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NEOCLEORDANE DITERPENOIDS AND THEIR ARTIFACTS FROM *TEUCRIUM OLIVARIANUM*

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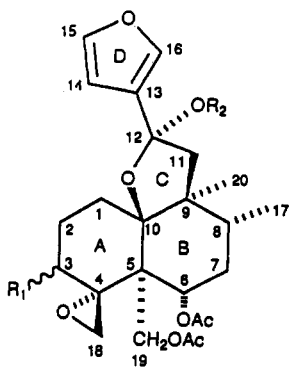
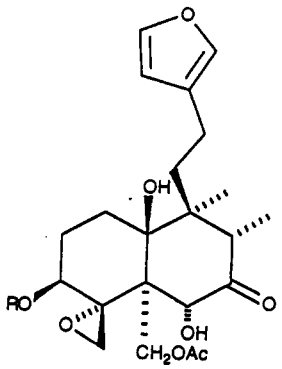
ABSTRACT.—The aerial parts of *Teucrium oliverianum* yielded five new neocleordane diterpenoids (teucrolins A [**4**], B [**5**], C [**6**], D [**7**], and E [**8**]), three neocleordane diterpene artifacts (12-*O*-methylteucrolivin A [**9**], 12-*O*-methylteucrolin A [**10**], and 12-*O*-ethylteucrolin A [**11**]), and the three known diterpenoids teucrolivins A [**1**], B [**2**], and C [**3**]. In addition, four other known compounds were isolated: the sterol 24(*S*)-stigmasta-5,22,25-trien-3β-ol, the iridoid 8-*O*-acetylharpagide, and the flavones eupatorin and cirsiliol. The structural assignments of all new diterpenoids and their artifacts were based on 1D and 2D nmr spectral data, chemical derivatization, and X-ray crystallographic analysis of **10**; the latter established the relative stereochemistry and the presence of the rare axial substitution at C-3 in **10** and related compounds.

Teucrium oliverianum (Ging. ex Benth.) R.Br. (Labiatae), a perennial herb, is one of five species of *Teucrium* distributed throughout Saudi Arabia (1–3). This plant is used in traditional Saudi medicine for the treatment of diabetes and is well known for its hypoglycemic activity (4). Earlier phytochemical work on the aerial parts of this plant yielded the three C-10 oxygenated neocleordane diterpenes teucrolivins A [**1**], B [**2**], and C [**3**] (5) and teucrolivins D–F (6). The structure and relative stereochemistry of **1** were unambiguously determined by X-ray crystallography. However, other species of *Teucrium* are known to exhibit a wide array of neocleordane and 19-norneocleordane diterpenoids (7,8), flavanoids (9,10), and iridoid glycosides (11), exhibiting various types of biological



	R_1	R_2
1	=O	H
4	α-OAc	H
9	=O	Me
10	α-OAc	Me
11	α-OAc	Et
12	β-OH	Me
13	β-OAc	Me
14	β-OAc	H

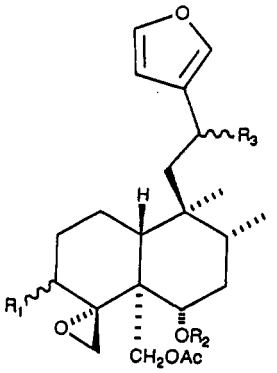


2 R=Ac
3 R=H

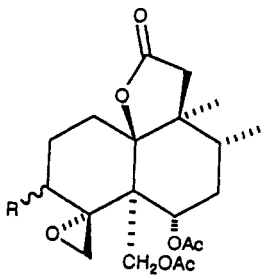
activities (12,13). We herein report on the isolation and characterization of five new diterpenoids from the aerial parts of *T. oliverianum*, namely, the 3α-acetylneocleordane diterpenes teucrolins A [**4**], B [**5**], and C [**6**] and the 3α-acetyltetranorneocleordane teucrolin D [**7**], as well as teucrolin E [**8**]. In addition, the same plant material yielded the neocleordane diterpene artifacts 12-*O*-methylteucrolivin A [**9**], 12-*O*-methylteucrolin A [**10**], and 12-*O*-ethylteucrolin A [**11**], the known neocleordanes teucrolivins A [**1**], B [**2**], and C [**3**] (5), the sterol 24(*S*)-stigmasta-5,22,25-trien-3β-ol (14), the iridoid 8-*O*-acetylharpagide (11,15), and the flavonoids eupatorin and cirsiliol (16,17).

RESULTS AND DISCUSSION

The $CHCl_3$ solubles of the 95% MeOH extract of *T. oliverianum* were flash chromatographed (18) on Si gel to give a number of fractions from which the major products **1–3** were obtained in 0.05%, 0.018%, and 0.014% yields, respectively. Compounds **1–3** were identified as teucrolivins A–C, respectively, by comparison of their physical and spectroscopic data with those previously reported (5). Further purification of fraction A (Table 1) by chromatography gave teucrolin A [**4**], $C_{26}H_{34}O_{10}$, as colorless plates. On methylation, **4** afforded the corresponding 12-*O*-methylteucrolin A [**10**] (δ 3.01, 3H, s; δ_C 51.21, q), confirming the presence of a hydroxyl group. Comparison of the ^{1}H- and ^{13}C-nmr spectral data of **4** and **1** [Tables 2 and 3, and Bruno *et al.* (5)] suggested that **4** was likely to be the 3-acetyl derivative of **1**. The ^{1}H-nmr spectrum of **4** (Table 2) contained a signal at δ 4.62 (t, J=4.2 Hz, H_β-3) suggesting the presence of an axially disposed 3α-OAc group. The related 3β-acetoxy derivatives of **10** and **4** were obtained from 12-*O*-methylteucrolivin A [**9**] (see Experimental) by $NaBH_4$ reduction, which yielded compound **12** as the major product. Acetylation of **12** afforded 3-*epi*-12-*O*-methylteucrolin A [**13**] and the by-product 3-*epi*-teucrolin A [**14**]. The ^{1}H-nmr spectra of **13** and **14** (Table 2) clearly showed the strong deshielding of their H-3α protons due to equatorial (β) orientation of their 3-OAc groups in contrast to axial disposition in the natural 3α-OAc epimer **4**. Furthermore, the ^{13}C-nmr spectrum of **14** (Table 3) revealed strong shielding of C-3 (δ_C 67.47) and C-18 (δ_C 44.53) compared to the corresponding centers [$\delta_{C\text{-}3}$ 76.45, $\delta_{C\text{-}18}$ 50.64] in **4**, due to the 3β-OAc group. The structure of teucrolin A [**4**] was tentatively proposed on the basis of its ^{13}C-nmr spectral



	R_1	R_2	R_3
5	α-OAc	H	OH
6	α-OAc	Ac	=O
15	β-OH	H	OAc
16	α-OAc	H	OAc
17	α-OAc	OAc	OAc
18	H	OAc	=O



7 R=α-OAc
19 R=O

TABLE 1. Column Chromatography (cc) and Centrifugal Preparative Tlc[a] (CPtlc) of the $CHCl_3$ Fraction.

