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NEW LABDANE DITERPENOIDS FROM *SIDERITIS CHAMAEDRYFOLIA**

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Key Word Index—*Sideritis chamaedryfolia*; Labiatae; new labdane diterpenoids; *ent*-kaurene derivatives.

Abstract—From the aerial parts of *Sideritis chamaedryfolia* six previously known *ent*-kaurene diterpenoids have been isolated. In addition, seven new labdane derivatives have also been obtained from the same source. The structures of these new natural diterpenoids have been established by chemical and spectroscopic means and by correlation with known products.

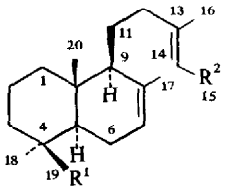
INTRODUCTION

In a previous communication [1] we reported sideridiol (*ent*-7α, 18-dihydroxy-kaur-15-ene) [2] and foliol (*ent*-3β, 7α, 18-trihydroxy-kaur-16-ene) [3] as the major diterpenic constituents of *Sideritis chamaedryfolia*. A study of the minor diterpene constituents of this plant (16% of the total diterpene fraction) has now allowed the isolation of four known substances: siderol (*ent*-7α-acetoxy-18-hydroxy-kaur-15-ene) [2], 7-acetyl-epi-candi candiol (*ent*-7α-acetoxy-18-hydroxy-kaur-16-ene) [4], 7-epicandicandiol (*ent*-7α, 18-dihydroxy-kaur-16-ene) [5] and isofoliol (*ent*-3β, 7α, 18-trihydroxy-kaur-15-ene) [3] plus seven labdane derivatives which are new natural products.

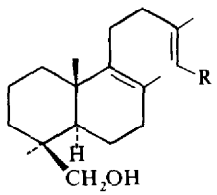
RESULTS AND DISCUSSION

The first of the new diterpenoids (villenol, **1**), $C_{20}H_{34}O_2$ had an IR spectrum which showed hydroxyl and olefinic absorptions and no CO bands. Villenol on acetylation gave a diacetate **2**, thus establishing the hydroxylic nature of the two oxygen atoms. The PMR spectrum of villenol showed signals for two overlapping olefinic protons (δ 5.46, one of which was a triplet, J = 7 Hz), a doublet for an allylic hydroxymethylene (4.18, J = 7 Hz), an AB quartet centered at 3.68 ($J \approx 11$ Hz) assigned to the C-19 axial hydroxymethylene [6], two methyl groups on an olefinic carbon at 1.71, and two methyl singlets at 0.97 and 0.74. All these data suggested structure **1** for villenol, in which the *E* stereochemistry of the side chain double bond was indicated by the chemical shift of the allylic methyl groups [7, 8]. The ^{13}C-NMR spectrum of **1** confirmed this structure with the carbon resonances being in agreement with a labdane skeleton [9, 10] possessing an hydroxyl group at the C-19 axial position (C-18 and C-19 at 26.7 and 64.7 ppm, respectively) [11], a C-7 double bond (C-7, 122.3; C-8 135.4; C-17, 22.2 ppm) and a 13*E* unsaturated side chain with an allylic alcohol at C-15 (C-13, 140.0; C-14, 123.7; C-15, 59.4 and C-16, 16.4 ppm) [12].

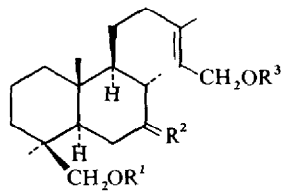
Oxidation of villenol (**1**) with CrO_3 in HMPA [13, 14] gave in 90% yield the α, β-unsaturated aldehyde **3** and a small quantity (~7%) of the dialdehyde **4**. The PMR spectra of compounds **3** and **4** showed a doublet for the C-16 methyl group (δ 2.20, $J \approx 1.5$ Hz) which confirmed the 13*E* stereochemistry of the side chain



	R^1	R^2
(1)	CH_2OH	CH_2OH
(2)	CH_2OAc	CH_2OAc
(3)	CH_2OH	CHO
(4)	CHO	CHO
(5)	CH_2OH	COOH
(6)	CH_2OH	COOMe
(9)	CH_2OAc	CH_2OH



	R
(7)	$COOCH_3$
(8)	CH_2OH



	R^1	R^2	R^3
(10)	H	O	H
(11)	Ac	O	Ac
(12)	Ac	OH, H	Ac
(13)	Ac	H, OH	Ac
(14)	Ac	OTs, H	Ac
(15)	H	H, OH	H
(16)	Ac	O	H

*Part 37 in the series 'Studies on diterpenes from *Sideritis* genus'. For part 36 see Valverde, S. and Rodríguez, B. (1977) *Phytochemistry* **16**, 1841.

double bond [15–17]. In dialdehyde **4** the C-19 proton appeared as a doublet (δ9.98. J = 1 Hz) characteristic of an axial aldehyde on C-4 [18].

NaOH–$AgNO_3$ treatment of hydroxyaldehyde **3** gave the acid **5**, the methyl ester of which (**6**) was subjected to isomerization with I_2 [19] yielding a compound (**7**) identical to a product previously described by Caputo *et al.* [20]. On the other hand, $LiAlH_4$ reduction of **7** or treatment of villenol (**1**) with I_2 in benzene solution [19] afforded the same known product (**8**) [20–22].

These correlations firmly establish the structure and absolute stereochemistry of villenol as 15, 19-dihydroxy-labda-7,13*E*-diene (**1**), except for the stereochemistry at C-9 which by biosynthetic reasons [23] must be 9*S*. However, a spectroscopic proof of this point was obtained in the study of the structure of villenolone (**10**, see below).

A C-19 monoacetate of villenol (**9**) was also present in *S. chamaedryfolia*. The PMR spectrum of this compound was identical with the spectrum of **1**, except for the presence of an additional signal due to the acetyl group (δ2.05, singlet) and the paramagnetic shift showed by the C-19 methylene protons (AB system centered at δ4.17). Treatment of compound **9** with Ac_2O–Py gave a substance identical in all respects to villenol diacetate (**2**).

