Pergamon 0031-9422(94)00412-9 Phytochemistry, Vol 37, No. 4, pp. 1109–1114, 1994

0031-9422/94 $7.00+0.00

LABDANES FROM *CRYPTOMERIA JAPONICA*

WEN-CHIUNG SU, JIM-MIN FANG and YU-SHIA CHENG*

Department of Chemistry, National Taiwan University, Taipei, Taiwan 106, Republic of China

(*Received* 22 *March* 1994)

Key Word Index—*Cryptomeria japonica*; Taxodiaceae; leaves; diterpenes; labdane-type.

Abstract—Twenty-seven labdanes were isolated from the leaves of *Cryptomeria japonica*. The new compounds include 15-(2-oxopropylidene)labd-8(17)-en-19-oic acid, 15-oxolabda-8(17),13*E*-dien-19-oic acid, 7β-acetoxy-15-hydroxylabda-8(17),13*E*-dien-19-oic acid methyl ester, 14-hydroxy-15-norlabd-8(17)-en-19-oic acid methyl ester, 15-hydroxylabda-8(17),13*Z*-dien-19-oic acid methyl ester, 15,16-epoxylabda-13(16),14-dien-8α,19-diol, 8α-hydroxylabda-13(16),14-dien-19-yl *p*-methoxycinnamate, an ester formed by 15-acetylisocupressic acid and cryptomeridiol and an ether formed by isocupressic acid and cryptomeridiol.

INTRODUCTION

The Japanese cedar, *Cryptomeria japonica* D. Don., is a widely distributed conifer called 'sugi' in Japanese. We recently reported the isolation and structural determination of chamaecydin triterpenes [1] and abietane and kaurane diterpenes [2] from the ethyl acetate-soluble part of the leaves of *C. japonica*. As a continuation of this study, we describe herein 27 constituents of labdane derivatives including nine novel compounds **5**, **19**–**23** and **25**–**27**.

RESULTS AND DISCUSSION

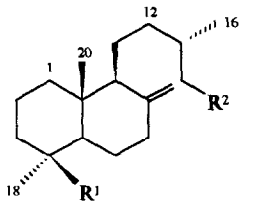
The known diterpenes imbricatolic acid (**1**) [3–5], imbricatolic acid methyl ester (**2**) [4, 5], 15-acetoxyimbricatolic acid (**3**) [5], labd-8(17)-en-15,19-dioic acid dimethyl ester (**4**) [6], 13-epimanool (**6**) [7, 8], 13-epitorulosol (**7**) [7], 19-acetoxy-13*S*-hydroxylabda-8(17),14-diene (**8**) [7], 13-epitorulosal (**9**) [9], 13-epicupressic acid (**10**) [10], agathadiol (**11**) [11, 12], 15-acetylagathadiol (**12**) [11], 19-acetylagathadiol (**13**) [11], 15,19-diacetylagathadiol (**14**) [11], isoagatholal (**15**) [13, 14], 15-acetylisoagatholal (**16**) [13], isocupressic acid (**17**) [15], 15-acetylisocupressic acid (**18**) [16], and 15-acetoxylabda-8,13*E*-dien-19-oic acid (**24**) [16] were identified by comparison of their physical and spectral data (mp, [α], mass, IR, ^{1}H and ^{13}C NMR) with the literature data.

The exact mass measurement of the $[M]^+$ of **5** (*m/z* 360.265) indicated a molecular formula $C_{23}H_{36}O_3$. The ^{13}C NMR signals (Table 1) at δ26.8, 132.4, 147.5 and 198.7 were attributed to an enone moiety C=C–COMe. The corresponding IR and UV absorptions appeared at 1686 cm^{-1} and 225 nm, respectively. In the ^{1}H NMR spectrum (Table 2), the methyl group gave rise to a signal at δ2.21 (*s*) and the two olefinic protons to two signals at δ6.03 and 6.74 with a coupling constant 16 Hz compatible to the *E*-configuration. The structure of **5** was assigned as 15-(2-oxopropylidene)labd-8(17)-en-19-oic acid. This was confirmed by C–H COSY and HMBC experiments. Enone **5** was subjected to ozonization to give aldehyde **5a**. The CD spectrum of **5a** showed a negative Cotton effect with $[\theta]_{min}$ at 292.5 nm, indicating the 13*S*-configuration [17]. Compound **5** is probably an artifact formed by condensation of imbricataloic acid and acetone.

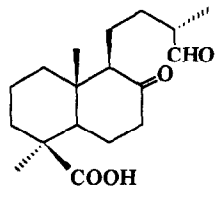
Compound **19** was assigned the molecular formula $C_{20}H_{30}O_3$ ($[M]^+ = m/z$ 318.219). Its ^{1}H NMR spectrum contained a signal for an aldehyde proton at δ9.98 (*d*, J = 8 Hz). Its structure was determined to be 15-oxolabda-8(17),13*E*-dien-19-oic acid by analysis of its NMR spectra (Tables 1 and 2). The *E*-configuration was supported by a 12.3% NOE of the aldehyde proton upon irradiation of Me-13 at δ2.14. The Me-10 occurred at a high field (δ0.58) due to the shielding effect of the carboxyl group at C-4. A related compound, 19-oxolabda-8(17),13*E*-dien-15-oic acid has been found in *Agathis microstachya* [18].

Compound **20** was assigned the molecular formula $C_{23}H_{36}O_5$ ($[M]^+ = m/z$ 392.256). The ^{1}H NMR spectrum showed an acetoxyl group at δ2.13 (*s*), a methoxycarbonyl group at δ3.60 (*s*), a vinyl methyl at δ1.63 (*s*) and two quaternary methyls at δ0.50 (*s*, Me-10) and 1.17 (*s*, Me-4). On the basis of these data and the ^{13}C NMR spectrum, **20** was assigned as 7β-acetoxy-15-hydroxylabda-8(17),13*E*-dien-19-oic acid methyl ester. The acetoxyl group is equatorially oriented as the geminal H-7 gives rise to a signal at δ4.96 as a double doublet (J = 5, 11.5 Hz). It was noted that the acetoxyl substituent caused a down-shift of H-17 ($\Delta\delta \sim 0.2$ ppm) as well as up-shifts of C-8 and C-17 ($\Delta\delta \sim 2.5$ ppm) compared to the corresponding resonances of other labdenes.