	Solvent						Weight		R_f[b]	Mp, $[\alpha]_D$[c]	Lit. mp, $[\alpha]_D$[d]	Identity
	Petroleum ether	EtOAc	MeOH	Et_2O	Me_2CO	$CHCl_3$	(g)	(%)				
Cc												
	9.0	1.0					0.24	0.008	0.85	[e] (−50.4°, c=0.01)		**11**
							1.711	0.057	0.82	205–206°, +27.5° (c=0.13)		**9**
							0.511	0.017	0.80	177–179°, −31.3° (c=0.01)		**10**
	8.5	1.5					0.045	0.0014	0.72	77–79°, −53° (c=0.084)		**7**
							1.59	0.05	0.65	199–200°, +46° (c=0.1, $CHCl_3$) +25° (c=0.1)	185–187°, +54.1° ($CHCl_3$)	**1**
							—	—	—	—	—	mixture A (2.5 g)
	7.0	3.0					0.533	0.018	0.55	[e] +29.7° (c=0.13)	104–106° +22.3° ($CHCl_3$)	**2**
	6.5	3.5					—	—	—	—	—	mixture B (3.0 g)
	1	1					0.428	0.014	0.35	[e] +19.1° (c=0.11, $CHCl_3$)	95–105°, +15.9° ($CHCl_3$)	**3**
Cptlc												
Mixture A	4			6			0.310	0.01	0.60[f]	119–120°, −45.2° (c=0.1)	—	**4**
							0.055	0.002	0.50[f]	152–153°, −72.8° (c=0.11)	—	**6**
Mixture B					0.25	100	0.105	0.004	0.60[g]	173–174°, −48.5° (c=0.07)	—	**5**
							0.040	0.0013	0.35[g]	78–79°, −35.4° (c=0.05)	—	**8**

[a]Using chromatotron (Si gel P_{254}, 2 mm disk).
[b]Si gel G 254, solvent petroleum ether-EtOAc (1:9).
[c]Optical rotation data recorded for diterpenes in C_6H_6 are likely to be more reliable than those recorded in halogenated solvents.
[d]Data in this column are from Bruno *et al.* (5).
[e]Amorphous solid.
[f]Solvent Et_2O.
[g]Solvent $CHCl_3/Me_2CO$.

TABLE 2. ^{1}H-nmr Chemical Shift Values (in δ ppm) and Coupling Constants (Hz, in parentheses) for Diterpenes **4**, **7**, **9**–**14**.[a]

Proton	Compound								
	4	**7**	**9**	**10**		**11**	**12**	**13**	**14**
				($CDCl_3$)	(C_6D_6)			(C_6D_6)	(C_6D_6)
H-1	2.0–2.10 m	1.95–2.05 m	2.0–2.20 m 2.45–2.50 m	2.0–2.08 m	+[b]	+	+	+	+
H-2	2.20–2.30 m 1.75–1.85 m[c]	1.80–1.90 m	2.62–2.64 m	2.2–2.24 m 1.87–1.89 m	+	1.75–1.85 m	1.95–2.2 m	+	+
H-3	4.62 t (4.2)[d]	4.63 t (3.5)[d]	—	4.62 brt (3.5)[d]	4.81 dd (1.6,3.8)	4.63 t (3.0)[d]	4.19 dd (4.8,12.0)	5.65 dd (5.4,11.4)	5.67 dd (5.6,12.5)
H-6	5.33 dd (6.4,10.6)	5.21 dd (6.0,9.4)	5.30 dd (5.8,10.8)	5.30 dd (4.5,11.5)	5.57 ddd (1.4,6.2, 11.0)	5.35 dd (6.0,10.0)	5.35 brdd (4.0,11.4)	5.55 dd (6.4,10.4)	5.52 ddd (1.3,5.1, 10.5)
H-7	1.40–1.48 m	1.70–1.82 m	1.38–1.41 m	1.65–1.70 m 1.37 dt (3.8,9.0)	+	1.35–1.45 m	1.34–1.48 m	+	+
H-8	1.75–1.85 m[c]	1.60–1.75 m	1.85–1.95 m	1.82–1.85 m	+	1.75–1.85 m	1.79–1.84 m	+	+
H-11	2.23 d (12.6) 2.34 d (13.0)	2.22 d (9.2) 2.44 d (10.0)	2.31 d (13.2) 2.47 d (13.8)	2.17 d (13.5) 2.31 d (13.5)	2.05 d (13.4) 2.15 d (13.8)	2.27 d (12.0) 2.33 d (12.0)	2.16 d (13.0) 2.32 d (13.0)	2.10 d (13.0) 2.03 d (13.2)	1.96 d (13.2) 2.09 d (13.6)
H-14	6.39 dd (1.2,2.0)	—	6.29 dd (1.4,2.6)	6.26 dd (1.0,1.9)	6.01 t (1.0)	6.28 dd (1.0,2.0)	6.27 brs	6.11 d (2.0)	6.16 dd (1.0,2.0)
H-15	7.39 d (1.7)	—	7.44 t (2.0)	7.41 t (1.7)	6.99 t (1.2)	7.40 t (1.6)	7.41 d (1.2)	6.98 d (1.6)	6.96 t (2.4)
H-16	7.48 d (1.3)	—	7.43 t (1.4)	7.45 dd (1.0,1.6)	7.49 t (1.0)	7.44 t (1.0)	7.45 brd (1.2)	7.16 brs	7.40 dd (1.2,2.2)
H-17	0.75 d (6.6)	0.95 d (5.6)	0.78 d (7.2)	0.72 d (6.7)	0.36 d (7.0)	0.73 d (6.2)	0.72 d (6.0)	0.31 d (6.2)	0.30 d (7.2)
H_A-18[e]	2.50 d (4.4)	2.54 d (4.2)	2.67 d (5.4)	2.51 d (4.1)	2.22 d (4.2)	2.52 d (4.2)	2.98 d (4.0)	2.84 d (4.2)	2.89 d (4.8)
H_B-18[f]	3.19 d (4.4)	3.18 d (3.8)	3.23 d (6.0)	3.23 d (4.3)	3.37 d (3.8)	3.24 d (4.2)	3.0 d (3.9)	3.28 d (4.0)	3.27 d (4.8)
H_A-19	4.60 brd (11.2)[d]	4.57 dd (2.4,12.0)[d]	4.37 d (11.4)	4.58 d (12.9)[d]	4.75 dd (1.4,12.4)	4.60 d (12.0)[d]	4.27 d (11.8)	4.18 dd (1.8,12.0)	4.19 dd (1.2,13.0)
H_B-19	5.09 d (12.4)	5.13 d (12.0)	4.81 d (11.8)	5.10 d (12.0)	5.16 d (12.2)	5.09 d (12.2)	5.07 d (12.0)	4.98 d (12.4)	4.95 d (13.0)
H-20	0.96 s	1.05 s	1.02 s	0.92 s	0.56 s	0.94 s	0.87 s	0.39 s	0.37 s
-OMe	—	—	3.03 s	3.01 s	2.83 s	—	3.04 s	2.90 s	—
-OAc	2.10, 2.06, 1.96 (3×s)	2.12, 2.08, 1.97 (3×s)	2.06, 2.04, 2.02 (3×s)	2.10, 2.06, 1.96 (3×s)	1.86, 1.84, 1.56 (3×s)	2.11, 2.07, 1.97 (3×s)	2.11, 1.99 (2×s)	2.15, 1.85, 1.70 (3×s)	2.13, 1.85, 1.72 (3×s)
-OEt	—	—	—	—	—	4.13, 3.71 dd (7.6,12.0) 1.04 t (7.8)	—	—	—

[a]Spectra for **4**, **7**, **9**, **11**, and **12**–**14** recorded at 200 MHz and for **10** at 300 MHz.
[b]+ =overlapped signals.
[c,d]Signals superimposed on each other.
[e]*exo*-Hydrogen with respect to ring B (5).
[f]*endo*-Hydrogen with respect to ring B (5).

