), 33). (Found: C, 65.80; H, 7.75. Calcd for $C_{17}H_{24}O_5$: C, 66.23; H, 7.79%). The mother liquor containing herbolides B and C was separated on 0.8 mm PLC plates by elution (×3 or ×4) with $CHCl_3$–MeOH (100:1) and extraction with $CHCl_3$–MeOH (8.2). In addition to pure herbolide B, crystalline herbolide C was obtained by crystallization from EtOH–petrol, mp 197–198°; $[\alpha]_D^{25} = -26°$ (*c*, 0.1, EtOH); IR ν_{max}^{KBr} cm^{-1}: 1770 (γ-lactone), 1730 (acetate), 1670 (C = C), 1250, 1240, 1175, 900, 865 and 830, MS (*m/e* (rel. int.) 308 (M^+, 13), 266 ($M^+ - 42$) 100) and 248 ($M^+ - 60$, 86). (Found: C, 66.02; H, 7.76. Calcd for $C_{17}H_{24}O_5$: C, 66.23; H, 7.79%).

Deacetylherbolide A (2). (*a*) *mild basic hydrolysis.* A soln of herbolide A (1) (250 mg) in MeOH (2 ml) was stirred for 16 hr with 2.5 ml aq. K_2CO_3 (11%) at room temp. The reaction mixture was diluted with H_2O (5 ml), neutralized with 1% HCl and extracted with Et_2O. The extract was washed with a satd NaCl soln and dried over $MgSO_4$. The filtrate yielded on evaporation an oil (138 mg) giving crystals on treatment with Et_2O–petrol, mp 54°; $[\alpha]_D^{25}$ + 100° (*c* 0.66, $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3550, 1765, 1635, 1600, 1155 and 960; MS *m/e* (rel. int.): 250 (M^+, 40), 232 ($M^+ - 18$, 100). The remaining neutral layer was carefully acidified to pH 4–5, left overnight and then extracted with Et_2O. The ethereal phase was washed with H_2O, dried ($MgSO_4$) and evapd. The residue (20 mg) $[\alpha]_D^{25}$ + 82, had IR and NMR spectra identical with 2 and a mixed mp of the two was undepressed. Acetylation of 2 yielded herbolide A (mp, mmp, IR and NMR spectra).

(*b*) *Strong basic hydrolysis.* Carried out as described by Yoshioka *et al.* [17]. The product obtained was identical with 2. Reacetylation afforded herbolide A (1).

Tetrahydroherbolide A (3). A soln of herbolide A (1), (450 mg) in HOAc (60 ml) was hydrogenated over PtO_2 (50 mg) (Adam's

catalyst) in a Parr hydrogenator (40 psi pres.) at room temp. After 2 hr the reaction mixture was filtered and conc to give a colourless oil (453 mg). PLC (C_6H_6–Me_2CO 100:4) yielded an oily substance (**3**) (410 mg), which could not be crystallized: $[\alpha]_D^{25}$ − 11.1° (*c* 1.0; EtOH) IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1780, 1735 and 1260; MS *m/e* (rel. int.): 296 (M^+, 3.3, 254 (M^+–42), 6.6), 236 (M^+–60, 20) and 208 (100).

Deacetyltetrahydroherbolide A (**4**). Tetrahydroherbolide A (**3**), (250 mg) was dissolved in MeOH (3 ml) and hydrolysed with 3 ml aq. K_2CO_3 (11%). The reaction mixture was stirred for 2 days and then extracted with Et_2O. The extract was washed with a satd NaCl soln and dried over $MgSO_4$. Evaporation of the solvent afforded an oil (85 mg), crystallization from Me_2CO–petrol afforded pure **4**, mp 60–62°; $[\alpha]_D^{25}$ − 12° (C 1.4; EtOH); IR ν_{max} cm^{-1}: 3450, 1745 and 1200; MS *m/e* (rel. int.): 254 (M^+, 8, 239 (M^+15, 8, 236) (M^+–18, 11), 210 (M^+–44, 32), 181 (100) and 163 (54).