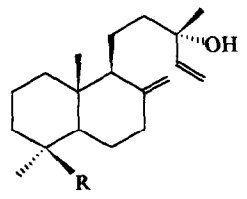
Compound **21** was assigned the molecular formula $C_{20}H_{34}O_3$ ($[M]^+ = m/z$ 332.252). The methoxycarbonyl group was inferred from the IR absorption at 1719 cm^{-1} and the ^{1}H NMR resonance at δ3.57 (*s*). The ^{1}H NMR



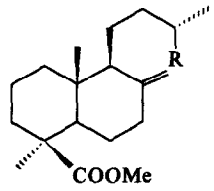
	R^1	R^2
1	COOH	CH_2OH
2	COOMe	CH_2OH
3	COOH	CH_2OAc
4	COOMe	COOMe
5	COOH	$CH\overset{E}{=}CHCOMe$



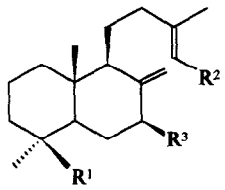
5a



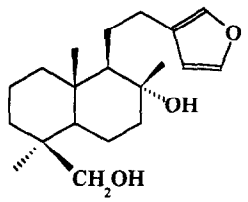
	R
6	Me
7	CH_2OH
8	CH_2OAc
9	CHO
10	COOH



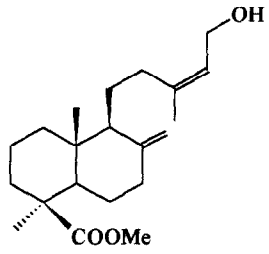
21 R = CH_2OH
21a R = CHO



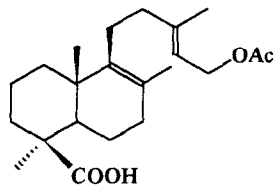
	R^1	R^2	R^3
11	CH_2OH	CH_2OH	H
12	CH_2OH	CH_2OAc	H
13	CH_2OAc	CH_2OH	H
14	CH_2OAc	CH_2OAc	H
15	CHO	CH_2OH	H
16	CHO	CH_2OAc	H
17	COOH	CH_2OH	H
18	COOH	CH_2OAc	H
19	COOH	CHO	H
20	COOMe	CH_2OH	OAc



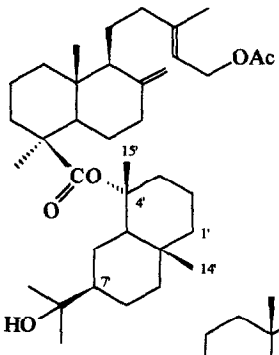
23



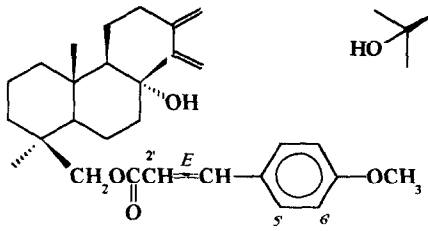
22



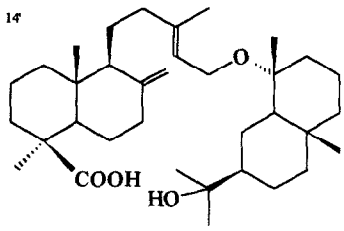
24



26



25



27

spectrum also showed resonances at δ4.46 (*s*) and 4.80 (*s*) for a terminal double bond and at δ3.35 (*dd*, $J=6$, 10.5 Hz) and δ3.48 (*dd*, $J=6$, 10.5 Hz) for two non-equivalent protons geminal to a hydroxyl group. Compound **21** was determined to be a norlabdene, 14-hydroxy-15-norlabd-8(17)-en-19-oic acid methyl ester. The 20 signals in the ^{13}C NMR spectrum were in agreement with this assignment. Oxidation of **21** with pyridinium dichromate (PDC) gave an aldehyde (**21a**), which exhibited a positive Cotton effect with $[\theta]_{max}$ at 292.5 nm attributable to the 13*S*-configuration [17].

Compound **22** was assigned the molecular formula $C_{21}H_{34}O_3$ ($[M]^+ = m/z$ 334.251). The structure 15-hydroxylabda-8(17),13*Z*-dien-19-oic acid methyl ester, was determined from its ^{1}H and ^{13}C NMR spectra. Irradiation of Me-13 caused a 15% NOE of H-14, supporting the assigned *Z*-configuration. The proton resonance of Me-13 appeared at a higher field (δ1.71),

Table 1. ^{13}C NMR spectral data of the new compounds (75 MHz, $CDCl_3$, δ values in ppm)

C	5*	19	20†	21	22	23	25‡	26§	27‖
1	39.1	39.1	38.9	39.2	39.1	40.0	39.5	39.4	39.1
2	19.9	19.9	19.8	20.0	20.0	18.1	18.0	19.6	19.9
3	37.9	37.9	37.5	38.3	38.2	35.7	36.3	38.4	38.0
4	44.1	44.1	44.1	44.3	44.3	38.6	37.1	45.3	44.1
5	56.5	56.1	53.2	56.4	56.3	56.8	56.6	56.3	56.3
6	26.0	26.0	32.2	26.2	26.3	20.9	20.7	26.5	26.1
7	38.7	38.6	75.5	38.8	38.7	45.0	44.6	38.9	38.7
8	148.2	147.5	145.2	148.2	148.1	74.0	74.0	148.1	147.9
9	56.3	56.4	53.5	56.7	55.1	61.5	61.6	55.4	55.6
10	40.5	40.5	39.7	40.3	40.2	39.0	38.8	40.5	40.4
11	21.2	21.4	21.0	21.2	21.9	26.2	24.6	22.1	22.0
12	35.9	39.5	38.1	32.4	30.5	28.0	34.9	38.5	38.6
13	33.3	164.8	139.1	36.4	140.4	125.6	147.2	142.9	138.6
14	39.6	127.2	124.0	68.1	124.7	111.1	138.7	118.1	122.2
15	147.5	191.4	59.4	—	59.1	138.8	115.6	61.4	56.8
16	19.8	17.7	16.0	16.9	23.3	142.7	113.4	16.5	16.5
17	106.3	106.6	103.8	106.3	106.5	23.8	23.8	106.4	106.4
18	29.0	28.9	28.6	28.8	28.8	27.0	27.5	29.1	29.0
19	183.6	182.8	177.3	177.8	177.7	65.5	66.8	175.9	183.2
20	12.7	12.8	12.5	12.5	12.6	16.0	15.9	13.5	12.8
OMe			51.3	51.1	51.1		55.3		