TABLE 3. ^{13}C-nmr Spectral Data for Diterpenoids **1**, **4**, **7**, **9–12**, and **14**.[a]

Carbon	Compound							
	1	**4**	**7**	**9**	**10**	**11**	**12**	**14**
C-1	28.21	24.40	24.70	28.42	24.65	24.65	27.65[b]	27.43[b]
C-2	36.17	25.68	25.27	35.97	25.49	25.44	27.60[b]	26.41[b]
C-3	205.32	76.45	75.39	205.08	76.38	76.58	65.83	67.47
C-4	63.0	60.93	60.35	61.90	60.75	60.78	64.40	62.41
C-5	48.76[b]	47.20[b]	46.69	48.72[b]	47.21[b]	47.30[b]	47.93[c]	48.40[c]
C-6	68.75	70.13	69.30	68.81	69.70	69.97	69.34	68.88
C-7	32.89	32.74	32.19	32.93	32.67	32.74	32.71	33.03
C-8	33.76	33.70	35.28	33.73	33.67	33.72	33.52	33.58
C-9	49.18[b]	48.48[b]	44.98	48.91[b]	47.90[b]	47.82[b]	48.02[c]	48.41[c]
C-10	90.14	91.73	93.22	90.47	92.10	90.08	92.25	91.62
C-11	50.58	49.40	42.80	51.50	51.40	49.19	51.19	50.52
C-12	100.81	101.08	173.95	104.47	104.75	104.29	104.28	101.05
C-13	131.91	132.27	—	127.88	128.0	128.77	128.22	132.92
C-14	108.16	108.37	—	108.68	108.68	108.82	108.79	108.65
C-15	143.97	143.79	—	144.08	143.83	143.77	143.83	143.72
C-16	138.49	138.56	—	140.15	140.20	139.93	140.28	138.88
C-17	15.94	16.18	16.36	15.97	16.08	16.14	16.15	15.76
C-18	52.51	50.64	49.48	52.35	49.15	51.73	44.23	44.53
C-19	61.03	62.32	62.16	61.90	62.18	62.27	61.07	60.91
C-20	15.04	13.96	13.30	15.07	14.05	14.13	13.77	13.19
OMe	—	—	—	51.31	51.21	—	51.19	—
OAc's	170.21	170.84	170.54	170.19	170.74	170.85	170.53	170.34
	169.97	170.01	169.75	169.89	170.02	170.08	169.86	169.48
	—	170.01	169.66	—	169.90	170.02	—	169.14
	21.26	21.33	21.29	21.30	21.62	21.32	21.22	21.11
	20.56	21.27	21.20	20.54	21.24	21.32	21.16	20.99
		21.19	21.15		21.18	21.26		20.63
OEt						58.98		
						14.90		

[a]Spectra recorded for **1** and **10** at 75 MHz, and for **4**, **7**, **9**, **11**, **12**, and **14** (in C_6D_6) at 50 MHz. Multiplicities of the carbon signals of all compounds were determined by APT and DEPT experiments, also aided (for **1** and **10**) by 2D nmr COSY and HETCOR experiments.
[b,c]Signals in the same column with the same superscript are interchangeable.

data and those of its derivatives **1** (5), **9–12**, and **14** (Table 3); singlets at δ 91.73 and δ 101.08 for C-10 and C-12, respectively, in the C-12(10β)-hemiacetal moiety of **4** with C-12 as the spiro center [versus $\delta_{C\text{-}10}$ 90.09, $\delta_{C\text{-}12}$ 100.77 of **1** (5)].

X-ray crystallographic analysis unambiguously established the complete structure and relative stereochemistry of **10** (the methyl ether of **4**). Carbon and oxygen atom fractional coordinates[1] are listed in Table 4. Bond lengths, in general, lie close to expected values (19). A view of the solid-state conformation is presented in Figure 1. [Endocyclic torsion angles ω_{ij} (σ 0.5–0.9°) about the bonds between atoms *i* and *j* follow: $\omega_{1,2}$ −52.0, $\omega_{2,3}$ 48.0, $\omega_{3,4}$ −54.2, $\omega_{4,5}$ 57.4, $\omega_{5,10}$ −58.8, $\omega_{10,1}$ 58.9° in ring A; $\omega_{5,6}$ −55.2, $\omega_{6,7}$ 61.8, $\omega_{7,8}$ −54.3, $\omega_{8,9}$ 43.3, $\omega_{9,10}$ −40.8, $\omega_{10,5}$ 44.9° in ring B; $\omega_{9,11}$ 34.1, $\omega_{11,12}$ −12.4, $\omega_{12,25}$ −17.1, $\omega_{25,10}$ 39.0, $\omega_{10,9}$ −43.9° in ring C; $\omega_{13,14}$ −2.0, $\omega_{14,15}$ 3.4, $\omega_{15,27}$ −3.4, $\omega_{27,16}$ 2.1, $\omega_{16,13}$ −0.1° in ring D]. Rings A and B are in somewhat flattened chair conformations, ring C approximates to a half-chair form with its C_2 symmetry axis passing through C-12 and the mid-point of the C-9–C-10 bond, and ring D is essentially planar.

Teucrolin B [**5**] was isolated as colorless needles and analyzed for $C_{24}H_{34}O_8$. Its ^{1}H- and ^{13}C-nmr spectral data (Tables 5 and 6) were generally similar to those of the previously isolated furano neocleordane diterpene teugraciline C [**15**] (20), except for the presence of signals for acetoxy and hydroxyl groups at C-3 and C-12, respectively. The ^{1}H-nmr spectrum of **5** contained a signal at δ 4.56 (t, J=3.4 Hz; δ_C 76.46; δ (C_6

[1]Atomic coordinates for compound **10** have been deposited at the Cambridge Crystallographic Data Centre, and can be obtained on request from Dr. Olga Kennard, University Chemical Laboratory, 12 Union Road, Cambridge CB2 1EW, UK.