Another of the new diterpenoids isolated from *S. chamaedryfolia*, villenolone (**10**), had a molecular formula $C_{20}H_{34}O_3$ and possessed a ketone function (ν_{CO} 1703 cm^{-1}). The PMR spectrum (see Experimental) of **10** suggested a structure closely related to villenol (**1**) with an identical side chain and a hydroxyl function on C-19, but lacking the C-7 double bond of villenol, which was substituted by the keto group and a secondary methyl group (δ1.06, 3H, *d*, J = 7 Hz). This structural hypothesis was confirmed by transforming villenolone (**10**) into villenol (**1**). Acetylation of compound **10** gave the diacetate **11** which was treated with $NaBH_4$ to give two C-7 epimeric alcohols (**12** and **13**) whose stereochemistry was established by PMR and by application of Horeau's method [24] (see Experimental). The major β-alcohol (equatorial) (**12**) was treated with tosyl chloride yielding derivative **14**, which by reaction with potassium acetate in DMF and final alkaline hydrolysis gave 60% of the triol **15**, 30% of villenol (**1**) and small quantities of an uncharacterized compound, probably the Δ^6 isomer of **1**.

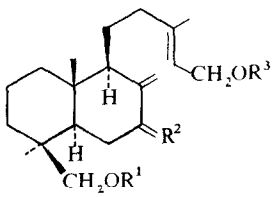
This correlation confirmed the structure **10** for villenolone except for the stereochemistry at C-8, which was established by the following criteria. (i) Compound **10** was recovered unchanged after prolonged treatment with NaOMe, this being indicative of an equatorial orientation of the C-17 methyl group [25]. (ii) By irradiation of the doublet for the C-17 methyl group in the PMR spectrum of compound **11**, a complex signal at δ2.20 collapsed to a doublet (J = 10 Hz), thus establishing a *trans* diaxial relationship between protons C-8 and C-9. This result also confirmed the stereochemistry on C-9 of villenol (**1**). (iii) In the PMR spectrum of compound **13** the C-7 equatorial proton appeared as a narrow multiplet ($W_{\frac{1}{2}}$ = 6 Hz) at δ3.80, whereas the C-7 axial proton of the epimeric compound (**12**) showed a six line signal at δ3.07 with two axial–axial (J = 10 Hz) and one axial-equatorial (J = 4 Hz) coupling-constants, which also confirmed the configuration of the C-17 methyl group as α (and equatorial). (iv) The small negative Cotton effect showed by villenolone (**10**) ($\Delta\varepsilon_{290} = -0.21$) further confirmed this point [25]. Villenolone is thus 15, 19-dihydroxy-8α-labd-13*E*-en-7-one (**10**).

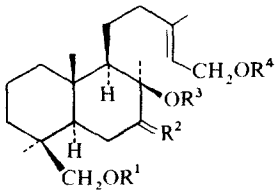
The C-19 acetyl derivative of villenolone (**16**) was also present in *S. chamaedryfolia*. Treatment of **16** with Ac_2O–Py yielded a product identical to **11**. The PMR spectrum of compound **16** confirmed the presence of the acetoxyl group (δ2.07, 3H, singlet) attached to C-19 (AB system centered at δ4.11).

Two new diterpene constituents of this plant were villenatriol (**17**) and its 19-acetyl derivative (**18**). On acetylation both compounds yielded the same triacetate (**19**). The paramagnetic shift ($\Delta\delta$ = +0.42) undergone by the C-19 methylene protons in compound **18** with respect to villenatriol (**17**) confirmed the attachment of the acetoxyl group at C-19.

The IR spectrum of **17** showed hydroxyl and exocyclic methylene absorptions (3340; 3080, 1640, 902 cm^{-1}) and its PMR spectrum presented signals for an exocyclic methylene (δ5.08 and 4.68, *br s*) and a secondary allylic hydroxyl group (δ4.37) axially oriented ($W_{\frac{1}{2}}$ = 6 Hz), besides the characteristic resonances for the C-19 hydroxymethylene function and the side chain previously found in villenol (**1**) and villenolone (**10**).

The base peak at *m/e* 123 in the MS of compounds **17** and **18** suggested a secondary hydroxyl group at the C-7 position [26]. Ac_2O–Py treatment of compound **17** or **18** at 0° for a short time give almost quantitatively the diacetate **20**, which by oxidation with CrO_3 in HMPA yielded an α,β-unsaturated ketone (λ_{max} 229 nm, ε 5.600) (**21**) thus confirming C-7 as the location of the secondary alcohol. Reduction of compound **21** by Huang-Minlon procedure gave in low yield two isomeric products, villenol (**1**) and agathadiol (**22**), previously obtained from agatholic acid [27]. The α configuration of the secondary hydroxyl group of villenatriol was suggested by the PMR signal of its geminal proton [26] (see above) and confirmed by application of Horeau's method [24] to compound **20** (see Experimental). Thus, villenatriol is 7α, 15, 19-trihydroxy-labda-8(17), 13*E*-diene (**17**).





	R¹	R²	R³
(17)	H		H
(18)	Ac		H
(19)	Ac		Ac
(20)	Ac		Ac
(21)	Ac	O	Ac
(22)	H	H_2	H

	R¹	R²	R³	R⁴
(23)	H	O	H	H
(24)	Ac	O	Ac	Ac
(25)	Ac	O	H	Ac
(26)	Ac		Ac	Ac

The last diterpenoid isolated from *S. chamaedryfolia* has been named villenatriolone (**23**) and its molecular formula was $C_{20}H_{34}O_4$. The IR spectrum of this substance showed hydroxyl (3520, 3410, 3360 cm^{-1}) and carbonyl (1703 cm^{-1}) absorptions. Treatment of **23** with Ac_2O–Py gave a triacetyl derivative (**24**) besides minor quantities of a diacetate (**25**) the IR spectrum of which showed residual OH absorption (3480 cm^{-1}). The PMR spectrum of derivative **24** showed signals for an acetylated C-19 hydroxymethylene grouping and for a C-15 acetylated primary allylic alcohol identical in all respect with the signals observed in the diterpenoids previously described. In addition, compound **24** showed a methyl singlet δ 1.44 assigned to a Me group geminal to a tertiary acetoxyl function. The presence of a tertiary hydroxyl group in the molecule of villenatriolone was also supported by the fact that compound **25** was isolated from the acetylation reaction.