*The resonances for =CH–COMe appeared at δ132.4, 198.7 and 26.8.

†The resonances for OAc appeared at δ170.2 and 21.2.

‡The rest of the resonances appeared at δ114.2 (C-6′, C-8′), 115.6 (C-2′), 127.0 (C-4′), 129.6 (C-5′, C-9′), 144.2 (C-3′), 161.2 (C-7′) and 167.5 (C-1′).

§The rest of the resonances appeared at δ18.5 (C-15′), 19.1 (C-14′), 20.1 (C-2′), 21.8 (C-6′), 22.4 (C-8′), 26.7 (C-12′), 27.9 (C-13′), 34.7 (C-10′), 37.8 (C-3′), 40.5 (C-1′), 44.8 (C-9′), 50.0 (C-7′), 52.7 (C-5′), 72.8 (C-11′), 85.8 (C-4′), 171.1 and 21.1 (OAc).

‖The rest of the resonances appeared at δ19.2 (C-14′), 19.7 (C-15′), 19.8 (C-2′), 21.6 (C-6′), 22.4 (C-8′), 26.9 (C-12′), 27.3 (C-13′), 34.5 (C-10′), 37.2 (C-3′), 40.9 (C-1′), 45.0 (C-9′), 49.7 (C-7′), 50.7 (C-5′), 73.1 (C-11′) and 76.6 (C-4′).

whereas the C-16 resonance occurred at a lower field (δ23.3) compared with the analogue **17** having the 13*E*-configuration.

Compound **23** ($C_{20}H_{32}O_3$) exhibited proton resonances at δ7.33 (*br s*), 7.22 (*br s*) and 6.28 (*br s*) as well as carbon signals at δ111.1, 125.6, 138.8 and 142.7 attributable to a β-substituted furan ring. Three singlets occurring at δ_H1.11, 0.96 and 0.78 were assigned to the methyl groups at C-8, C-4 and C-10, respectively. The structure of **23** was determined to be 15,16-epoxylabda-13(16),14-dien-8α,19-diol. The stereochemistry was established as such by irradiation of Me-10 to cause a 9% NOE of H-19 and a 7% NOE of Me-8.

Compound **25** was determined to be 8α-hydroxylabda-13(16),14-dien-19-yl *p*-methoxycinnamate from its spectroscopic properties. The *p*-hydroxycinnamate analogue has been found in *Juniperus thurifer* leaves [12]. Saponification of **25** gave a diol **25a** and *p*-methoxycinnamic acid (*E*-configuration). The UV absorption at 225 nm and the ^{13}C signals at δ113.5 (*t*), 115.6 (*t*), 138.8 (*d*) and 147.3 (*s*) were consistent with a conjugated diene moiety. Irradiation of Me-10 caused a 9% NOE of H-19 and a 12% NOE of Me-8, supporting the assigned stereochemistry.

Compound **26** ($C_{37}H_{60}O_5$) showed carbon resonances at δ175.9 (*s*) and 171.1 (*s*) attributable to two carboxylate groups. Saponification of **26** gave isocupressic acid (**17**) and cryptomeridiol [19]. The structure of **26** was assigned as an ester formed by 15-acetylisocupressic acid (**18**) linked with the C-4 hydroxyl group of cryptomeridiol. The C-4 resonance in cryptomeridiol occurred at a higher field (δ72.3) than the corresponding resonance in **26** (at δ85.8), whereas values for the resonances of C-11 in both compounds were similar.

By analysis of its spectroscopic properties, **27** ($C_{35}H_{58}O_4$) was determined to be an ether derived from isocupressic acid and cryptomeridiol. The ether linkage was formed between the C-15 of isocupressic acid and the C-4 of cryptomeridiol. The assignment was supported by C–H COSY and HMBC experiments.

In summary, we have isolated 27 labdane derivatives from *C. japonica*. Among them, **26** and **27** are especially noteworthy as their skeletons incorporate both labdane–diterpene and a cryptomeridiol–sesquiterpene.

EXPERIMENTAL

General. Merck silica gel 60F sheets were used for analytical TLC. HPLC was carried out on a Hibar Lichrosorb Si 60 (7 or 10 μm) column (25 × 1 cm).

Table 2. ^{1}H NMR spectral data of the new compounds (300 MHz, $CDCl_3$, δ values in ppm, J values in Hz)

