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10-DESMETHYL-1-METHYL-EUDESMANES FROM *OCOTEA CORYMBOSA**

JUCENI PEREIRA CHAVEZ,† OTTO R. GOTTLIEB‡ and MASSAYOSHI YOSHIDA§

Instituto de Química, Universidade de São Paulo, 05508-900 São Paulo, SP, Brazil

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Key Word Index—*Ocotea corymbosa*; Lauraceae; fruits; rearranged eudesmanes; sesquiterpenoids; *p*-menthanes; monoterpenoids.

Abstract—Unripe fruits of *Ocotea corymbosa* contain the known monoterpenes carvacrol and *cis*-3-hydroxy-*p*-menth-1-en-6-one, besides three novel rearranged sesquiterpenes possessing the apparently rare carbon skeleton of 10-desmethyl-1-methyl-eudesmane.

INTRODUCTION

The tropical South American genus *Ocotea* is well known as a source of shikimate-derived aromatics such as benzylisoquinoline alkaloids and neolignans. Even its essential oils have been found to contain mostly phenylpropanoid derivatives. The search for terpenoid constituents has so far provided comparatively modest results. The present paper describes the isolation from unripe fruits of *O. corymbosa* (Meissn.) Mez of three novel sesquiterpenoids, either possessing (**1**, **2**) or derived from (**3**) the apparently rare carbon skeleton of occidol, rishitinol and the emmotins [2]. The same source yielded additionally two known *p*-menthane monoterpenoids, carvacrol and *cis*-3-hydroxy-*p*-menth-1-en-6-one [3], as well as the ubiquitous sitosterol and stigmasterol.

RESULTS

The molecular formulae, $C_{15}H_{26}O$ (**1**), $C_{15}H_{24}O_2$ (**2**) and $C_{15}H_{24}O_2$ (**3**), as well as the ^{13}C and ^1H NMR spectra (Tables 1 and 2), revealed the close structural relationship of all three compounds, and indicated that most probably they were sesquiterpenes with two methyl groups and one isopropenyl group each. The oxygen atoms were easily assigned to a tertiary hydroxyl in **1**, a tertiary hydroxyl and a carbonyl in **2** and two carbonyls in **3**. Hence, while **1** and **2** were bicyclic, **3** had a monocyclic system. The NMR spectral assignments (Tables 1 and 2), achieved by short and long range ^1H–^{13}C correlations, led to substructures A, B and C for **1**, D, E and F for **2**, and G, H and I for **3**.

The relative placements of the substructures as shown in formula **1** were deduced by interpretation of the spectra obtained in the presence of the lanthanide reagent Eu(fod)$_3$. The induced ^1H NMR spectral shifts allowed not only some proton couplings to be measured accurately, but also many ^1H–^1H correlations to be observed (Table 1). Such data provided evidence for the connections of substructure A through its terminal C-2 to C-3 of substructure B and through its terminal C-10 (via CH_2-9) to C-8 of substructure C. This left only two possibilities for the insertion of the remaining CH_2-6, either between C-5 and C-7 (as shown in **1**) or between C-5 and C-10. The latter alternative could be discarded. Thus H-10 was represented by a *ddd*, the coupling constants (J = 9.2, 8.4, 3.5 Hz) revealing two axial–axial and one axial–equatorial relationships. Hence H-10 was axial and must be flanked by a methylene (at position 9) and an axial methine (at position 5). Proton couplings were also helpful in the definition of other conformational features. Thus, H-2_{eq} was represented by a *dddd* (J = 13.0, 3.5, 2.5, 2.5 Hz) in contrast to H-2_{ax} which was represented by a *ddd* (J = 13.0, 9.0, 3.5). The additional small coupling of the former was evidence for a *W*-interaction with the, hence equally equatorial, H-4. The eudesmanes **4** (δ150.5, C-11; 108.2, C-12 [4]), with an equatorial isopropenyl, and **5** (δ146.8, C-11, 110.7, C-12 [5]), with an axial isopropenyl, are close structural analogues of compound **1**. Hence it was highly probable that the orientation of the isopropenyl in **1** (δ152.3, C-11; 107.1, C-12) was again equatorial. Finally the chirality at C-1 was established by interpretation of the Eu(fod)$_3$ induced proton signal shifts. These shifts were stronger for H-5_{ax} (1.1 ppm), H-7_{ax} (1.0 ppm) and H-9_{ax} (1.5 ppm), than for H-4_{eq}

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†Present address: Faculdade de Fármacia, Universidade Federal da Bahia, Salvador, BA, Brazil.