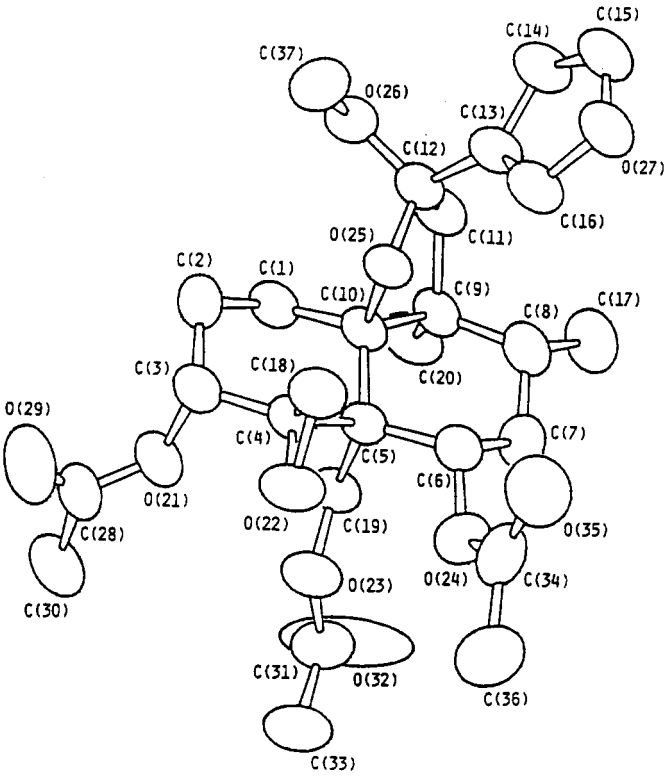


FIGURE 1. Atom numbering scheme and solid-state conformation of 12-*O*-methylteucrolin A [**10**]; hydrogen atoms have been omitted for clarity.

D_6) 4.70, t, J=2.2 Hz) due to an axially disposed 3α-OAc group, as observed for **4**. On acetylation, teucrolin B [**5**] afforded the corresponding triacetate **16** and tetraacetate **17**, with the ^{1}H-nmr spectrum of the latter showing the anticipated deshielding of both H-6 and H-12 to δ 4.75 (ddd, J=1.4, 9.8 Hz) and 5.89 (dd, J=3.3, 7.9 Hz), respectively, versus $\delta_{H\text{-}6}$ 3.66, $\delta_{H\text{-}12}$ 4.79 for **5**, thus confirming the presence of hydroxyl groups at C-6 and C-12 positions in **5**. The ^{13}C-nmr spectrum of the tetraacetate **17** revealed deshielding of C-12 to δ_C 64.65 and shielding of C-13 to δ_C 126.09 (versus $\delta_{C\text{-}12}$ 63.12 and

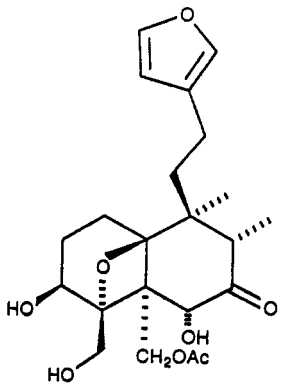


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TABLE 4. Non-hydrogen Atom Fractional Coordinates and Equivalent Isotropic Thermal Parameters for 12-*O*-Methylteucrolin A [**10**], with Estimated Standard Deviations in Parentheses.

Atom	*x*	*y*	*z*	*B*eq(Å^2)
C-1	0.0960 (8)	0.6291 (7)	−0.0160 (1)	6.2 (2)
C-2	−0.0506 (8)	0.5168 (9)	−0.0326 (1)	7.2 (2)
C-3	0.0165 (8)	0.4582 (8)	−0.0517 (1)	6.4 (2)
C-4	0.1272 (7)	0.3830 (7)	−0.0442 (1)	5.3 (1)
C-5	0.2808 (6)	0.5004 (6)	−0.0290 (1)	4.9 (1)
C-6	0.3850 (7)	0.4169 (7)	−0.0206 (1)	5.8 (1)
C-7	0.5156 (8)	0.5224 (9)	−0.0039 (2)	7.0 (2)
C-8	0.4342 (9)	0.5496 (8)	0.0168 (1)	6.9 (2)
C-9	0.3163 (8)	0.6266 (6)	0.0116 (1)	5.8 (1)
C-10	0.1957 (7)	0.5406 (6)	−0.0088 (1)	4.9 (1)
C-11	0.1748 (9)	0.5668 (7)	0.0299 (1)	6.5 (2)
C-12	0.0355 (8)	0.3888 (7)	0.0222 (1)	5.6 (1)
C-13	0.0163 (8)	0.2333 (7)	0.0347 (1)	5.7 (1)
C-14	−0.0377 (10)	0.1920 (8)	0.0571 (1)	7.0 (2)
C-15	−0.0478 (9)	0.0409 (8)	0.0614 (1)	7.6 (2)
C-16	0.0405 (9)	0.1057 (7)	0.0273 (1)	6.7 (2)
C-17	0.5639 (11)	0.6460 (14)	0.0349 (2)	10.3 (3)
C-18	0.0389 (8)	0.1958 (7)	−0.0427 (1)	6.2 (2)
C-19	0.4071 (7)	0.6703 (7)	−0.0406 (1)	5.8 (1)
C-20	0.4152 (11)	0.8289 (8)	0.0106 (1)	8.3 (2)
O-21	0.1150 (7)	0.6014 (6)	−0.0667 (1)	7.8 (1)
O-22	0.1518 (6)	0.2830 (6)	−0.0606 (1)	7.2 (1)
O-23	0.4512 (5)	0.6348 (6)	−0.0619 (1)	7.0 (1)
O-24	0.4649 (5)	0.3792 (5)	−0.0385 (1)	6.9 (1)
O-25	0.0741 (4)	0.3696 (4)	−0.0000 (−)[a]	5.0 (1)
O-26	−0.1259 (5)	0.3913 (4)	0.0234 (1)	6.2 (1)
O-27	0.0050 (6)	−0.0139 (5)	0.0438 (1)	7.2 (1)
C-28	0.0495 (9)	0.5931 (10)	−0.0862 (1)	8.3 (2)
O-29	−0.0883 (9)	0.4890 (10)	−0.0919 (1)	12.4 (2)
C-30	0.1760 (13)	0.7500 (12)	−0.0996 (2)	10.4 (3)
C-31	0.5960 (8)	0.7340 (8)	−0.0704 (1)	7.5 (2)
O-32	0.6948 (10)	0.8632 (11)	−0.0617 (2)	23.9 (3)
C-33	0.6246 (10)	0.6772 (10)	−0.0919 (2)	8.5 (2)
C-34	0.4372 (8)	0.2180 (8)	−0.0412 (2)	7.2 (2)
O-35	0.3507 (8)	0.1014 (6)	−0.0287 (1)	10.5 (2)
C-36	0.5125 (11)	0.1999 (11)	−0.0616 (2)	9.6 (3)
C-37	−0.2746 (9)	0.2295 (8)	0.0168 (2)	7.5 (2)

[a]The *z*-coordinate of O-25 was held constant throughout the analysis to define the space group origin in this direction.

$\delta_{C\text{-}13}$ 130.90 for **5**), in agreement with those previously reported for **15** (20,21), thus formulating the structure of this new diterpene as teucrolin B [**5**].