H	5*	19	20†	21	22	23	25‡	26§	27‖
7α			4.96 (*dd*, *J* = 5, 11.5)						
14		5.86 (*d*, *J* = 8)	5.34 (t, *J* = 7)	3.35 (*dd*, *J* = 6, 10.5) 3.48 (*dd*, *J* = 6, 10.5)	5.39 (t, *J* = 7)	6.28 (*br s*)	6.33 (*d*, *J* = 10.5, 17.5)	5.28 (t, *J* = 7)	5.21 (t, *J* = 7)
15	6.74 (*dt*, *J* = 16, 7)	9.98 (*d*, *J* = 8)	4.12 (*d*, *J* = 7)		4.03 (*d*, *J* = 7)	7.33 (*br s*)	5.04 (*d*, *J* = 10.5) 5.28 (*d*, *J* = 17.5)	4.55 (*d*, *J* = 7)	3.80 (*dd*, *J* = 7, 9) 3.87 (*dd*, *J* = 7, 9)
16	0.88 (*d*, *J* = 6.5)	2.14 (s)	1.63 (s)	0.89 (*d*, *J* = 6.5)	1.71 (s)	7.22 (*br s*)	4.99 (*br s*)	1.66 (s)	1.60 (s)
17	4.43 (s)	4.47 (s)	4.63 (s)	4.46 (s)	4.54 (s)	1.11 (s)	1.12 (s)	4.50 (s)	4.49 (s)
	4.80 (s)	4.86 (s)	5.00 (s)	4.80 (s)	4.87 (s)			4.84 (s)	4.81 (s)
18	1.21 (s)	1.22 (s)	1.17 (s)	1.14 (s)	1.15 (s)	0.96 (s)	1.00 (s)	1.12 (s)	1.20 (s)
19						3.43 (*d*, *J* = 10.5) 3.66 (*d*, *J* = 10.5)	3.98 (*d*, *J* = 11) 4.26 (*d*, *J* = 11)		
20	0.56 (s)	0.58 (s)	0.50 (s)	0.46 (s)	0.47 (s)	0.78 (s)	0.81 (s)	0.59 (s)	0.56 (s)
OMe			3.60 (s)	3.57 (s)	3.58 (s)		3.81 (s)		

*The resonances for =CH–COMe appeared at δ6.03 (*d*, *J* = 16) and 2.21 (s).
†The resonance for OAc group appeared at δ2.13 (s).
‡The rest of the resonances appeared at δ6.27 (*d*, *J* = 16, H-2'), 7.59 (*d*, *J* = 16, H-3'), 7.45 (*d*, *J* = 8.5, H-5', 9'), 6.87 (*d*, *J* = 8.5, H-6', 8').
§The rest of the resonances appeared at δ1.17 (s, H-12'), 1.19 (s, H-13'), 0.88 (s, H-14'), 1.35 (s, H-15'), 2.03 (s, OAc).
‖The rest of the resonances appeared at δ1.16 (s, H-12'), 1.17 (s, H-13'), 0.86 (s, H-14'), 1.06 (s, H-15').

Plant material. The plant used in this study was introduced from Japan and is cultivated in the Taipei suburbs. A voucher specimen has been deposited in our laboratory. The leaves (1.4 kg) of *C. japonica* D. Don. were exhaustively extracted with Me_2CO. The Me_2CO extract was passed through a pad of charcoal, concd and re-extracted with EtOAc. The EtOAc-soluble portion (45 g) was chromatographed on a silica gel column by elution with gradient of hexane and EtOAc. The appropriate frs were combined and purified by HPLC to give **14** (15 mg), **4** (20 mg), **6** (45 mg), **16** (22 mg), **21** (26 mg), **22** (9 mg), **2** (40 mg), **8** (10 mg), **3** (10 mg), **18** (20 mg), **26** (9 mg), **24** (10 mg), **20** (15 mg), **1** (15 mg), **9** (12 mg), **10** (75 mg), **7** (20 mg), **27** (20 mg), **12** (15 mg), **17** (25 mg), **25** (50 mg), **5** (30 mg), **19** (8 mg), **13** (11 mg), **15** (15 mg), **11** (15 mg) and **23** (5 mg), in the order of increasing polarity.

Imbricatolic acid (**1**). Oil, $[\alpha]_D^{25}$ +50° ($CHCl_3$; *c* 1.5). ^{13}C NMR ($CDCl_3$, 75 MHz): δ12.7 (C-20), 19.8 (C-2, 16), 21.1 (C-11), 26.0 (C-6), 29.0 (C-18), 30.2 (C-13), 36.4 (C-12), 38.0 (C-3), 38.7 (C-7), 39.1 (C-1), 39.5 (C-14), 40.5 (C-10), 44.1 (C-4), 56.3 (C-5), 56.6 (C-9), 61.2 (C-15), 106.3 (C-17), 148.2 (C-8), 183.3 (C-19).

Imbricatolic acid methyl ester (**2**). Oil, $[\alpha]_D^{20}$ +47° ($CHCl_3$; *c* 3.9). ^{13}C NMR ($CDCl_3$, 75 MHz): δ12.5 (C-20), 19.8 (C-16), 20.0 (C-2), 21.1 (C-11), 26.2 (C-6), 28.8 (C-18), 30.3 (C-13), 36.4 (C-12), 38.3 (C-3), 38.8 (C-7), 39.2 (C-1), 39.6 (C-14), 40.3 (C-10), 44.3 (C-4), 51.1 (MeO), 56.4 (C-5), 56.6 (C-9), 61.1 (C-15), 106.3 (C-17), 148.3 (C-8), 177.8 (C-19).

15-Acetoxyimbricatolic acid (**3**). Oil, $[\alpha]_D^{25}$ +19° ($CHCl_3$; *c* 1). ^{13}C NMR ($CDCl_3$, 75 MHz): δ12.7 (C-20), 19.7 (C-16), 19.9 (C-2), 21.0 (C-11), 26.1 (C-6), 29.0 (C-18), 30.6 (C-13), 35.2 (C-14), 36.1 (C-12), 38.0 (C-3), 38.8 (C-7), 39.2 (C-1), 40.6 (C-10), 44.2 (C-4), 56.4 (C-5), 56.6 (C-9), 63.1 (C-15), 106.4 (C-17), 148.2 (C-8), 183.7 (C-19), 21.2, 171.2 (OAc).

Labd-8(17)-en-15,19-dioic acid dimethyl ester (**4**). Oil, $[\alpha]_D^{20}$ +48° ($CHCl_3$; *c* 1.5). ^{13}C NMR ($CDCl_3$, 75 MHz): δ12.5 (C-20), 20.0 (C-2, 16), 21.2 (C-11), 26.2 (C-6), 28.8 (C-18), 31.1 (C-13), 35.9 (C-12), 38.2 (C-3), 38.8 (C-7), 39.1 (C-1), 40.3 (C-10), 41.4 (C-14), 44.3 (C-4), 51.1 (MeO), 51.3 (MeO), 56.3 (C-5), 56.4 (C-9), 106.3 (C-17), 148.2 (C-8), 173.8 (C-15), 177.8 (C-19).