When villenatriolone (**23**) was reduced by the Huang–Minlon procedure, only villenol (**1**) arising from a Kishner elimination reaction was obtained. This result firmly established the structure and absolute stereochemistry of compound **23** and located the ketone function on C-7 and the tertiary alcohol on C-8. The β-configuration (axial) of the latter was confirmed as follows: (i) The frequencies of the carbonyl absorptions in the IR spectra of compounds **23** and **10** were identical (1703 cm^{-1}), which suggested a no-coplanar relationship between the CO and OH groups in **23** [28], thus the tertiary alcohol on C-8 must be axial (β). (ii) The carbonyl absorption band in the UV spectrum of villenolone (**10**) appeared at λ 282.5 nm (ε 50) whereas compound **23** showed for the same absorption a maximum at λ 301 nm (ε 41). This bathochromic shift was also indicative of an axial stereochemistry for the tertiary alcohol [29]. (iii) The strong negative Cotton effect ($\Delta\varepsilon_{304} = -2.46$) showed by villenatriolone (**23**) in comparison with the small negative value observed in compound **10** ($\Delta\varepsilon_{290} = -0.21$) further confirmed this point [30, 31]. (iv) The $NaBH_4$ reduction of the triacetate **24** yielded predominantly the 7α-OH epimer (**26**) requiring a favoured attack by the most hindered β side, whereas compound **11** in the same reaction gave mainly the 7β-OH epimer (see above). This difference may be rationalized by the presence of an 8β-acetoxyl substituent in compound **24** [32]. Villenatriolone is thus 8β, 15, 19-trihydroxy-labd-13*E*-en-7-one (**23**).

Sideritis chamaedryfolia is a member of the Labiatae which is endemic at the Iberian Peninsula and grows only in low areas near Villena (Alicante). This plant is the first species of *Sideritis* in which the co-occurrence of diterpenoids with normal and antipodal A/B ring junction have been found.

EXPERIMENTAL

All mps were determined in a Kofler apparatus and are uncorr. The PMR and ^{13}C-NMR spectra were recorded in $CDCl_3$ soln with Me_4Si as an int. stand. Elemental analyses were carried out in this laboratory with the help of an automatic analyzer.

Isolation of the diterpenoids. Dried and finely powdered *S. chamaedryfolia* Cav. plants (10 kg), collected near Villena (Alicante), were extracted for 100 hr with petrol (20 l.) in a Soxhlet. The extract was concd under vacuum to 3 l. and repeatedly extracted with 90% aq. MeOH (6 × 300 ml). The MeOH extract was concd to 1 l., diluted with H_2O (4 l.) and extracted with $CHCl_3$ (6 × 400 ml). The $CHCl_3$ extract was dried, filtered and concd under vacuum to leave a residue (92 g) which was repeatedly chromatographed on Si gel and Si gel plus $AgNO_3$ (12%) columns with C_6H_6 and C_6H_6–EtOAc mixtures as eluents, yielding the following compounds in order of elution. 19-acetylvillenol (**9**, 820 mg), 7-acetyl-epicandicandiol (50 mg) [4], siderol (2.2 g) [2], 19-acetyl-villenolone (**16**, 910 mg), villenol (**1**, 1.15 g), 7-epicandicandiol (250 mg) [5], sideridiol (35 g) [2], 19-acetylvillenatriol (**18**, 780 mg), villenolone (**10**, 1.2 g), villenatriolone (**23**, 170 mg), villenatriol (**17**, 1.37 g), foliol (23.8 g) [3], and isofoliol (2.3 g) [3]. The previously known diterpenoids were identified by their physical (mp, $[\alpha]_D$) and spectroscopic (IR, NMR, MS) data and by comparison with authentic samples.

Villenol (**1**). Mp 106–108° (Me_2CO–*n*-hexane or C_6H_6–*n*-hexane), $[\alpha]_D^{23°}$ + 4.3° (*c* 0.41, $CHCl_3$), +3.7° (*c* 0.83, EtOH). IR ν_{max}^{KBr} cm^{-1}: 3320, 3040, 1665, 1015, 830. PMR: δ5.46 (2H, *m* and *t*, *J* = 7 Hz, H-7 and H-14), 4.18 (2H, *d*, *J* = 7 Hz, 2H-15), 3.68 (2H, AB *q*, *J* = 11 Hz, 2H-19), 1.71 (6H, *br*, *s*, allylic Me C-16 and C-17), C-Me singlets at 0.97 and 0.74 ^{13}C-NMR (assignments were made with the aid of off-resonance and noise-decoupled ^{13}C-NMR spectrum). carbon atom (chemical shift ppm) 1 (39.2)†, 2 (18.5), 3 (38.0)†, 4 (42.1), 5 (54.7), 6 (25.8)¶, 7 (122.3), 8 (135.4), 9 (51.2), 10 (35.3), 11 (23.4)¶, 12 (36.8), 13 (140.0), 14 (123.7), 15 (59.4), 16 (16.4), 17 (22.2), 18 (26.7), 19 (64.7), 20 (14.7) (Assignments marked † or ¶ could be reversed). MS (70 eV, direct inlet) *m/e* (rel.int.): 306 (M^+ 0.2), 288 (0.3), 275 (2.2), 253 (3.1), 220 (90), 205 (14), 202 (20), 187 (28), 132 (42), 109 (98), 81 (100). (Found: C, 78.23; H, 11.09. $C_{20}H_{34}O_2$ requires: C, 78.38; H, 11.18%).

Diacetylvillenol (**2**). Treatment of compound **1** (40 mg) with Ac_2O–Py (0.5–1 ml) as usual gave **2**, a syrup, $[\alpha]_D^{18°}$ −4.8° (*c* 1.33, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 3030, 1735, 1665, 1240, 1035. PMR: δ5.32 (2H, *m* and *t*, *J* = 7 Hz, H-7 and H-14 respectively), 4.56 (2H, *d*, *J* = 7 Hz, 2H-15), 4.12 (2H, AB *q*, *J* = 11 Hz, 2H-19), 2.02 (6H, *s*, two -OAc), 1.70 (6H, *br*. *s*, allylic Me C-16 and C-17), C-Me singlets at 0.94 and 0.77. (Found: C, 73.58; H, 9.92. $C_{24}H_{38}O_4$ requires: C, 73.80; H, 9.81%).

Oxidation of **1**: *compounds* **3** *and* **4**. A soln of **1** (450 mg) in HMPA (1 ml) was added to an stirred soln of CrO_3 (300 mg) in HMPA (3 ml) and left at room temp. for 36 hr. The soln was then diluted with H_2O (20 ml) and extracted with Et_2O. Evapn of the solvent left a residue which was separated by PLC on Si gel plates (C_6H_6–EtOAc, 3:2) into two components, **3** (most polar, 360 mg) and **4** (28 mg).