In addition, three minor diterpenoids **6–8** were isolated (for yield, mp, and specific rotation; see Table 1). One of these, teucrolin C [**6**], was obtained as colorless plates that analyzed for $C_{26}H_{34}O_9$. The ^{1}H- and ^{13}C-nmr spectra of **6** (Tables 5 and 6) were found to be generally similar to those of 6β,12-diacetylteucrolin B [**17**] except for the difference associated with the presence of a ketone at C-12 (ν max 1665 cm^{-1}; δ_C 193.05, s). The ^{1}H-nmr (C_6D_6) spectrum of **6** showed signals at δ 4.57 (t, J=2.2 Hz) for H-3β and at δ 2.32 and 2.18 (each d, J=16.7 Hz) due to the AB system of H_2-11. The ^{1}H-nmr spectrum also revealed the anticipated deshielding of H-14 and H-16 to δ 6.58 and 7.36, respectively (versus $\delta_{H\text{-}14}$ 6.08 and $\delta_{H\text{-}16}$ 7.06 for **5**), due to the presence of the ketone at C-12 (22). The ^{1}H-nmr chemical shift values (in $CDCl_3$) of H-11 and H-14–H-16 for

TABLE 5. ^{1}H-nmr Chemical Shift Values (δ ppm) and Coupling Constants (Hz, in parentheses) for Diterpenes **5**, **6**, **8**, **16**, and **17**.[a]

Proton	Compound					
	5		**6**	**8**	**16**	**17**
	($CDCl_3$)	(C_6D_6)	(C_6D_6)			
H-1	+[b]	+	+	2.08–2.15 m[c] 1.70–1.90 m	+	+
H-2	2.08 m 1.80 m	+	1.96 m	2.10 m[c] 1.88–1.98 m	+	1.82 m
H-3	4.56 t (3.4)	4.70 t (2.2)	4.57 t (2.2)	3.97 dd (5.6,9.2)	4.55 t (2.8)	4.52 t (2.4)
H-6	3.66 ddd (1.4,4.3, 10.1)	3.55 dd (5.6,11.0)	4.98 brdd (4.9,10.9)	4.72 d —	3.60 ddd (1.5,4.5, 9.5)	4.75 ddd (1.3,5.4, 9.8)
H-7	1.50–1.60 m	+	1.50–1.60 m	3.37 q (7.0)	+	1.45–1.55 m
H-8	1.65 m	+	+	+	+	1.62 m
H-11	1.85–1.95 m	+	2.32 d (16.7) 2.18 d (16.7)	2.34 dd (5.8,14.8) 1.45–1.55 m	+	+
H-12	4.79 brd (8.0)	4.35 dd (1.6,7.3)	—	2.90 dd (4.4,13.6)	5.89 dd (3.4,7.2)	5.89 dd (3.3,7.9)
H-14	6.37 d (1.0)	6.08 t (1.2)	6.58 dd (1.0,2.0)	6.26 d (1.0)	6.36 dd (1.0,2.0)	6.37 dd (1.0,2.0)
H-15	7.39 d (1.2)	7.06 t (1.2)	6.84 t (1.6)	7.35 d (1.2)	7.38 m	7.42 d (1.2)
H-16	7.37 brd	7.04 d (1.4)	7.36 t (1.0)	7.20 d (1.0)	7.38 m	7.37 dd (1.4,2.2)
H-17	0.83 d (6.8)	0.53 d (6.6)	0.49 d (6.8)	1.08 d (7.4)	0.79 d (6.8)	0.86 d (6.4)
H_A-18	2.55 d (3.6)[d]	1.99 d (3.8)[d]	1.77 d (3.80)[d]	4.37 d (8.8)	2.53 d (3.6)[d]	2.31 d (3.6)[d]
H_B-18	3.42 brd (3.2)[e]	2.96 d (3.8)[e]	3.05 d (3.8)[e]	3.82 dd (2.0,9.4)	3.31 d (3.2)[e]	3.18 d (3.6)[e]
H_A-19	4.58 d (13.4)	4.81 d (11.4)	4.63 dd (1.6,11.6)	4.16 d (12.4)	4.58 d (13.0)	4.48 brd (10.8)
H_B-19	4.67 d (14.6)	4.92 d (11.0)	4.99 d (11.2)	4.35 d (12.4)	4.70 brd (12.6)	4.92 d (11.8)
H-20	0.75 s	0.46 s	0.49 s	0.74 s	0.75 s	0.78 s
OAc	2.07, 2.04 (2×s)	1.84, 1.83 (2×s)	1.87, 1.83 1.83 (3×s)	2.04 s	2.07, 2.04 2.0 (3×s)	2.09, 2.05 2.0, 1.95 (4×s)
OH			2.80–2.95 brs			

[a]Spectra recorded at 200 MHz.
[b]+ = overlapped signals.
[c]Signals superimposed on each other.
[d]*exo*-Hydrogen with respect to ring B (19).
[e]*endo*-Hydrogen with respect to ring B (19).

6 were also in agreement with those previously reported for the oxidation product **18** of 6,19-diacetylteumassilin (22), thus assigning the structure of this new compound as teucrolin C [**6**].

The second minor diterpenoid teucrolin D [**7**], $C_{22}H_{30}O_9$, gave ^{1}H- and ^{13}C-nmr spectral data (Tables 2 and 3) that were almost indistinguishable from those of teucrolin A [**4**], except for the absence of the signals for the β-substituted furan and deshielded resonance of the spiro carbon. The presence of a C-12(10β)-γ-lactone was inferred from the spectral data [$\delta_{C\text{-}12}$ 173.95 and $\delta_{C\text{-}10}$ 92.33, ν max 1780 cm^{-1} (γ-lactone)]. Furthermore, the ^{1}H-nmr spectrum of **7** showed a signal at δ 4.63 (t, J=3.5 Hz; δ_C 75.39) due to an axial α-OAc group at C-3 like that observed for **4**–**6**. Based on foregoing data and also by comparing the ^{13}C-nmr chemical shift values for previously isolated tetranorneocleordane teucrolivin F [**19**] (6), this minor diterpene was formulated as teucrolin D [**7**]. The relative stereochemistry of teucrolin D depicted in **7** was based on

TABLE 6. ^{13}C-nmr Spectral Data for Diterpenoids **3**, **5**, **6**, **8**, and **17**.[a]

Carbon	Compound				
	3	**5**	**6**[b]	**8**	**17**
C-1	27.06[c]	17.17	17.82	27.18	17.22
C-2	26.92[c]	30.24	30.31	25.80	30.22
C-3	63.35	76.46	76.86	68.72	76.49
C-4	66.56	65.11	63.54	84.08	63.48
C-5	54.72	44.76	45.46	58.24	45.11
C-6	75.44	74.98	73.09	75.02	73.09
C-7	209.0	34.01	33.48	210.87	32.79
C-8	45.29	35.01	35.43	43.79	35.19
C-9	49.83	39.39	40.94	48.28	39.22
C-10	81.81	47.87	47.49	90.10	48.68
C-11	38.98	45.02	45.88	38.68	42.34
C-12	21.79	63.12	193.05	21.08	64.65
C-13	125.14	130.90	129.58	125.32	126.09
C-14	110.60	108.20	108.47	110.63	108.47
C-15	143.13	143.75	146.91	142.67	143.56
C-16	138.53	138.21	144.46	123.83	139.88
C-17	8.10	15.56	15.39	7.71	15.39
C-18	46.42	47.46	47.13	68.63	46.91
C-19	63.73	63.65	62.68	61.75	62.43
C-20	18.22	18.17	17.53	18.60	17.53
-OAc	170.16	170.93	170.22	169.73	170.85
	—	170.04	169.08	—	169.85
	—	—	168.96	—	169.81 (2×C)
	21.0	21.24	21.03	20.77	21.45
		21.20	21.03		21.27
			20.95		21.19
					21.15

[a]All spectra recorded at 50 MHz in $CDCl_3$. Multiplicities of the carbon signals of all compounds were determined by APT and DEPT experiments.