15-(2-Oxopropylidene)labd-8(17)-en-19-oic acid (**5**). Oil $[\alpha]_D^{30}$ +32° ($CHCl_3$; *c* 2.6). TLC (18% EtOAc in CH_2Cl_2) R_f 0.58. IR ν_{max}^{neat} cm^{-1}: 3072, 3000–2500, 1686, 887; UV λ_{max}^{MeOH} nm (ε): 225 (16 500), 212 (13 800), 208 (14 300); EIMS (70 eV) *m/z* (rel. int.): 360 $[M]^+$ (3), 342 (7), 317 (10), 302 (12), 189 (15), 161 (25), 121 (50), 43 (100); HRMS for $C_{23}H_{36}O_3$ requires 360.2666; found 360.2654.

Ozonization of **5**. A soln of **5** (25 mg) in CH_2Cl_2 (5 ml) was stirred at −78° and bubbled with O_3 for 1 min. Dimethylsulphide (3 ml) was then added and the mixt. stirred at 20° for 2 hr. The mixt. was sepd by HPLC with elution with EtOAc–hexane (3:7) to give ketone **5a** (18 mg), 8,15-dioxo-17-norlabdan-19-oic acid. Oil, $[\alpha]_D^{20}$ −31° ($CHCl_3$; *c* 0.4). TLC (30% EtOAc in hexane) R_f 0.55. IR ν_{max}^{neat} cm^{-1}: 3000–2500, 2729, 1717, 1703, 1694; CD ($CHCl_3$): $[\theta]_{350}$ −20, $[\theta]_{292.5}$ −750, $[\theta]_{230}$ −50; ^{1}H NMR ($CDCl_3$, 300 MHz): δ0.58 (s, H-20), 0.92

(*d*, $J=7$ Hz, H-16), 1.30 (*s*, H-18), 9.72 (*t*, $J=2$ Hz, H-15); ^{13}C NMR ($CDCl_3$, 75 MHz): δ13.2 (C-20), 19.4 (C-11), 19.6 (C-2), 20.1 (C-16), 25.5 (C-6), 28.6 (C-13), 28.9 (C-18), 36.8 (C-12), 37.7 (C-3), 39.4 (C-1), 43.1 (C-7), 43.8 (C-10), 44.2 (C-4), 50.7 (C-14), 55.0 (C-5), 63.6 (C-9), 182.7 (C-19), 203.2 (C-15), 211.4 (C-8); EIMS (70 eV) *m/z* (rel. int.): 322 $[M]^+$ (5), 307 (8), 279 (60), 261 (7), 233 (12), 224 (35), 209 (100). HRMS for $C_{19}H_{30}O_4$ requires 322.2145; found 322.2151.

13-*Epimanool* (**6**). Oil, $[\alpha]_D^{25}$ +51° ($CHCl_3$; *c* 3.2).

13-*Epitorulosol* (**7**). Mp 111–113°. $[\alpha]_D^{25}$ +43° ($CHCl_3$; *c* 2). ^{13}C NMR ($CDCl_3$, 75 MHz): δ15.2 (C-20), 17.8 (C-11), 19.0 (C-2), 24.4 (C-6), 27.1 (C-16), 28.0 (C-18), 35.4 (C-3), 38.6 (C-7), 38.8 (C-4), 39.0 (C-1), 39.7 (C-10), 41.3 (C-12), 56.3 (C-5), 57.3 (C-9), 65.0 (C-19), 73.6 (C-13), 106.6 (C-17), 111.6 (C-15), 145.1 (C-14), 148.2 (C-8).

19-*Acetoxy*-13S-*hydroxylabda*-8(17),14-*diene* (**8**). Oil, $[\alpha]_D^{25}$ +41° ($CHCl_3$; *c* 1). ^{13}C NMR ($CDCl_3$, 75 MHz): δ15.2 (C-20), 17.8 (C-11), 18.9 (C-2), 24.5 (C-6), 27.5 (C-16), 28.1 (C-18), 36.3 (C-3), 37.3 (C-4), 38.5 (C-7), 38.9 (C-1), 39.7 (C-10), 41.3 (C-12), 56.3 (C-5), 57.3 (C-9), 66.8 (C-19), 73.6 (C-13), 106.8 (C-17), 111.7 (C-15), 145.1 (C-14), 147.9 (C-8), 20.9, 171.3 (OAc).

13-*Epitorulosal* (**9**). Oil, $[\alpha]_D^{20}$ +35° ($CHCl_3$; *c* 1). ^{13}C NMR ($CDCl_3$, 75 MHz): δ13.5 (C-20), 17.9 (C-11), 19.2 (C-2), 24.0 (C-6), 24.3 (C-18), 28.1 (C-16), 34.4 (C-1), 38.4 (C-3, 7), 40.2 (C-10), 41.3 (C-12), 48.6 (C-4), 55.8 (C-5), 55.9 (C-9), 73.6 (C-13), 107.3 (C-17), 111.7 (C-15), 145.0 (C-14), 147.5 (C-8), 205.7 (C-19).

13-*Epicupressic acid* (**10**). Oil, $[\alpha]_D^{20}$ +57° ($CHCl_3$; *c* 4.5). ^{13}C NMR ($CDCl_3$, 75 MHz): δ12.7 (C-20), 17.8 (C-11), 19.8 (C-2), 26.0 (C-6), 27.9 (C-16), 28.9 (C-18), 37.9 (C-3), 38.7 (C-7), 39.1 (C-1), 40.6 (C-10), 41.3 (C-12), 44.1 (C-4), 56.3 (C-5), 56.4 (C-9), 73.8 (C-13), 106.5 (C-17), 111.7 (C-15), 144.7 (C-14), 148.0 (C-8), 183.5 (C-19).