Deacetylherbolide B (**6**). A soln of 500 mg of **5** in MeOH (5 ml) was hydrolysed with 5 ml aq. K_2CO_3. The mixture was stirred 12 hr at room temp., then H_2O was added (5 ml) and the reaction mixture was carefully neutralized with 1% HCl. The MeOH (with some of the H_2O) was evap. under red. press. at 30° and the remaining 3 or 4 ml aq. soln was extracted with Et_2O. The Et_2O extract was washed with satd NaCl, dried ($MgSO_4$), and the solvent evaporated. The residue (177 mg) was crystallized from Et_2O–petrol to yield pure **7**; mp 162°; $[\alpha]_D^{25}$ −11.5° (*c* 0.62, $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3550, 1765, 1575, 1190 and 990; MS *m/e* (rel. int.): 266 (M^+, 36, 248 (M^+–18, 100), 230 (3) and 175 (90). (Found: C, 67.27; H, 8.28. Calcd for $C_{15}H_{22}O_4$: C, 67.67; H, 8.27%). The neutral reaction mixture was then carefully acidified to pH 4–5, left overnight and then extracted with Et_2O. The Et_2O soln was washed with H_2O, dried ($MgSO_4$) and evap. Acetylation of this product yielded after purification by column chromatography (eluent: petrol–*iso*-PrOH, 20:1) 50 mg of pure herbolide B. (mp, mmp, IR, NMR).

Dihydroherbolide B **7**. A soln of 240 mg of **5** in 20 ml of EtOAc was hydrogenated over Adam's catalyst (50 mg) in a Parr hydrogenator at room temp. (*ca* 40 psi). After 4 hr the catalyst was filtered off and the solvent evap. The residue (238 mg) was purified by column chromatography (petrol–*iso*-PrOH, 24:1) to yield 130 mg of **7** crystallized from C_6H_6, mp 155°; $[\alpha]_D^{25}$ −26.4° (C 0.25, $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1775, 1735 and 1230 MS *m/e* (rel. int.): 295 (M^+–15, 22,) 268 (M^+–42, 100) and 250 (M^+–60, 55).

Deacetyldihydroherbolide B (**8**). Dihydroherbolide B (**7**) (145 mg) dissolved in MeOH (2 ml) was hydrolysed with 1 ml of 11% aq. K_2CO_3. The reaction was allowed to stand overnight and then extracted with Et_2O (fraction a). The aq. soln was then acidified and again extracted (fraction b), The Et_2O extracts were treated separately, each was washed with satd NaCl, dried over $MgSO_4$ and evap. to give a white solid which crystallized from Et_2O; fraction a, 70 mg and fraction b, 14 mg. Purification by column chromatography, (eluent $CHCl_3$–MeOH, 100:1) yielded identical deacetylhydroherbolide B (**8**) from both extracts mp 121–123°; $[\alpha]_D^{25}$ − 45° (*c* 0.24; $CHCl_3$); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3595, 1770, 1460 and 1180; mpm no depression. MS *m/e* (rel. int.): 268 (M^+, 100) and 250 (M^+–18, 100). Reacetylation of fraction b afforded **7**.

Epoxidation of herbolide A to monoepoxides **5** and **9**. To a soln of 300 mg herbolide A in $CHCl_3$ (10 ml) an equimolar amount of *m*-chloroperoxybenzoic acid (180 mg) was added. The reaction mixture was allowed to stand for 3 hr in the dark at room temp. The soln was washed with 5% aq. $NaHCO_3$ and H_2O, dried ($MgSO_4$) and the solvent was evap. The residue (270 mg) was chromatographed on PLC using the same procedure as described for the mixture of the natural epoxides. The 2 products obtained were shown to be identical with herbolides B and C (mp, mmp, IR and NMR spectra).

Epoxidation of herbolide A to the diepoxide **10**. Herbolide A (165 mg) in $CHCl_3$ (10 ml) was allowed to react with an excess of *m*-chloroperoxybenzoic acid (150 mg) for 24 hr at room temp. The soln was then processed as described above. The product (158 mg) which still contained small amounts of monoepoxides was purified by column chromatography. Elution with $CHCl_3$–MeOH (240:1), gave 50 mg of the diepoxyherbolide (**10**): mp 215–216°; $[\alpha]_D^{25}$ − 38° (*c* 0.5, $CHCl_3$); IR ν_{max}^{KBr} cm^{-1}: 1770, 1250, 1240, 1175 and 900; MS *m/e* (rel. int.): 324 (M^+, 5)282 (M^+–42, 23), 281 (M^+–43, 43), 264 (M^+–60, 20), 263 (18), 239 (39) and 238 (100).

Epoxidation of herbolides B and C to the diepoxide **10**. A mixture of herbolides B and C (20 mg) was allowed to react with an a excess of *m*-chroroperoxybenzoic acid following the same procedure described above. The purified product (5 mg) was shown to be identical with the diepoxide **10** (mp, mmp and IR spectrum).

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