[b]Spectrum recorded in C_6D_6.

[c]Interchangeable signal.

the ^{1}H- and ^{13}C-nmr spectral data as well as biogenetic correlation with teucrolin A [**4**] and related compounds **1** and **19** (5,6).

^{1}H- and ^{13}C-nmr spectral data (Tables 5 and 6) for the remaining minor diterpene, teucrolin E [**8**], were remarkably similar to those of teucrolivin C [**3**] except for the absence of signals associated with the C-4(18)-epoxide group. Instead, **8** was concluded to have a hydroxymethyl group at C-4 (δ 3.82 and 4.37; δ_C 68.63, t) and a C-4(10β) inner oxide group, as suggested by its ^{13}C-nmr spectral data ($\delta_{C\text{-}4}$ 84.08 and $\delta_{C\text{-}10}$ 90.1).

In the course of isolation of the above-mentioned compounds, the 12-*O*-methyl ethers of **1** and **4**, namely, 12-*O*-methylteucrolivin A [**9**] and 12-*O*-methylteuerolin A [**10**], as well as the 12-*O*-ethyl ether of **4**, 12-*O*-ethylteucrolin A [**11**], were also isolated as pure entities. They are apparently artifacts arising from the reaction between the extraction solvents MeOH and EtOH (contained in $CHCl_3$ as a stabilizer) and the respective precursor for each. Confirmation of this fact was obtained by treating **1** and **4** with 95% MeOH to give **9** and **10**, respectively, while **11** was obtained by reacting **4** with 95% EtOH. All products were obtained in excellent yields (see Experimental).

Other natural products isolated from *T. oliverianum* in the course of this work include 24(*S*)-stigmasta-5,22,25-trien-3β-ol, 8-*O*-acetylharpagide, and two flavones eupatorin

and cirsiliol. These compounds were characterized by comparing their physical and spectral data with those reported.

It is noteworthy from a phytochemical point of view that although more than 120 diterpenoids possessing the neoclerodane skeleton have been isolated from *Teucrium* species, teucrolins A [**4**], B [**5**], C [**6**], and D [**7**] are the first to date with a unique 3α-acetyl substituent to be found as natural products. Moreover, 24(*S*)-stigmasta-5,22,25-trien-3β-ol and eupatorin have not been previously reported from *Teucrium* species.

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—Mp's uncorrected; uv cyclohexane (unless otherwise stated), ir KBr. The nmr spectra were taken on Varian instruments at 300 (or 200) MHz (^{1}H) and 75 (or 50) MHz (^{13}C) in $CDCl_3$ (unless otherwise stated) using TMS as internal standard. Multiplicity determinations (APT and DEPT/or DEPTGL) and 2D nmr spectra (COSY and HETCOR) were obtained using standard Varian software. Eims was obtained on a Finnigan 3300 at 70 eV, and cims was recorded using NH_3 as the ionizing gas. Specific rotations were obtained at ambient temperature in C_6H_6, unless otherwise stated, with a Perkin-Elmer 241 MC polarimeter. Tlc was performed on Si gel 60 F254, using petroleum either (bp 60–80°)-EtOAc (1:9) as solvent, with visualization using vanillin/H_2SO_4 spray reagent. Centrifugal preparative tlc (CPtlc, using chromatotron®, Harrison Research Inc. model 7924) was run with either 1-mm or 2-mm Si gel P_{254} disks, using a flow rate of 4 ml/min.

PLANT MATERIAL.—The aerial parts of *T. oliverianum* were collected in Rudhet Khraim, Gassim, Saudi Arabia in April 1990. A voucher specimen was deposited at the harbarium of MAPPRC, College of Pharmacy, King Saud University, Riyadh, Saudi Arabia.

EXTRACTION AND ISOLATION.—The dried ground aerial parts (leaves and stems, 3 kg) were percolated at room temperature with 95% MeOH (3×5 liters), and the extract was evaporated in vacuo to leave 105 g of residue. The crude extract (100 g), dissolved in 95% MeOH, was subjected to solvent partitioning with *n*- hexane (3×5 liters), followed by $CHCl_3$ (3×5 liters), presaturated with each other, to yield 22 g, 12 g, and 63 g in these phases, respectively. The $CHCl_3$ fraction (62 g) was subjected to flash chromatography over Si gel (3.1 kg) and eluted with petroleum ether (bp 60–80°) followed by increasing concentrations of EtOAc in petroleum ether to give seven pure diterpenoids, four other known compounds, and two mixtures (Table 1). Each mixture was subsequently separated by centrifugal preparative tlc (using Si gel P_{254} 2 mm disks as shown in Table 1).

Further, the same material (*T. oliverianum*; 50 g) was extracted by percolation with absolute EtOH and the extract was dried in vacuo (yield 15.5 g). A portion of this extract (10 g) was subjected to solvent partitioning between *n*-hexane and MeCN (yields 2.5 g and 4.5 g, respectively); the latter fraction showed the absence of the artifacts **9–11**, those isolated from the $CHCl_3$ partition of 95% MeOH extract.

Teucrolin A [**4**].—Colorless plates from *n*- hexane/EtOAc: mp and [α]D see Table 1; uv λ max nm 205 (log ε 4.16) 250 sh (log ε 2.6); ir (KBr) ν max cm^{-1} 3420 (OH), 1730 (br, OH), 1500, 1365, 1240 br, 1150, 1070, 1030, 965, 870, 800, 600; ^{1}H nmr see Table 2; ^{13}C nmr see Table 3; cims *m/z* (rel. int.) $[M\cdot NH_4]^+$ 524 ($[C_{26}H_{34}O_{10}\cdot NH_4]^+$) (12), $[M]^+$ 506 ($[M\cdot NH_4-NH_4]^+$) (90), $[M-OH]^+$ 489 (100), $[M-59]^+$ 447 (12), $[489-60]^+$ 429 (48), $[429-60]^+$ 369 (45), $[369-60]^+$ 309 (20), 174 (8), 161 (10), 95 (7).

Teucrolin B [**5**].—Colorless needles from *n*-hexane/EtOAc: mp and [α]D see Table 1; uv λ max nm 200 (log ε 4.08) 265 (log ε 2.45); ir (KBr) ν max cm^{-1} 3390 (OH), 1745 (OAc), 1730 (br, OAc), 1365, 1250 (br), 1145, 1100, 1085, 1030, 1015, 870, 770, 600; ^{1}H nmr see Table 5; ^{13}C nmr see Table 6; cims *m/z* (rel. int.) $[MH]^+$ 451 ($[C_{24}H_{34}O_8\cdot H]^+$) (12), $[MH-60]^+$ 391 (35), $[MH-(60+42)]^+$ 349 (87), $[MH-(2\times60)]^+$ 331 (7), $[331-H_2O]^+$ 313 (50), $[313-H_2O]^+$ 295 (88), 261 (88), 219 (90), 201 (100), 189 (8), 163 (7), 95 (3).