Agathadiol (**11**). Mp 106–107°. $[\alpha]_D^{25}$ +30° ($CHCl_3$; *c* 1.5).

15-*Acetylagathadiol* (**12**). Oil, $[\alpha]_D^{25}$ +23° ($CHCl_3$; *c* 1.5). ^{13}C NMR ($CDCl_3$, 75 MHz): δ15.3 (C-20), 16.4 (C-16), 18.9 (C-2), 21.7 (C-11), 24.4 (C-6), 27.0 (C-18), 35.4 (C-3), 38.2 (C-7), 38.6 (C-12), 38.8 (C-4), 39.0 (C-1), 39.5 (C-10), 56.2 (C-5), 56.3 (C-9), 61.4 (C-15), 64.9 (C-19), 106.5 (C-17), 118.0 (C-14), 142.9 (C-13), 147.9 (C-8), 21.0, 171.1 (OAc).

19-*Acetylagathadiol* (**13**). Oil, $[\alpha]_D^{26}$ +19° ($CHCl_3$; *c* 1.1). ^{13}C NMR ($CDCl_3$, 75 MHz): δ15.2 (C-20), 16.3 (C-16), 18.9 (C-2), 21.8 (C-11), 24.4 (C-6), 27.5 (C-18), 36.2 (C-3), 37.3 (C-4), 38.3 (C-7), 38.5 (C-12), 38.9 (C-1), 39.5 (C-10), 56.2 (C-5), 56.3 (C-9), 59.4 (C-15), 66.8 (C-19), 106.7 (C-17), 123.1 (C-14), 140.4 (C-13), 147.8 (C-8), 21.0, 171.3 (OAc).

15,19-*Diacetylagathadiol* (**14**). Oil, $[\alpha]_D^{28}$ +19° ($CHCl_3$; *c* 1). ^{13}C NMR ($CDCl_3$, 75 MHz): δ15.3 (C-20), 16.5 (C-16), 18.9 (C-2), 21.7 (C-11), 24.4 (C-6), 27.5 (C-18), 36.2 (C-3), 37.3 (C-4), 38.3 (C-7), 38.5 (C-12), 38.8 (C-1), 39.5 (C-10), 56.2 (C-5, 9), 61.4 (C-15), 66.8 (C-19), 106.7 (C-17), 118.1 (C-14), 142.9 (C-13), 147.7 (C-8), 21.0, 21.1, 171.1, 171.3 (OAc).

Isoagatholal (**15**). Oil, $[\alpha]_D^{25}$ +19° ($CHCl_3$; *c* 1.5).

15-*Acetylisoagatholal* (**16**). Oil, $[\alpha]_D^{26}$ +22° ($CHCl_3$; *c* 2.2). ^{13}C NMR ($CDCl_3$, 75 MHz): δ13.5 (C-20), 16.5 (C-16), 19.2 (C-2), 21.8 (C-11), 24.0 (C-6), 24.3 (C-18), 34.4 (C-3), 38.2 (C-7), 38.4 (C-1, 12), 40.0 (C-10), 48.6 (C-4), 54.7 (C-5), 56.0 (C-9), 61.3 (C-15), 107.3 (C-17), 118.2 (C-14), 142.6 (C-13), 147.2 (C-8), 205.6 (C-19), 21.0, 171.1 (OAc).

Isocupressic acid (**17**). Mp 117–119°, $[\alpha]_D^{25}$ +42° ($CHCl_3$; *c* 2.5). ^{13}C NMR ($CDCl_3$, 75 MHz): δ12.8 (C-20), 16.3 (C-16), 19.9 (C-2), 21.9 (C-11), 26.0 (C-6), 28.9 (C-18), 37.9 (C-3), 38.4 (C-7), 38.7 (C-12), 39.1 (C-1), 40.4 (C-10), 44.1 (C-4), 55.5 (C-5), 56.3 (C-9), 59.2 (C-15), 106.4 (C-17), 122.8 (C-14), 140.3 (C-13), 147.9 (C-8), 183.2 (C-19).

15-*Acetylisocupressic acid* (**18**). Oil, $[\alpha]_D^{32}$ +34° ($CHCl_3$; *c* 1.5). ^{13}C NMR ($CDCl_3$, 75 MHz): δ12.7 (C-20), 16.4 (C-16), 19.8 (C-2), 21.7 (C-11), 26.0 (C-6), 28.9 (C-18), 37.9 (C-3), 38.3 (C-7), 38.6 (C-12), 39.0 (C-1), 40.3 (C-10), 44.1 (C-4), 55.3 (C-5), 56.3 (C-9), 61.3 (C-15), 106.3 (C-17), 118.0 (C-14), 142.7 (C-13), 147.7 (C-8), 183.5 (C-19), 20.9, 171.1 (OAc).

15-*Oxolabda*-8(17),13E-*dien*-19-*oic acid* (**19**). Oily solid, $[\alpha]_D^{28}$ +47.5° (MeOH; *c* 0.8). TLC (18% EtOAc in CH_2Cl_2) R_f 0.57. IR ν_{max}^{neat} cm^{-1}: 3075, 3000–2500, 1710, 1686, 889; UV λ_{max}^{MeOH} nm (ε): 238 (16400), 217 (11000); EIMS (70 eV) *m/z* (rel. int.): 318 $[M]^+$ (7), 303 (18), 274 (15), 235 (37), 189 (57), 161 (22), 121 (70), 41 (100); HRMS for $C_{20}H_{30}O_3$ requires 318.2196; found 318.2191.

7β-*Acetoxy*-15-*hydroxylabda*-8(17),13E-*dien*-19-*oic acid methyl ester* (**20**). Oil, $[\alpha]_D$ +14° ($CHCl_3$; *c* 0.5). TLC (50% EtOAc in hexane) R_f 0.7. IR ν_{max}^{neat} cm^{-1}: 3446, 1719, 1642, 897; EIMS (70 eV) *m/z* (rel. int.): 392 $[M]^+$ (3), 374 (5), 332 (22), 255 (30), 187 (60), 159 (50), 121 (75), 43 (100); HRMS for $C_{23}H_{36}O_5$ requires 392.2564; found 392.2565.