‡Present address: Departamento de Fisiologia e Farmacodinâmica, Instituto Oswaldo Cruz, FIOCRUZ, Rio de Janeiro, RJ, Brazil.

§Author to whom correspondence should be addressed.

Table 1. NMR spectral data of compound **1**

	1			**1** (30 mg)/Eu (fod)$_3$ (8 mg)		
Atom	^{13}C	^{1}H	*J* (Hz)	^{13}C	^{1}H	*J* (Hz)
1	74.7	—		81.2	—	
2	36.1	1.57 *m*		38.8	3.50 *ddd*	13.0, 9.0, 3.5
		1.88 *m*			3.70 *dddd*	13.0, 3.5, 2.5, 2.5
3	31.0	1.30 *m*		31.8	2.20 *m*	
		1.60 *m*			2.80 *m*	
4	38.8	1.97 *m*		39.4	2.40 *m*	
5	45.7	1.97 *m*		47.4	3.05 *m*	
6	28.5	1.16 *m*		29.6	2.08 *m*	
		1.36 *m*			2.08 *m*	
7	46.0	2.19 *m*		46.6	3.15 *m*	
8	28.5	1.79 *m*		29.7	2.08 *m*	
9	26.1	1.46 *m*		27.4	2.95 *m*	
		1.71 *m*			2.95 *m*	
10	55.4	2.11 *m*		56.8	4.38 *ddd*	9.2, 8.4, 3.5
11	152.3	—		152.7	—	
12	107.7	4.58 *dq*	2.0, 1.4	108.0	4.76 *dq*	2.0, 1.4
		4.66 *dq*	2.0, 0.7		4.92 *dq*	2.0, 0.7
13	19.8	1.65 *br s*		20.1	1.94 *s*	
14	29.6	1.14 *s*		31.9	3.09 *s*	
15	16.0	0.83 *s*	6.5	16.4	1.26 *d*	6.9

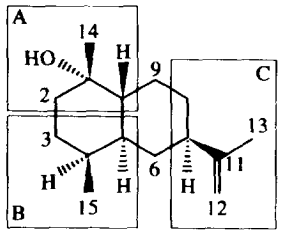
^{1}H–^{13}C HETCOR (*J* = 10 Hz). 1—H-7: 28.5 (C-8), 107.7 (C-12), 152.2 (C-11); H-12: 19.8 (C-13), 46.0 (C-7), 152.3 (C-11); H-13: 46.0 (C-7), 107.7 (C-12), 152.3 (C-11); H-14: 36.1 (C-2), 55.4 (C-10), 74.4 (C-1); H-15: 31.0 (C-3), 38.8 (C-4), 45.7 (C-5).

^{1}H–^{1}H COSY. H-13: 4.58 (H-12), 4.66 (H-12); H-15: 1.97 (H-4). 1[+ Eu(fod)$_3$] H-2$_{ax}$: 2.20 (H-3$_{ax}$), 2.80 (H-3$_{eq}$), 3.70 (H-2$_{eq}$); H-2$_{eq}$: 2.20 (H-3$_{ax}$), 2.80 (H-3$_{eq}$); H-3$_{ax}$: 3.50 (H-2$_{ax}$); H-3$_{eq}$: 3.70 (H-2$_{eq}$); H-8: 2.95 (H-9); H-9: 4.38 (H-10); H-13: 4.76 (H-12), 4.92 (H-12); H-15: 2.40 (H-4).