Teucrolin C [**6**].—Colorless plates from *n*-hexane/EtOAc: mp and [α]D see Table 1; uv (EtOH) λ max nm 215 (log ε 4.26), 250 (log ε 3.86); ir (KBr) ν max cm^{-1} 1730 (br, OAc), 1665 (CO), 1550, 1500, 1460, 1365, 1240 (br), 1150, 1080, 1030, 870, 805, 795, 635, 600; ^{1}H nmr see Table 5; ^{13}C nmr see Table 6; ms *m/z* (rel. int.) $[M]^+$ 490 ($C_{26}H_{34}O_9$) (6), $[M-C_6H_5O_2]^+$ 381 (30), $[381-60]^+$ 321 (20), $[381-2\times60]^+$ 261 (45), $[381-3\times60]^+$ 201 (67), 187 (85), 159 (65), 110 (55), 95 (100), 69 (17).

Teucrolin D [**7**].—Powder: mp and [α]D see Table 1; uv λ max nm 200 (log ε 3.88), 225 (sh, log ε 3.62), 275 (log ε 2.85); ir (KBr) ν max cm^{-1} 1780 (lactone), 1730 (OAc), 1460, 1365,1230, 1170, 1040, 1020, 970, 920, 810, 680, 600; ^{1}H nmr see Table 2; ^{13}C nmr see Table 3; ms *m/z* (rel. int.) $[M]^+$ 438 ($C_{22}H_{30}O_9$) (2), 366 (100), $[366-60]^+$ 306 (25), $[366-2\times60]^+$ 245 (45), $[246-59]^+$ 187 (50).

Teucrolin E [**8**].—Colorless plates: mp and [α]D see Table 1; uv λ max nm 205 (log ε 4.22), 275 (br, log ε 2.75); ir (KBr) ν max cm^{-1} 3460 (br, OH), 1740 (br, OAc), 1720 (CO), 1500, 1450, 1390, 1360, 1230 (br), 1150, 1070, 1035, 1015, 905, 870, 770, 600; ^{1}H nmr see Table 5; ^{13}C nmr see Tables 6; cims *m/z* (rel. int.) $[M\cdot NH_4]^+$ 440 ($[C_{22}H_{30}O_8\cdot NH_4]^+$) (100), $[MH]^+$ 423 ($[M\cdot NH_4-NH_3]^+$) (2), $[423-H_2O]^+$ 405 (8), $[423-44]^+$ 379 (30), $[423-59]^+$ 362 (12), $[379-H_2O]^+$ 311 (12), 314 (14), 88 (25), 59 (85).

12-O-Methylteucrolin A [**10**].—Colorless plates from *n*-hexane/EtOAc: mp and [α]D see Table 1; ir (KBr) ν max cm^{-1} 1735 (OAc), 1720 (OAc), 1550, 1420, 1285 (br), 1200, 1150, 1080, 1020, 920, 845, 650; ^{1}H nmr see Table 2; ^{13}C nmr see Table 3; cims *m/z* (rel. int.) $[M\cdot NH_4]^+$ 538 ($[C_{27}H_{56}O_{10}\cdot NH_4]^+$) (10), $[MH]^+$ 521 ($[M\cdot NH_4-NH_3]^+$) (12), $[521-Me]^+$ 506 (7), $[521-OMe]^+$ 489 (90), $[489-60]^+$ 429 (15), $[489-2\times60]^+$ 369 (5), 83 (65), 59 (100).

12-O-Methylteucrolivin A [**9**].—Colorless plates from *n*-hexane/EtOAc: mp and [α]D see Table 1; ir (KBr) ν max cm^{-1} 1740 (OAc), 1730 (OAc), 1715 (-C=O), 1500, 1460, 1390, 1370, 1240 (br), 1150, 1140, 1090, 1030, 960, 860, 795, 600; ^{1}H nmr see Table 2; ^{13}C nmr see Table 3; fabms *m/z* (rel. int.) $[M+H]^+$ 477 ($[C_{25}H_{32}O_9+H]^+$) (25), $[M+H-OMe]^+$ 446 (47), 429 (22), $[446-60]^+$ 386 (10), 343 (10), $[386-60]^+$ 326 (22), 309 (20), 275 (15), 247 (15), 215 (100), 201 (57).

12-O-Ethylteucrolin A [**11**].—Powder: [α]D see Table 1; ir (KBr) ν max cm^{-1} 1730 (br, OAc), 1500, 1460, 1365, 1240 (br), 1160, 1030 (br), 955, 870, 800, 600, ^{1}H nmr see Table 2; ^{13}C nmr see Table 3; cims *m/z* (rel. int.) $[M+H]^+$ 535 ($[C_{28}H_{38}O_{10}+H]^+$) (12), $[535-EtOH]^+$ 489 (75), $[535-60]^+$ 475 (20), $[489-60]^+$ 429 (70), $[429-60]^+$ 369 (78), $[369-60]^+$ 309 (100), 291 (15), 281 (18), 259 (16), 217 (16), 199 (75), 171 (20), 161 (15), 137 (12), 95 (20).

REDUCTION OF COMPOUND **9** WITH $NaBH_4$.—Compound **9** (150 mg) in absolute EtOH (10 ml) was stirred with $NaBH_4$ (75 mg) at room temperature for 1 h. The reaction mixture was acidified with glacial HOAc (0.1 ml), then diluted with H_2O (30 ml) and extracted into Et_2O from which the major product **12** was separated from several minor side products by chromatography [CPtlc, 1 mm Si gel P_{254} disk; solvent EtOAc-CH_2Cl_2 (6:4)] as colorless transparent glass (80 mg): [α]D +7.9° (*c*=0.102, C_6H_6), ir (KBr) ν max cm^{-1} 3440 (OH), 1730 (br, OAc), 1500, 1385, 1360, 1230 (br), 1150, 1065, 1040, 1015, 870, 775, 600; ^{1}H nmr see Table 2; ^{13}C nmr see Table 3; ms *m/z* (rel. int.) $[M]^+$ 478 (1), $[M-OMe]^+$ 447 (75).

ACETYLATION OF COMPOUND **12**.—Compound **12** (40 mg) was dissolved in pyridine and treated with Ac_2O at room temperature for 4 h. Regular workup gave a mixture (38 mg) of compounds **13** and **14**, which was separated on a short Si gel column, using *n*-hexane–EtOAc (75:25) as solvent, to give **13** (7 mg) and **14** (16 mg) as colorless solids.

3-epi-12-O-Methylteucrolin A [**13**].—Solid: [α]D +6.5° (*c*=0.052, C_6H_6); ir (KBr) ν max cm^{-1} 1740 and 1720 sh (OAc), 1500, 1460, 1370, 1350, 1260, 1240, 1160, 1140, 1120, 1080, 1030, 930, 910, 875, 795, 725, 600; ^{1}H nmr see Table 2; ms *m/z* (rel. int.) $[M]^+$ 520 (3), $[M-OMe]^+$ 489 (85).

3-epi-Teucrolin A [**14**].—Solid: [α]D +11.7° (*c*=0.102, C_6H_6); ir (KBr) ν max cm^{-1} 1735 (br, OAc), 1500, 1460, 1380, 1360, 1245 (br), 1155, 1130, 1100, 1070 (br), 1040, 990, 965, 910, 870, 795, 600. ^{1}H nmr see Table 2; ^{13}C nmr see Table 3; ms *m/z* (rel. int.) $[M]^+$ 506 (5), $[M-H_2O]^+$ 488 (35).