14-*Hydroxy*-15-*norlabd*-8(17)-*en*-19-*oic acid methyl ester* (**21**). Oil, $[\alpha]_D^{20}$ +50.5° ($CHCl_3$; *c* 2.6). TLC (10% EtOAc in hexane) R_f 0.4. IR ν_{max}^{neat} cm^{-1}: 3391, 3080, 1719, 1637, 1151, 887; EIMS (70 eV) *m/z* (rel. int.): 322 $[M]^+$ (5), 262 (20), 221 (10), 189 (7), 181 (10), 161 (15), 121 (100); HRMS for $C_{20}H_{34}O_3$ requires 322.2509; found 322.2517.

Oxidation of **21**. A soln of **21** (20 mg) in CH_2Cl_2 (5 ml) was stirred with PDC (1.2 equivalent) and a molecular sieve (4 Å) at 20° for 16 hr. The mixt. was filtered and concd to give aldehyde **21a** (19 mg), 14-oxo-15-norlabd-8(17)-en-19-oic acid methyl ester. Oil, $[\alpha]_D^{20}$ +58.5° ($CHCl_3$; *c* 2.0). TLC (10% EtOAc in hexane) R_f 0.6. IR ν_{max}^{neat} cm^{-1}: 3079, 2705, 1718, 1637, 1151, 888; CD ($CHCl_3$): $[\theta]_{340}$ +80, $[\theta]_{292.5}$ +770, $[\theta]_{250}$ +310, $[\theta]_{230}$ +20; ^{1}H NMR ($CDCl_3$, 300 MHz): δ0.45 (*s*, H-20), 1.05 (*d*, $J=7$ Hz, H-16), 1.15 (*s*, H-18), 3.58 (*s*, OMe), 4.47 (*s*, H-17), 4.82 (*s*, H-17), 9.56 (*d*, $J=2$ Hz, H-14); ^{13}C NMR ($CDCl_3$, 75 MHz): δ12.5 (C-20), 13.6 (C-16), 19.9 (C-2), 21.2 (C-11), 26.2 (C-6), 28.8 (C-18), 29.9 (C-12), 38.2 (C-3), 38.7 (C-7), 39.1 (C-1), 40.3 (C-10), 44.3 (C-4), 46.8 (C-13), 51.1 (OMe), 56.3 (C-5), 56.4 (C-9), 106.5 (C-17), 147.8 (C-8), 177.7 (C-19), 205.2 (C-14); EIMS (70 eV): *m/z* (rel. int.) 320 $[M]^+$ (22), 302 (10), 262 (40), 181 (20), 161 (15), 121 (100), 109 (27); HRMS for $C_{20}H_{32}O_3$ requires 320.2352; found 320.2345.

15-*Hydroxylabda*-8(17),13Z-*dien*-19-*oic acid methyl ester* (**22**). Oil, $[\alpha]_D^{20}$ +30° ($CHCl_3$; *c* 0.9). TLC (10% EtOAc in hexane) R_f 0.38. IR ν_{max}^{neat} cm^{-1}: 3397, 3080, 1719, 1636, 1151, 886; EIMS (70 eV) *m/z* (rel. int.): 319 [M

$-Me]^+$ (7), 301 (5), 274 (8), 257 (12), 241 (15), 189 (25), 161 (18), 121 (100); HRMS for $C_{21}H_{34}O_3$ requires 334.2509; found 334.2515.

15,16-*Epoxylabda*-13(16),14-*dien*-8α,19-*diol* (**23**). Crystals from $CHCl_3$–hexane (7:3), Mp 163–164°. $[\alpha]_D^{20}$ +20° ($CHCl_3$; *c* 0.5). TLC (30% EtOAc in hexane) R_f 0.3. IR ν_{max}^{KBr} cm^{-1}: 3360, 885; EIMS (70 eV) *m/z* (rel. int.) 302 $[M-H_2O]^+$ (18), 287 (5), 271 (10), 208 (25), 177 (70), 121 (15), 95 (25), 81 (100); HRMS for $C_{20}H_{32}O_3$ requires 320.2353, 302.2247 $[M-H_2O]^+$, found 302.2250 $[M-H_2O]^+$.

15-*Acetoxylabda*-8,13E-*dien*-19-*oic acid* (**24**). Oil, $[\alpha]_D^{20}$ +110° ($CHCl_3$; *c* 1). ^{13}C NMR ($CDCl_3$, 75 MHz): δ16.5 (C-16), 18.0 (C-20), 19.5 (C-2), 19.7 (C-17), 20.7 (C-6), 26.8 (C-11), 28.6 (C-18), 34.3 (C-7), 37.2 (C-3), 37.5 (C-1), 39.8 (C-10), 40.1 (C-12), 43.7 (C-4), 53.5 (C-5), 61.4 (C-15), 117.7 (C-14), 127.1 (C-8), 138.7 (C-9), 143.0 (C-13), 182.8 (C-19), 21.0, 171.2 (OAc).

8α-*Hydroxylabda*-13(16),14-*dien*-19-*yl* p-*methoxycinnamate* (**25**). Oil, $[\alpha]_D^{28}$ +12° (MeOH; *c* 5.0). TLC (18% EtOAc in CH_2Cl_2) R_f 0.6. IR ν_{max}^{neat} cm^{-1}: 3483, 3077, 1698, 1627, 1600, 1570, 984, 907; UV λ_{max}^{MeOH} nm (ε): 393 (410), 369 (350), 309 (27 200), 249 (2100), 225 (31 600); EIMS (70 eV) *m/z* (rel. int.): 466 $[M]^+$ (27), 448 (10), 288 (8), 189 (21), 178 (15), 161 (100), 133 (13); HRMS for $C_{30}H_{42}O_4$ requires 466.3085; found 466.3089.