Hydroxyaldehyde **3**. A syrup, $[\alpha]_D^{21°}$ +6.5° (*c* 0.70, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 3450, 3030, 1665, 1630, 1610, 1030. UV λ_{max}^{EtOH} nm (log ε). 238.5 (4.15). PMR: δ10.08 (1H, *d*, *J* = 8 Hz, H-15), 5.95 (1H, *d*, *J* = 8 Hz, with small allylic coupling, H-14), 5.45 (1H, *m*, $W_{\frac{1}{2}}$ = 8 Hz, H-7), 3.70 (2H, AB *q*, *J* = 11 Hz, 2H-19), 2.20 (3H, *d*, *J* = 1.5 Hz, 3H-16), 1.70 (3H, *br*. *s*, 3H-17) C-Me singlets at 0.98 and 0.76. (Found: C, 78.71; H, 10.43. $C_{20}H_{32}O_2$ requires: C, 78.89; H, 10.59%).

Dialdehyde **4**. A syrup, $[\alpha]_D^{22°}$ −17.0° (*c* 1.00, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 3030, 2730, 1710, 1670, 1625, 1610. PMR: δ10.09 (1H, *d*, *J* = 8 Hz, H-15), 9.98 (1H, *d*, *J* = 1 Hz, H-19), 5.94 (1H, *d*, *J* = 8 Hz, with small allylic coupling, H-14), 5.47 (1H, *m*, $W_{\frac{1}{2}}$ = 9 Hz, H-7), 2.19 (3H, *d*, *J* = 1.5 Hz, 3H-16), 1.70 (3H, *br*. *s*, 3H-17), C-Me singlets at 1.02 and 0.66. MS (70 eV, direct inlet) *m/e* (rel. int.) 302 (M^+ 1.1), 287 (2.3), 218 (50), 200 (19), 190 (12), 119 (100), 109 (88), 81 (96). (Found: C, 79.30; H, 9.89. $C_{20}H_{30}O_2$ requires: C, 79.42; H, 10.00%).

Bis-semicarbazone of **4**. A mixture of **4** (12 mg) and semicarbazide hydrochloride (30 mg) in EtOH (4 ml) was refluxed for 4 hr. After cooling, a crystalline ppt. was collected and crystallized from aq. EtOH: mp 207–210°. IR ν_{max}^{KBr} cm^{-1}: 3470, 3180, 1685, 1575, 1115, 765. (Found: C, 63.61; H, 8.45; N, 19.99. $C_{22}H_{36}O_2N_6$ requires: C, 63.43; H, 8.71; N, 20.18%).

Hydroxy acid **5**. To a vigorously stirred mixture of compound **3** (300 mg) and finely powdered $AgNO_3$ (650 mg) in EtOH (6 ml), a soln of NaOH (360 mg) in EtOH–H_2O (9:1, 10 ml) was added. After 24 hr, the mixture was diluted with H_2O, acidified with 5% aq. H_2SO_4 and extracted with Et_2O. Evapn

of the solvent left a residue (300 mg) which was crystallized from C_6H_6–*n*-hexane, giving pure **5** (260 mg), mp 143–146°, $[\alpha]_D^{22}$ +22.5° (*c* 0.56, $CHCl_3$). IR ν_{max}^{KBr} cm^{-1}: 3420, 3030, 2740, 2650, 2570, 1675, 1635, 1230, 1170, 1020, 865, 705. UV λ_{max}^{EtOH} nm (log ε): 218 (4.09). PMR: δ5.75 (1H, *m*, $W_{\frac{1}{2}}$ = 5 Hz, H-14), 5.43 (1H, *m*, $W_{\frac{1}{2}}$ = 9 Hz, H-7), 3.69 (2H, AB *q*, *J* = 11 Hz, 2H-19), 2.18 (3H, *d*, *J* = 1.5 Hz, 3H-16), 1.70 (3H, *br. s*, 3H-17), C-Me singlets at 0.96 and 0.74. MS (70 eV, direct inlet) *m/e* (rel. int.) 320 (M^+ 0.3), 305 (0.2), 302 (1.2), 289 (4), 220 (22), 202 (4), 109 (100), 81 (71). (Found: C, 74.81; H, 10.11. $C_{20}H_{32}O_3$ requires: C, 74.96; H, 10.06%).

Methyl ester **6**. An Et_2O soln of **5** (200 mg) was treated with CH_2N_2 to give the ester **6** (202 mg), a syrup, $[\alpha]_D^{20}$ +17° (*c* 0.11, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 3450, 1710, 1660, 1610, 1150, 865. PMR δ5.72 (1H, *m*, $W_{\frac{1}{2}}$ = 5 Hz, H-14), 5.43 (1H, *m*, $W_{\frac{1}{2}}$ = 9 Hz, H-7), 3.70 (3H, *s*, —COOMe), 3.67 (2H, AB *q*, *J* = 11 Hz, 2H-19), 2.18 (3H, *d*, J = 1.5 Hz, 3H-16) 1.69 (3H, *br. s*, 3H-17), C-Me singlets at 0.95 and 0.72.

Isomerization of **6** *to* **7**. A C_6H_6 soln (20 ml) of **6** (100 mg) was treated with I_2 (10 mg) under reflux for 12 hr. After cooling, the soln was diluted with C_6H_6 (100 ml) and washed with aq $Na_2S_2O_3$ and H_2O. Evapn of the C_6H_6 and final PLC purification gave **7** (oil, 70 mg), $[\alpha]_D^{22}$ +53.8° (*c* 0.81, $CHCl_3$). PMR. δ5.73 (1H, *m*, $W_{\frac{1}{2}}$ = 4 Hz, H-14). 3.70 (3H, *s*, —COOMe), 3.65 (2H, AB *q*, *J* = 11 Hz, 2H-19), 2.19 (3H, *d*, *J* = 1.5 Hz, 3H-16), 1.58 (3H, *s*, 3H-17), C-Me singlets at 0.97 and 0.92. (Found: C, 75.26; H, 10.09. Calc. for $C_{21}H_{34}O_3$: C, 75.40; 10.25%). Identical in all respects to the described compound [20].

$LiAlH_4$ reduction of **7** *to* **8**. A THF soln of compound **7** (50 mg) was treated with $LiAlH_4$ in the usual manner giving **8**, mp 142–144 (C_6H_6–*n*-hexane), $[\alpha]_D^{20}$ +54.6° (*c* 0.87, $CHCl_3$). IR ν_{max}^{KBr} cm^{-1}: 3500, 3380. PMR: 5.47 (1H, *t*, *J* = 7 Hz, with small allylic coupling, H-14), 4.15 (2H, *d*, *J* = 7 Hz, 2H-15), 3.63 (2H, AB *q*, *J* = 11 Hz, 2H-19), 1.70 (3H, *d*, *J* = 1.5 Hz, 3H-16), 1.64 (3H, *s*, 3H-17), C-Me singlets at 0.98 and 0.93. (Found: C, 78.26; H, 11.06. Calc. for $C_{20}H_{34}O_2$ C, 78.38; H, 11.18%). Identical in all respects with the previously reported compound [20–22].