METHYLATION OF COMPOUNDS **1** AND **4**.—Compounds **1** and **4** (each 20 mg) were treated separately with 95% MeOH at room temperature for 5 h. The reaction mixtures were dried in vacuo to afford the colorless crystals **9** and **10** (each ca. 18 mg), respectively. The physical (R_f, mp, mmp, and [α]D) and ^{1}H-nmr data of **9** and **10** were indistinguishable from those of 12-*O*-methylteucrolivin A and 12-*O*-methylteucrolin A, respectively.

ACETYLATION OF TEUCROLIN B [**5**].—Compound **5** (40 mg) was acetylated for 24 h, as described above for **12**, to afford a mixture of compounds **16** and **17**. Separation of this mixture (35 mg) by CPtlc [using 1 mm Si gel P_{254} disk, solvent *n*-hexane–EtOAc (88:12)] gave triacetate **16**, as a gum, and tetraacetate **17**, as colorless needles (6 and 16 mg, respectively).

12-Acetylteucrolin B [**16**].—Gum: [α]D −29.5° (*c*=0.05, C_6H_6); ir (KBr) ν max cm^{-1} 3500 (br, OH), 3130, 1735 (br, OAc), 1500, 1440, 1360, 1245 (br), 1160, 1130, 1070, 1010, 950, 855, 810, 750, 665, 600; ^{1}H nmr see Table 5; ms *m/z* (rel. int.) $[M]^+$ 492 (5).

6α,12-Diacetylteucrolin B [**17**].—Needles: mp 163–164°; [α]D −35.8° (*c*=0.086, C_6H_6); ir (KBr) ν max cm^{-1} 3130, 1730 (br, OAc), 1500, 1435, 1370, 1365, 1240 (br), 1150, 1125, 1075, 1060, 1020 (br), 940, 865, 815, 755, 670, 600; ^{1}H nmr see Table 5; ^{13}C nmr see Table 6; ms *m/z* (rel. int.) $[M]^+$ 534 (7).

ETHYLATION OF COMPOUND **4**.—Treatment of compound **4** (20 mg) with absolute EtOH-H_2O (95:5) at room temperature for 6 h afforded **11** as a colorless solid (17 mg). The physical (R_f and [α]D) and spectroscopic data (^{1}H and ^{13}C nmr) of **11** were indistinguishable from those of 12-*O*-ethylteucrolin A.

24(S)-Stigmasta-5,22,25-trien-3β-ol.—Needles from hot *n*-hexane: mp, [α]D, ir, and ^{1}H nmr were indistinguishable from those reported previously (14); ^{13}C nmr (no. of bonded H) 12.02 (3, C-18), 12.12 (3, C-27), 19.37 (3, C-19), 20.20 (3, C-21), 20.78 (3, C-29), 21.04 (2, C-11), 24.29 (2, C-15), 25.67 (2, C-28), 31.61 (2, C-2), 31.86 (2, C-7), 31.86 (1, C-24), 36.47 (0, C-10), 37.23 (2, C-1), 39.64 (2, C-16), 40.17 (1, C-20), 42.22 (2, C-4), 42.26 (0, C-13), 50.11 (1, C-9), 51.96 (1, C-8), 55.84 (1, C-17), 56.81 (1, C-14), 71.74 (1, C-3), 109.49 (2, C-26), 121.64 (1, C-6), 129.99 (1, C-22), 137.16 (1, C-23), 140.72 (0, C-23), 148.56 (0, C-25), hrms *m/z* (rel. int.) $[M]^+$ 410.3503 (20).

8-O-Acetylharpagide.—Plates from MeOH/EtOAc: mp, [α]D, and ^{1}H-nmr data were indistinguishable from those reported previously (11); ^{13}C nmr (CD_3OD, no. of bonded H) 24.11 (3, C-10), 47.63 (2, C-7), 57.08 (1, C-9), 64.45 (2, C-6′), 73.28 (1, C-4′), 74.91 (0, C-5), 76.12 (1, C-2′), 79.24 (1×2c, C-6 and C-5′), 79.74 (1, C-3′), 90.20 (0, C-8), 96.13 (1, C-1), 101.48 (1, C-1′), 108.50 (1, C-4), 145.44 (1, C-3), 174.91, 23.82 (OAc); the mp 184–185° and [α]D −123° (*c*=0.2, $CHCl_3$) of the heptaacetate were indistinguishable from those previously reported [lit. (11) mp 185–189° and $[\alpha]^{22}$D −118° (*c*=0.99, $CHCl_3$)].

X-RAY CRYSTAL STRUCTURE ANALYSIS OF 12-*O*-METHYLTEUCROLIN A [**10**].—Crystal data: $C_{27}H_{36}O_{10}$, MW=520.58, hexagonal, $a=b=8.902(1)$, $c=60.940(5)$ Å (from 25 orientation reflections, $35°<\theta<40°$), V=4182(1) Å^3, Z=6, $D_c=1.240$ g cm^{-3}, μ (CuKα radiation, λ=1.5418 Å)=7.5 cm^{-1}; crystal dimensions 0.23×0.23×0.50 mm.

Preliminary unit-cell parameters and space group information were derived from oscillation and Weissenberg photographs. Intensity data were recorded on an Enraf-Nonius CAD-4 diffractometer [CuKα radiation, graphite monochromator, ω–2θ scans, scan width (0.90+0.14 tan θ)°, θ max=75°; 2881 non-equivalent reflections]. The intensities of four reference reflections, monitored every 2 h during data collection, showed no significant variation (<1% overall). The data were corrected for the usual Lorentz and polarization effects, and those 1675 reflections with $I>3.0\sigma(I)$ were retained for the structure analysis and refinement.

The crystal structure was solved by direct methods (MULTAN11/82). Approximate carbon and oxygen atom coordinates were obtained from an E-map. Positional and thermal parameters (at first isotropic and then anisotropic) of these atoms were adjusted by means of several rounds of full-matrix least squares calculations; hydrogen atoms were incorporated at their calculated positions during the later iterations. The parameter refinement converged (max. shift; ESD=0.04) at $R=\Sigma||F_o|-|F_c||/\Sigma|F_o|=0.056$ $\{R_w=[\Sigma w(|F_o|-|F_c|)^2/\Sigma w|F_o|^2)]^{1/2}=0.083$, $GOF=[\Sigma w(|F_o|-|F_c|)^2/(N_{observations}-N_{parameters})]^{1/2}=1.66\}$. A final difference Fourier synthesis contained no unusual features ($\Delta\rho e/Å^3$: max. 0.25; min. −0.16).

Crystallographic calculations were performed on PDP11/44 and Micro VAX computers by use of the Enraf-Nonius Structure Determination Package (SDP). For all structure-factor calculations, neutral atom scattering factors and their anomalous dispersion corrections were from the literature (23). In the least-squares iterations, $\Sigma w\Delta^2[w=1/\sigma^2(|F_o|), \Delta=(|F_o|-|F_c|)]$ was minimized.

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