Table 2. NMR spectral data of compounds **2** and **3**

	2			**3**		
Atom	^{13}C	^{1}H	*J* (Hz)	^{13}C	^{1}H	*J* (Hz)
1	38.5	1.85		208.7	—	
2	32.3	2.36 *m*		41.2	2.30 *m*	
		2.54 *m*				
3	214.3	—		29.2	1.30 *m*	
4	40.1	2.52 *m*		38.5	1.80 *m*	
5	58.3	2.44 *m*		54.1	1.60 *m*	
6	24.9	1.45 *m*		32.7	1.58 *m*	
		1.80 *m*			1.80 *m*	
7	48.8	2.49 *m*		44.7	2.15 *m*	
8	29.4	1.45 *m*		26.7	1.30 *m*	
		1.80 *m*			1.55 *m*	
9	30.8	1.74 *m*		37.4	2.15 *m*	
		1.86 *m*			2.25 m	
10	78.3	—		220.9	—	
11	145.9	—		146.5	—	
12	111.9	4.59 *dq*	2.9, 1.4	113.4	4.67 *dq*	2.3, 1.6
		4.65 *dq*	2.9, 0.6		4.78 *dq*	2.0, 0.9
13	17.7	1.64 *br s*		17.2	1.57 *br s*	
14	13.3	1.01 *d*	7.3	29.9	2.09 *s*	
15	14.3	0.95 *d*	6.4	20.1	1.12 *d*	6.5

^{1}H–^{13}C HETCOR (*J* = 10 Hz). 2—H-13: 48.8 (C-7), 111.9 (C-12), 145.9 (C-11), 4.61 (C-12); H-14: 38.5 (C-1), 78.3 (C-10); H-15: 40.1 (C-4), 214.3 (C-3). 3—H-2: 208.7 (C-1); H-12: 17.2 (C-13); H-13: 44.7 (C-7), 113.4 (C-12), 146.5 (C-11); H-14: 208.7 (C-1); H-15: 29.2 (C-3), 38.5 (C-4), 54.1 (C-5).



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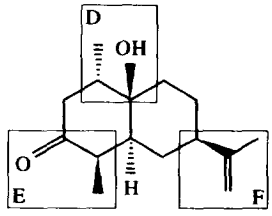

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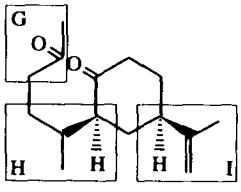

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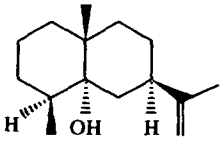

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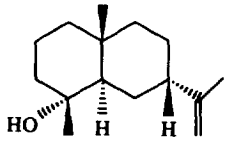

5

(0.4 ppm) and H-9_{eq} (1.2 ppm), indicating their *cis*-relationship with the hydroxyl group.

Confirmatory evidence for the localization of the isopropenyl at position 7 of **1** was provided by the Eu(fod)$_3$ induced ^{13}C-shifts. The methine carbon at this position showed the smallest effect and, therefore, had to be as far removed from the site of association (HO-1) as possible. Direct evidence for the insertion of the isopropenyl at C-7 also in **2**, was provided by the strong ^{1}H-^{13}C NMR correlation of H-7 with the bridgehead (δ58.3, C-5) establishing their separation by three bonds. Both additional methines being necessarily linked to the two methyls represented by ^{1}H NMR doublets (J = 7 Hz), the tertiary hydroxyl could only be located at the alternative bridgehead (δ78.3, C-10) and provided conclusive evidence for the placement of substructure D within the molecular framework. Not its methine (δ1.81), but the methine of substructure E (δ2.52) flanks the carbonyl. As suggested by the equally low field two-proton signal (δ2.36, 2.54), the other position relative to the carbonyl had to be occupied by a methylene as shown in **2**.

The substructures G, H and I, determined for **3**, only accounted for one carbonyl group (ν_{max} 1738 cm^{-1}). The additional carbonyl of this monocyclic compound thus had to be part of a cyclohexanone group (ν_{max} 1718 cm^{-1}). Groups flanking the two carbonyls comprise a methyl (δ2.09, *s*, Me-14) as well as a methylene (δ2.30, 2H-2) in substructure G, and a methylene (δ2.15, H-9_{ax}; 2.25, H-9_{eq}) as well as a methine (δ1.6, H-5_{ax}) in the cyclohexanone moiety. The relatively upfield position of this methine proton signal, jointly with the relative downfield position of the methine carbon signals (δ54.1, C-5; 44.7, C-7) provided evidence for the equatorial orientation of both substituents of the cyclohexanone as shown in **3**.

DISCUSSION

The occurrence of eudesmanes in an *Ocotea* species has been observed [6]. Thus, as in the case of the emmotins [2], the biosynthesis of **1**–**3** may conceivably also involve a methyl shift from C-10 to C-1 within a basic eudesmane type skeleton. In this connection it seems relevant to observe that oxygenation occurred in **1** at C-1, in **2** at C-10 and in **3** at both these positions.