Isomerization of villenol (**1**) *to* **8**. Isomerization of **1** (100 mg) was carried out under the conditions described for **6**, to give **8** (32 mg, after PLC purification).

19-Acetylvillenol (**9**). Natural diterpenoid **9** is an oil, bp 190° (0.07 mm Hg), n_D^{10} 1.5222, $[\alpha]_D^{20}$ −7.4° (*c* 1.13, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 3400, 3040, 1745, 1240. PMR: δ5.45 (2H, *m*, H-7 and H-14), 4.18 (2H, *d*, *J* = 7 Hz, 2H-15), 4.17 (2H, AB *q*, *J* = 11 Hz, 2H-19), 2.05 (3H, *s*, —OAc), 1.70 (6H, *br. s*, two allylic Me C-16 and C-17), C-Me singlets at 0.95 and 0.78. (Found: C, 75.90; H, 10.37. $C_{22}H_{36}O_3$ requires: C, 75.81; H, 10.41%). Ac_2O–Py treatment of **9** yielded a compound identical to villenol diacetate (**2**).

Villenolone (**10**). Mp 88–91° (spontaneously on cooling), $[\alpha]_D^{18}$ −4.1° (*c* 1.1, $CHCl_3$). IR ν_{max}^{KBr} cm^{-1}: 3360, 1703, 1670, 1035, 1010. UV λ_{max}^{EtOH} nm (ε): 282.5 (50). CD: $\Delta\varepsilon_{265}$ = 0, $\Delta\varepsilon_{290}$ = −0.21, $\Delta\varepsilon_{332}$ = 0 (*c* 0.250, EtOH). PMR δ5.43 (1H, *t*, J = 7 Hz, with small allylic coupling, H-14), 4.16 (2H, *d*, *J* = 7 Hz, 2H-15), 3.64 (2H, AB *q*, *J* = 11 Hz, 2H-19), 1.68 (3H, *br. s*, 3H-16), 1.06 (3H, *d*, *J* = 7 Hz, 3H-17), C-Me singlets at 1.01 and 0.94. MS (70 eV, direct inlet) *m/e* (rel. int.): 322 (M^+ 21), 307 (0.9), 304 (2), 249 (27), 236 (37), 123 (98), 109 (100), 81 (96), 55 (97) (Found: C, 74.30; H, 10.51. $C_{20}H_{34}O_3$ requires C, 74.49; H, 10.63%). Compound **10** was recovered unchanged after treatment with NaOMe–MeOH under reflux for 24 hr (identical mp, $[\alpha]_D$ and NMR spectrum).

Diacetylvillenolone (**11**). Treatment of villenolone (**10**, 900 mg) with Ac_2O–Py in the usual manner gave **11** (900 mg), a syrup, n_D^{19} 1.5027, $[\alpha]_D^{23}$ +5.7 (*c* 0.91, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 3030, 1740, 1710, 1240, 1030. PMR: δ5.38 (1H, *t*, *J* = 7 Hz, with small allylic coupling, H-14), 4.61 (2H, *d*, *J* = 7 Hz, 2H-15), 4.12 (2H, AB *q*, *J* = 11 Hz, 2H-19), 2.06 (6H, *s*, two —OAc), 1.71 (3H, *br. s*, 3H-16), 1.07 (3H, *d*, *J* = 7 Hz, 3H-17), C-Me singlets at 1.06 and 0.96. MS (70 eV, direct inlet) *m/e* (rel. int.) 406 (M^+ 40), 346 (11), 291 (31), 278 (30), 265 (17), 236 (32), 223 (50), 205 (30), 181 (51), 164 (41), 135 (42), 123 (70), 121 (59), 109 (75), 81 (100). (Found: C, 71.08; H, 9.36. $C_{24}H_{38}O_5$ requires: C, 70.90, H, 9.42%).

$NaBH_4$ reduction of **11** *to* **12** *and* **13**. To an EtOH–dioxane (1:1) soln (20 ml) of **11** (700 mg), $NaBH_4$ (350 mg) was slowly added and the mixture kept at room temp. for 2 hr. The reaction products were separated on PLC Si gel ($CHCl_3$–MeOH, 32:1) giving **12** (most polar component, 470 mg) and **13** (145 mg).

Compound **12**. A syrup, n_D^{18} 1.5067, $[\alpha]_D^{24}$ +20.3° (*c* 0.64, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 3460, 3030, 1740, 1240, 1025. PMR: δ5.30 (1H, *t*, *J* = 7 Hz, with small allylic coupling, H-14), 4.54 (2H, *d*, *J* = 7 Hz, 2H-15), 4.04 (2H, AB *q*, *J* = 11 Hz, 2H-19), 3.07 (1H, sextet, $J_{aa'} = J_{aa''}$ = 10 Hz, $J_{ae'}$ = 4 Hz, H-7), 2.01 (6H, *s*, two —OAc), 1.69 (3H, *br. s*, 3H-16), 1.04 (3H, *d*, *J* = 7 Hz, 3H-17), C-Me singlets at 0.95 and 0.83. MS (70 eV, direct inlet) *m/e* (rel. int.) 408 (M^+ 0.4), 393 (0.5), 390 (1.4), 348 (8), 330 (8), 317 (5), 288 (4), 280 (15), 262 (12), 207 (20), 205 (11), 202 (14), 189 (65), 187 (26), 135 (76), 123 (100), 121 (59), 109 (96). Hydrolysis of **12** with 4% ethanolic KOH gave a triol: mp 170–171 (Me_2CO–*n*-hexane), $[\alpha]_D^{23}$ + 22.9° (*c* 0.69, EtOH). IR ν_{max}^{KBr} cm^{-1}: 3350, 1670, 1020. MS (70 eV, direct inlet) *m/e* (rel. int.): 324 (M^+ 0.7), 306 (5), 275 (16), 238 (49), 220 (64), 207 (36), 189 (69), 123 (92), 109 (100), 81 (98). (Found: C, 73.86; H, 11.21. $C_{20}H_{36}O_3$ requires: C, 74.02; H, 11.18%)