Saponification of **25**. A soln of **25** (50 mg) in EtOH (5 ml) was treated with 10% KOH–EtOH (2 ml) at 20° for 16 hr. The mixt. was extracted with Et_2O. The organic phase was concd to give **25a** (27 mg), labda-13(16),14-diene-8,19-diol. The aq. phase was acidified with 1 N HCl, extracted with Et_2O and concd to give *p*-methoxycinnamic acid (14 mg), mp 173–174°. **25a**: needles from $CHCl_3$–hexane (7:3), mp 117–118°. $[\alpha]_D$ +25° ($CHCl_3$; *c* 1.0). TLC (30% EtOAc in hexane) R_f 0.33. IR ν_{max}^{KBr} cm^{-1}: 3335, 1587; UV λ_{max}^{MeOH} nm (ε): 225 (31 000); ^1H NMR ($CDCl_3$, 300 MHz): δ0.77 (*s*, H-20), 0.96 (*s*, H-18), 1.12 (*s*, H-17), 3.43 (*d*, *J* = 10.5 Hz, H-19), 3.66 (*d*, *J* = 10.5 Hz, H-19), 4.99 (*br s*, H-16), 5.04 (*d*, *J* = 10.5 Hz, H-15), 5.28 (*d*, *J* = 18 Hz, H-15), 6.33 (*dd*, *J* = 10.5, 18 Hz, H-14); ^{13}C NMR ($CDCl_3$, 75 MHz): δ16.0 (C-20), 18.1 (C-2), 20.8 (C-6), 23.9 (C-17), 24.7 (C-11), 26.9 (C-18), 35.0 (C-12), 35.6 (C-3), 38.5 (C-4), 39.0 (C-10), 39.8 (C-1), 44.9 (C-7), 56.7 (C-5), 61.8 (C-9), 65.3 (C-19), 74.1 (C-8), 113.5 (C-16), 115.6 (C-15), 138.8 (C-14), 147.3 (C-13); EIMS (70 eV) *m/z* (rel. int.): 288 $[M-H_2O]^+$ (5), 275 (25), 257 (30), 207 (31), 177 (40), 153 (15), 121 (35), 43 (100); HRMS for $C_{20}H_{34}O_2$ requires 306.2560; found 306.2551.

Cryptomeridiol-4-*yl*-19-*acetoxylabda*-8(17), 13E-*dien*-19-*oate* (**26**). Oil, $[\alpha]_D^{25}$ +14.5° ($CHCl_3$; *c* 0.9). TLC (10% EtOAc in hexane) R_f 0.2. IR ν_{max}^{neat} cm^{-1} 3455, 1735, 1705, 885; MS (FAB) *m/z* (rel. int.): 584 $[M]^+$ (1), 525 (1), 507 (1), 360 (2), 303 (27), 257 (23), 205 (100); HRMS for $C_{37}H_{60}O_5$ requires 584.4443; found 584.4435.

Saponification of **26** (9 mg) by a procedure similar to that for **25** gave isocupressic acid (5 mg) and cryptomeridiol (4 mg).

An ether from cryptomeridiol and isocupressic acid (**27**). Oil, $[\alpha]_D^{25}$ +20° ($CHCl_3$; *c* 1.9). TLC (10% EtOAc in CH_2Cl_2) R_f 0.29. IR ν_{max}^{neat} cm^{-1}: 3406, 3000–2500, 1687, 1637, 888; EIMS (70 eV) *m/z* (rel. int.): 542 $[M]^+$ (11), 302 (40), 287 (24), 257 (35), 205 (100), 189 (30), 149 (50), 123 (87); HRMS for $C_{35}H_{58}O_4$ requires 542.4337; found 542.4347.

Acknowledgment—We are grateful to the National Science Council for financial support (Grant NSC83-0208-M002-095).

REFERENCES

1. Su, W.-C., Fang, J.-M. and Cheng, Y.-S. (1993) *Phytochemistry* **34**, 779.
2. Su, W.-C., Fang, J.-M. and Cheng, Y.-S. (1994) *Phytochemistry*, **35**, 1279.
3. Spalding, B. P., Zinkel, D. F. and Roberts, D. R. (1971) *Phytochemistry* **10**, 3289.
4. Teresa, J. D. P., San Feliciano, A. and Mignel del Corral, M. J. (1974) *An. Quim.* **70**, 1015.
5. Weissmann, G., Bruns, K. and Gruetzmacher, H. Fr. (1965) *Tetrahedron Letters* 4623.
6. Calderon, J. S., Quijano, L., Gomez-Garibay, F., Moran, M. and Rios, T. (1987) *Phytochemistry* **26**, 2639.
7. Manning, T. D. R. (1973) *Aust. J. Chem.* **26**, 2735.
8. Bruns, K. (1970) *Tetrahedron Letters* 3263.
9. Caputo, R., Mangoni, L., Monaco, P. and Previtera, L. (1974) *Phytochemistry* **13**, 471.
10. Carman, R. M., Craig, W. G. and Shaw, I. M. (1973) *Aust. J. Chem.* **26**, 209.
11. Rowe, J. W. and Shaffer, G. W. (1965) *Tetrahedron Letters* 2633.
12. San Feliciano, A., Medarde, M., Lopez, J. L., Miguel del Corral, J. M., Puebla, P. and Barrero, A. F. (1988) *Phytochemistry* **27**, 2241.
13. Raldugin, V. A. and Pentegova, V. A. (1971) *Khim. Prir. Soedin.* 595.
14. Hasegawa, S. and Hirose, Y. (1980) *Phytochemistry* **19**, 2479.
15. Fang, J.-M., Lang, C.-I., Chen, W.-L. and Cheng, Y.-S. (1991) *Phytochemistry* **30**, 2793.
16. Caputo, R., Dovinola, V. and Mongoni, L. (1974) *Phytochemistry* **13**, 475.
17. Djerassi, C. and Geller, L. E. (1959) *J. Am. Chem. Soc.* **81**, 2789.
18. Carman, R. M. and Marty, R. A. (1968) *Aust. J. Chem.* **21**, 1923.
19. Evans, F. E., Miller, D. W., Cairns, T., Baddeley, G. V. and Wenkert, E. (1982) *Phytochemistry* **21**, 937.