EXPERIMENTAL

Botanical material and unripe fruits were collected near Campo Grande, Mato Grosso do Sul, and identified by Dr João Batista Baitello. A voucher numbered 12824 is deposited at the Herbarium Bento Pickel, Instituto Florestal de São Paulo.

Isolation of the constituents. Unripe fruits (1.32 kg) were extracted with EtOH. The solvent was evapd under red. pres. The oily residue was partitioned with hexane/EtOH–H_2O (7:3) and EtOAc/EtOH–H_2O (3:2). CC (silica gel, 300 g, hexane–EtOAc gradient) of the hexane extract (15.8 g) yielded 20 fractions. Fractions 1–5 and 12–20 contained essential oil and fatty material, respectively, and were not investigated. From the other fractions fats were pptd with MeOH. The methanolic layers of frs 7 (130 mg), 8 (155 mg) and 10 (155 mg), after prep. TLC, developed with hexane–EtOAc (9:1, 4:1 and 7:3, respectively) afforded carvacrol (17 mg), **1** (64 mg) and **3** (30 mg), besides sitosterol and stigmasterol. The methanolic layer of fr. 11 (333 mg), after prep. TLC developed with C_6H_6–EtOAc (7:3), yielded frs A and B. Further purification of A and B by prep. TLC developed with hexane–EtOAc (3:2) afforded **2** (30 mg) and 3-hydroxy-*p*-menth-1-en-6-one (20 mg), respectively.

rel-(1S,4S,5R,7R,10R)-10-*Desmethyl*-1-*methyl*-11-*eudesmene* (**1**). Oil, $[\alpha]_D^{25} - 10.5°$ ($CHCl_3$; *c* 0.524 × 10^{-2}). IR ν_{max}^{film} cm^{-1}: 3395, 1643, 1453, 1374, 1103, 886; EI-MS *m/z* (rel. int.): 222 $[M]^+$ (1), 204 $[M - H_2O]^+$ (2), 189 (5), 161 (6), 147 (5), 122 (11), 121 (14), 107 (20), 71 (32), 55 (38), 43 (100); ^{13}C NMR (50 MHz, $CDCl_3$) and ^1H NMR (200 MHz, $CDCl_3$): Table 1.

rel-(1S,4R,5R,7R,10R)-10-*Desmethyl*-10-*hydroxy*-1-*methyl*-3-*oxo*-11-*eudesmene* (**2**). Oil, $[\alpha]_D^{25} + 64.8°$ ($CHCl_3$; *c* 0.3 × 10^{-2}). IR ν_{max}^{film} cm^{-1}: 3345, 1706, 1645, 1455, 1377, 894; EI-MS *m/z* (rel. int.): 236 $[M]^+$ (8), 221 (85), 218 (54), 203 (70), 193 (29), 175 (88), 160 (82), 124 (32), 123 (54), 109 (100), 107 (91), 105 (98), 95 (84), 93 (94), 79 (62), 69 (40), 55 (66), 43 (43); ^{13}C NMR (50 MHz, $CDCl_3$) and ^1H NMR (200 MHz, $CDCl_3$): Table 2.

rel-(5R,7R)-10-*Desmethyl*-1-*methyl*-1,10-*dioxo*-1,10-*seco*-11-*eudesmene* (**3**). Oil, $[\alpha]_D^{25} - 1.48°$ ($CHCl_3$; *c* 0.508 × 10^{-2}). IR ν_{max}^{film} cm^{-1}: 1738, 1718, 1643, 1100, 890; EI-MS *m/z* (rel. int.): 236 (1), 140 (2), 123 (16), 111 (20), 110 (11), 109 (27), 108 (14), 98 (19), 97 (27), 95 (41), 93 (36), 83 (82), 82 (14), 81 (31), 69 (25), 67 (43), 55 (51), 43 (100); CI-MS *m/z* (rel. int.): 238 (20), 237 (100), 235 (6), 219 (58), 201 (23), 203 (13), 161 (6), 121 (8); ^{13}C NMR (50 MHz, $CDCl_3$) and ^1H NMR (200 MHz, $CDCl_3$): Table 2.

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