Application of Horeau's method [24] *to* **12**. A mixture of (±)-α-phenylbutyric anhydride (0.387 mmol) and **12** (0.123 mmol) in Py soln (2 ml) was kept at room temp for 18 hr. α_1 = +1.312; α_2 = +1.259; $\alpha_1 - 1.1\alpha_2$ = −0.073. Configuration 7*S*

Compound **13**. A syrup, n_D^{18} 1.5074, $[\alpha]_D^{24}$ −3.8° (*c* 0.70, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 3520, 1745, 1240, 1030. PMR: δ5.30 (1H, *t*, *J* = 7 Hz, with small allylic coupling, H-14) 4.55 (2H, *d*, *J* = 7 Hz, 2H-15), 4.03 (2H, AB *q*, *J* = 11 Hz, 2H-19), 3.80 (1H, *m*, $W_{\frac{1}{2}}$ = 6 Hz, equatorial H-7), 2.02 (6H, *s*, two —OAc), 1.68 (3H, *br. s*, 3H-16), 0.98 (3H, *d*, *J* = 7 Hz, 3H-17), C-Me singlets at 0.93 and 0.79. MS (70 eV, direct inlet) *m/e* (rel. int.): 390 (M^+ -18, 0.1), 348 (4), 317 (11), 280 (34), 189 (90), 123 (100), 109 (92). Hydrolysis of **13** with ethanolic KOH gave compound **15** (see below).

Application of Horeau's method to **13**. Performed in the usual manner [24]. **13** (0.042 mmol), (±)-α-phenylbutyric anhydride (0.152 mmol). α_1 = −0.036; α_2 = −0.057, $\alpha - 1.1\alpha_2$ = +0.026. Configuration 7*R*.

Villenol (**1**) *from* **12**. Compound **12** (250 mg) was dissolved in dry Py (3 ml). To this soln, cooled to 0°, was added *p*-toluenesulfonyl chloride (150 mg) and the mixture left at room temp. during 3 days, diluted with H_2O and extracted with $CHCl_3$. Evapn of the solvent left a syrup (236 mg) of compound **14**, which without further characterization, was dissolved in a soln of KOAc (354 mg) in DMF (5 ml) and H_2O (0.5 ml), and heated at 105° for 4 hr. The neutral product isolated then saponified with 4% ethanolic KOH by heating under reflux for 1 hr. The reaction products were separated by PLC on Si gel (C_6H_6–EtOAc, 1:1) yielding villenol (**1**, less polar component, 54 mg, identical in all respects with natural product), an uncharacterized compound (9 mg), and the triol **15** (103 mg, most polar), mp 180–181° (Me_2CO–*n*-hexane), $[\alpha]_D^{24}$ −10.4° (*c* 0.42, EtOH). IR ν_{max}^{KBr} cm^{-1}: 3460, 1680, 1025, 1010. MS (70 eV, direct inlet) *m/e* (rel. int.) 324 (M^+ 0.2), 309 (0.2), 306 (1.2), 275 (11), 238 (32), 220 (24), 207 (23), 189 (41), 123 (100), 109 (74), 55 (94). (Found: C, 73.92; H, 11.11 $C_{20}H_{36}O_3$ requires: C, 74.02; H, 11.18%).

19-Acetylvillenolone (**16**). Natural diterpenoid **16** was an oil, n_D^{12} 1.5194, $[\alpha]_D^{22}$ +5.2° (*c* 0.93, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 3420, 1730, 1705, 1230, 1025. PMR: δ5.43 (1H, *t*, *J* = 7 Hz, with small allylic coupling, H-14), 4.16 (2H, *d*, *J* = 7 Hz, 2H-15), 4.11 (2H, AB *q*, *J* = 11 Hz, 2H-19), 2.07 (3H, *s*, —OAc), 1.69 (3H, *br. s*, 3H-16), 1.07 (3H, *d*, *J* = 7 Hz, 3H-17), C-Me singlets at 1.05 and 0.95 (Found: C, 72.53; H, 9.87. $C_{22}H_{36}O_4$ requires: C, 72.49; H, 9.96%). Ac_2O–Py treatment of **16** yielded a compound identical to **11**.

Villenatriol (**17**). An amorphous solid that softened at 62–65°, $[\alpha]_D^{18}$ −41.2 (*c* 0.62, $CHCl_3$). IR ν_{max}^{KBr} cm^{-1}: 3340,

3080, 1660, 1640, 1020, 902. PMR. δ5.42 (1H, *t*, J = 7 Hz, with small allylic coupling, H-14), 5.08 and 4.68 (1H each, *br. s*, $W_{\frac{1}{2}}$ = 4 Hz, 2H-17), 4.37 (1H, *m*, $W_{\frac{1}{2}}$ = 6 Hz, equatorial H-7), 4.15 (2H, *d*, J = 7 Hz, 2H-15), 3.58 (2H, AB *q*, J = 11 Hz, 2H-19), 1.68 (3H, *br. s*, 3H-16), C-Me singlets at 0.98 and 0.66 (C-18 and C-20, respectively). MS (70 eV, direct inlet) *m/e* (rel. int.): 322 (M^+ 0.4), 307 (1), 304 (3), 291 (2), 289 (3), 286 (4), 273 (16), 259 (7), 255 (17), 236 (5), 187 (28), 153 (42), 151 (50), 123 (100), 109 (57), 107 (45), 81 (80). (Found: C, 74.53; H, 10.51. $C_{20}H_{34}O_3$ requires: C, 74.49; H, 10.63%).

19-Acetylvillenatriol (**18**). A syrup, $n_D^{10°}$ 1.5237, $[\alpha]_D^{20°}$ −30.0° (*c* 1.41, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 3380, 3080, 1735, 1665, 1640, 1245, 1030, 902. PMR. δ5.32 (1H, *t*, J = 7 Hz, with small allylic coupling, H-14), 5.01 and 4.61 (1H each, *br. s*, $W_{\frac{1}{2}}$ = 3 Hz, 2H-17), 4.30 (1H, *m*, $W_{\frac{1}{2}}$ = 6 Hz, H-7), 4.09 (2H, *d*, J = 7 Hz, 2H-15), 4.01 (2H, AB *q*, J = 11 Hz, 2H-19), 2.01 (3H, *s*, —OAc), 1.66 (3H, *br. s*, 3H-16), C-Me singlets at 0.95 and 0.67. MS (70 eV, direct inlet) *m/e* (rel. int.): 364 (M^+ 1.5), 349 (1), 346 (3), 331 (5), 328 (2), 286 (8), 255 (19), 218 (5), 187 (37), 182 (25), 164 (30), 123 (100), 121 (60), 109 (60), 107 (65). (Found: C, 72.36; H, 10.08. $C_{22}H_{36}O_4$ requires. C, 72.49; H, 9.96%).

Villenatriol triacetate (**19**). Ac_2O–Py treatment of villenatriol (**17**) or compound **18** gave the same product (**19**), a syrup, $n_D^{9°}$ 1.5042, $[\alpha]_D^{20°}$ +8.9° (*c* 1.25, $CHCl_3$). IR ν_{max}^{film} cm^{-1}. 3080, 1735, 1640, 1240, 1020, 903. PMR: δ5.36 (1H, *m*, $W_{\frac{1}{2}}$ = 6 Hz, equatorial H-7), 5.26 (1H, *t*, J = 7 Hz, with small allylic coupling, H-14), 5.16 and 4.75 (1H each *br. s*, $W_{\frac{1}{2}}$ = 3 Hz, 2H-17), 4.56 (2H, *d*, J = 7 Hz, 2H-15), 3.99 (2H, AB *q*, J = 11 Hz, 2H-19), 2.03 (6H, *s*, two —OAc), 2.01 (3H, *s*, —OAc), 1.67 (3H, *d*, J = 1 Hz, 3H-16), C-Me singlets at 0.91 and 0.69.

Villenatriol 15,19-diacetate (**20**). Ac_2O (3 ml) was added to a soln of **17** (or **18**) (400 mg) in Py (2 ml) and the mixture kept 1 hr at 0°. It was poured on ice-H_2O and extracted with $CHCl_3$. Vacuum distillation of the solvent left a residue (408 mg) which after PLC on Si gel (C_6H_6–EtOAc, 3:1) yielded 380 mg of **20**, a syrup, $n_D^{10°}$ 1.5143, $[\alpha]_D^{20°}$ −18.1° (*c* 0.61, $CHCl_3$). IR ν_{max}^{film} cm^{-1}. 3480, 3080, 1725, 1660, 1240, 902, 850. PMR. δ5.38 (1H, *t*, J = 7 Hz, with small allylic coupling, H-14), 5.10 and 4.70 (1H each, *br. s*, $W_{\frac{1}{2}}$ = 3 Hz, 2H-17), 4.63 (2H, *d*, J = 7 Hz, 2H-15), 4.39 (1H, *m*, $W_{\frac{1}{2}}$ = 7 Hz, H-7), 4.08 (2H, AB *q*, J = 11 Hz, 2H-19), 2.07 (6H, *s*, two —OAc), 1.71 (3H, *d*, J = 1 Hz, 3H-16), C-Me singlets at 0.98 and 0.69.

Application of Horeau's method to **20**. Performed in the usual manner. [24]. **20** (0.048 mmol), (±)-α-phenylbutyric anhydride (0.123 mmol), Py (2 ml). α_1 = +0.100; α_2 = −0.009; $\alpha_1 - 1.1\alpha_2$ = +0.109. Configuration 7*R*.

Ketone **21**. Oxidation of **20** (300 mg) was carried out with the same conditions described for **1**, to give **21** (260 mg), a syrup, IR ν_{max}^{film} cm^{-1}: 3080, 1730, 1690, 1640, 1605, 1235, 915. UV λ_{max}^{EtOH} nm (log ε). 229 (3.75). PMR: δ5.80 and 5.10 (1H each, *br. s*, $W_{\frac{1}{2}}$ = 3 Hz, 2H-17), 5.30 (1H, *t*, J = 7 Hz, with small allylic coupling, H-14), 4.56 (2H, *d*, J = 7 Hz, 2H-15), 4.05 (2H, AB *q*, J = 11 Hz, 2H-19), 2.02 (6H, *s*, two —OAc), 1.70 (3H, *d*, J = 1 Hz, 3H-16), C-Me singlets at 0.98 and 0.85.

Huang-Minlon reduction of **21** *to give* **1** *and* **22**. Compound **21** (250 mg) was treated under N_2 by the conditions of the Huang-Minlon reaction. The residue of this reaction (80 mg) was separated by PLC on 12% $AgNO_3$–Si gel into two components: **1** (36 mg, most polar, identical in all respects with natural villenol) and **22** (5 mg), mp 109–110° (MeOH), $[\alpha]_D^{22°}$ +31.6° (*c* 0.16, $CHCl_3$). IR ν_{max}^{KBr} cm^{-1}: 3460, 3080, 1640, 895. Agathadiol [20, 27], mp 109–110° $[\alpha]_D$ + 33°.

Villenatriolone (**23**). Mp 159–160° (Me_2CO–*n*-hexane), $[\alpha]_D^{23°}$ −78.6° (*c* 0.66, EtOH). IR ν_{max}^{KBr} cm^{-1}. 3520, 3410, 3360, 3005, 1703, 1680, 1020, 1000, 860. UV λ_{max}^{EtOH} nm (ε): 301 (41). CD: $\Delta\varepsilon_{255}$ = 0; $\Delta\varepsilon_{304}$ = −2.46; $\Delta\varepsilon_{340}$ = 0 (*c* 0.288, EtOH). PMR: δ5.31 (1H, *t*, J = 7 Hz, with small allylic coupling, H-14), 4.09 (2H, *d*, J = 7 Hz, 2H-15), 3.55 (2H, AB *q*, J = 11 Hz, 2H-19), 1.62 (3H, *br. s*, 3H-16), 1.25 (3H, *s*, 3H-17), C-Me singlets at 1.05 and 0.63. MS (70 eV, direct inlet) *m/e* (rel. int.). 338 (M^+ 2), 323 (5), 320 (32), 305 (5), 302 (19), 271 (15), 197 (44), 179 (25), 166 (32), 123 (96), 109 (100). (Found: C, 71.13; H, 10.17. $C_{20}H_{34}O_4$ requires. C, 70.97; H 10.13%).

Acetylation of **23**. Treatment of **23** (100 mg) with Ac_2O–Py at room temp. gave two products which were separated by PLC on Si gel ($CHCl_3$–MeOH, 46:1) into a triacetate (**24**, 80 mg, less polar component) and a diacetyl derivative (**25**, 23 mg). **24** was a syrup, $n_D^{15°}$ 1.4996, $[\alpha]_D^{23°}$ −18.7° (*c* 0.32, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 1735, 1670, 1240, 1025. PMR. δ5.37 (1H, *t*, J = 7 Hz, with small allylic coupling, H-14), 4.62 (2H, *d*, J = 7 Hz, 2H-15), 4.04 (2H, AB *q*, J = 11 Hz, 2H-19), 2.11 (3H, *s*, —OAc), 2.07 (6H, *s*, two —OAc), 1.70 (3H, *br. s*, 3H-16), 1.44 (3H, *s*, 3H-17), C-Me singlets at 1.05 and 0.68. **25** was also a syrup, $[\alpha]_D^{23°}$ −45.4° (*c* 0.11, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 3480, 1730, 1240, 1025. PMR. δ5.28 (1H, *t*, J = 7 Hz, with small allylic coupling, H-14), 4.59 (2H, *d*, J = 7 Hz, 2H-15), 4.06 (2H, AB *q*, J = 11 Hz, 2H-19), 2.08 (6H, *s*, two —OAc), 1.69 (3H, *br. s*, 3H-16), 1.31 (3H, *s*, 3H-17), C-Me singlets at 1.05 and 0.68. (Found: C, 68.31; H, 8.98. $C_{24}H_{38}O_6$ requires: C, 68.22; H, 9.07%).

Villenol (**1**) *from villenatriolone* (**23**). Compound **23** (50 mg) was treated under N_2 by the conditions of the Huang-Minlon reaction yielding only villenol (**1**, 38 mg, identical in all respects with natural compound).

$NaBH_4$ reduction of **24**. $NaBH_4$ reduction of **24** (70 mg) was carried out with the same conditions described for **11**, to give **26** as the major reaction product (51 mg after PLC on Si gel with C_6H_6–EtOAc, 3:1). Compound **26** was a syrup, $[\alpha]_D^{22°}$ −1.6° (*c* 0.64, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 3540, 1745, 1730, 1245, 1030, 800 cm^{-1}. PMR: δ5.40 (1H, *t*, J = 7 Hz, with small allylic coupling, H-14), 4.62 (2H, *d*, J = 7 Hz, 2H-15), 4.08 (2H, AB *q*, J = 11 Hz, 2H-19), 3.87 (1H, *m*, $W_{\frac{1}{2}}$ = 7 Hz, equatorial H-7), 2.05 (6H, *s*, two —OAc), 2.01 (3H, *s*, —OAc), 1.71 (3H, *br. s*, 3H-16), 1.58 (3H, *s*, 3H-17), C-Me singlets at 0.95 and 0.91. (Found: C, 66.81; H, 9.17. $C_{26}H_{42}O_7$ requires. C, 66.92; H, 9.07%).

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REFERENCES

1. Rodríguez, B., Valverde, S., Cuesta, R. and Peña, A. (1975) *Phytochemistry* **14**, 1670.
2. Piozzi, F., Venturella, P., Bellino, A. and Mondelli, R. (1968) *Tetrahedron* **24**, 4073.
3. De Quesada, T. G., Rodríguez, B., Valverde, S. and Huneck, S. (1972) *Tetrahedron Letters* 2187.
4. González, A. G., Fraga, M. B., Hernández, M. G. and Luis, J. G. (1973) *Phytochemistry* **12**, 2721.
5. Piozzi, F., Venturella, P., Bellino, A., Paternostro, M. P., Rodríguez, B. and Valverde, S. (1971) *Chem. Ind. (London)* 962.
6. Gaudemer, A., Polonsky, J. and Wenkert, E. (1964) *Bull. Soc. Chim. France* 407.
7. Bates, R. B. and Gale, D. M. (1960) *J. Am. Chem. Soc.* **82**, 5749.
8. Jefferies, P. R. and Payne, T. G. (1965) *Australian J. Chem.* **18**, 1441.
9. Almqvist, S. O., Enzell, C. R. and Wehrli, F. W. (1975) *Acta Chem. Scand.* **B29**, 695.
10. Buckwalter, B. L., Burfitt, I. R., Nagel, A. A., Wenkert, E. and Náf, F. (1975) *Helv. Chim. Acta* **58**, 1567.
11. Cambie, R. C., Burfitt, I. R., Goodwin, T. E. and Wenkert, E. (1975) *J. Org. Chem.* **40**, 3789.
12. Brouwer, H. and Stothers, J. B. (1972) *Can. J. Chem.* **50**, 1361.
13. Beugelmans, R. (1969) *Bull. Soc. Chim. France* 335.
14. Cardillo, G., Orena, M. and Sandri, S. (1976) *Synthesis* 394.
15. Bory, S., Fétizon, M. and Laszlo, P. (1963) *Bull. Soc. Chim. France* 2310.

16. McCrindle, R. and Nakamura, E. (1974) *Can. J. Chem.* **52**, 2029.
17. McCreadie, T. and Overton, K. H. (1971) *J. Chem. Soc. (C)*312.
18. Fétizon, M., Moreau, G. and Moreau, N. (1968) *Bull. Soc. Chim. France* 3295.
19. Ikekawa, N., Honma, Y., Morisaki, N. and Sakai, K. (1970) *J. Org. Chem.* **35**, 4145.
20. Caputo, R., Mangoni, L., Monaco, P. and Previtera, L. (1974) *Phytochemistry* **13**, 471.
21. Caputo, R., Dovinola, V. and Mangoni, L. (1974) *Phytochemistry* **13**, 475.
22. Marty, R. A. and Carman, R. M. (1969) *Australian J. Chem.* **22**, 491.
23. Hanson, J. R. (1971) *Fortsch. Chem. Org. Naturstoffe* **29**, 395.
24. Horeau, A. and Nouaille, A. (1971) *Tetrahedron Letters* 1939.
25. Grant, P. K., Huntrakul, C. and Weavers, R. T. (1972) *Australian J. Chem.* **25**, 365.
26. Cambie, R. C., Grant, P. K., Huntrakul, C. and Weston, R. J. (1969) *Australian J. Chem.* **22**, 1691.
27. Enzell, C. (1961) *Acta Chem. Scand.* **15**, 1303.
28. Bellamy, L. J. (1964) *The IR Spectra of Complex Molecules* p. 139. Methuen, London.
29. Cookson, R. C. and Dandegaonker, S. H. (1955) *J. Chem. Soc.* 352.
30. Dauben, W. G., Weinstein, B., Lim, P. and Anderson, A. B. (1961) *Tetrahedron* **15**, 217.
31. Djerassi, C., Halpern, O., Schindler, O. and Tamm, C. (1958) *Helv. Chim. Acta* **41**, 250
32 Monson, R. S., Przybycien, D. and Baraze, A. (1970) *J. Org. Chem.* **35**, 1700.