

SESQUITERPENES FROM *VANILLOSMOPSIS ARBOREA*MARIA ELISA O. MATOS, MIRIAN P. DE SOUSA, FRANCISCO JOSÉ A. MATOS,
and AFRÂNIO ARAGÃO CRAVEIRO**Laboratório de Produtos Naturais, Departamento de Química Orgânica e Inorgânica, Caixa Postal 3010,
Universidade Federal do Ceará, 60.000 Fortaleza, Ceará, Brazil*

The genus *Vanillosmopsis* (Compositae) is represented by seven species native to Brazil (1). Some of them have economic value due to their oil content, which is very similar to chamomile oil. *Vanillosmopsis arborea* Baker, popularly known as "candeieiro," is a small tree which grows in the Araripe National Forest, in the state of Ceará, Brazil. Its wood has a strong odor of chamomile and burns easily with a strong flame.

We have carried out a chemical investigation of the essential oil content of *V. arborea* by steam distillation and solvent extraction of its trunk wood.

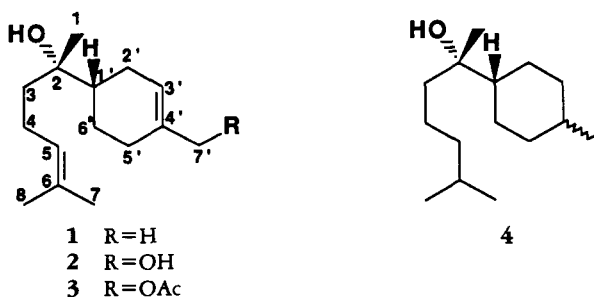
Ground trunk wood was steam distilled, giving 0.1% of volatile constituents as a clear oil with an odor resembling chamomile. Gc-ms computer analysis (2) allowed the identification of estragole, β -elemene, methyl eugenol, β -cubebene, β -himachalene, β -maaliene, δ -guaiene, β -bisabolene, elemicine, α -cadinol, and α -bisabolol as the major constituents.

The residual marc, after steam distillation, was extracted with hexane followed by EtOH. Chromatographic fractionation of the hexane extract on Si gel allowed the isolation of compound **1** as an oily substance. The EtOH extract similarly gave another pure component

2 that was acetylated to provide a monoacetate derivative **3**.

Compound **1** was obtained as an oil, $[\alpha]^{25}_D -48.9^\circ$ (1.06, EtOH). Comparison of its ir, $^1\text{H-nmr}$, and mass spectra with literature data (3,4) identified it as $(-)\text{-}\alpha\text{-bisabolol}$ [**1**].

Compound **2** was an oil, showing ir absorptions for hydroxyl groups (3360 cm^{-1}) and double bonds (1670 and 810 cm^{-1}). Its $^1\text{H-nmr}$ spectrum showed two signals at δ 5.60 and 5.09 attributed to the olefinic hydrogens, a broad signal at δ 3.89 corresponding to a methylene group bearing an oxygen (CH_2OH), two singlets at δ 1.68 and δ 1.62 attributed to two olefinic methyls, and a broad signal at 1.59 that disappeared on treatment with D_2O , corresponding to a hydroxyl proton. The overall spectrum is very similar to the spectrum of $(-)\text{-}\alpha\text{-bisabolol}$, except for the presence of an additional hydroxyl group attached to C-7', causing a downfield shift of the resonance of H-3' (δ 5.60) in comparison with H-3' in $\alpha\text{-bisabolol}$ (δ 5.37). The mass spectrum of **2** does not show a molecular ion at m/z 238 ($\text{C}_{15}\text{H}_{26}\text{O}_2$) but shows instead an ion at m/z 220 which is compatible with loss of H_2O from the parent ion $[\text{M}-18]^+$. Peaks at m/z 109 and 69 were also ob-



served in the fragmentation of α -bisabolol and are derived from the side chain, further supporting the location of the additional hydroxyl group at the C-7' position. To confirm the position of the hydroxyl group, **2** was acetylated to the monoacetylated derivative **3**, $[\alpha]^{25}_D -48.6^\circ$ (1.08, EtOH), showing a shift in the absorption of H-7' from δ 3.89 in **2** to δ 4.38 in **3** (CH₂OAc). Hydrogenation of **3** provided **4**. The absence of olefinic absorption and the presence of an additional methyl group in **4** are in agreement with hydrogenolysis of the allylic -OAc group and confirm its presence at C-7' in **3**.

¹³C-nmr data of **1** and **3** are shown in Table 1. The ¹³C absorptions for (-)- α -bisabolol [**1**], which are not totally correlated in the literature (4), were proposed with support from data for similar terpenes and by APT experiments. Comparison of the absorptions gives support for the proposed structure **2** including the stereochemistry 1'S 2S (3,4).

Furthermore, the absorptions for C-3' and C-5' in **3** are in agreement with the expected shifts for these carbons caused by the hydroxyl group in C-7', as can be seen from comparison with limonene [**5**] and its hydroxy and acetoxy derivatives **6** and **7**, respectively (5).

Compound **2** is, thus, a new natural dioxygenated sesquiterpene derived from (-)- α -bisabolol with the structure of (*S*)- α^4 -methyl- α^4 -(4-methyl-3-pentenyl)-1-cyclohexene-1,4-dimethanol.¹

TABLE 1. ¹³C-nmr Assignments of Compounds **1** and **3** in CDCl₃ (ppm).

Carbon	Compound	
	1 ^a	3 ^b
1	25.67	25.53
2	74.22	73.91
3	40.32	39.89
4	22.26	21.89
5	124.79	124.33
6	131.32	131.50
7	23.29	23.00
8	17.67	17.50
1'	43.23	42.59
2'	27.04	26.68
3'	120.78	124.33
4'	133.87	132.75
5'	31.24	26.50
6'	23.29	22.61
7'	23.29	68.27
-OCOCH ₃	—	20.79
-OCOCH ₃	—	170.91

^aRecorded at 75 MHz in CDCl₃.

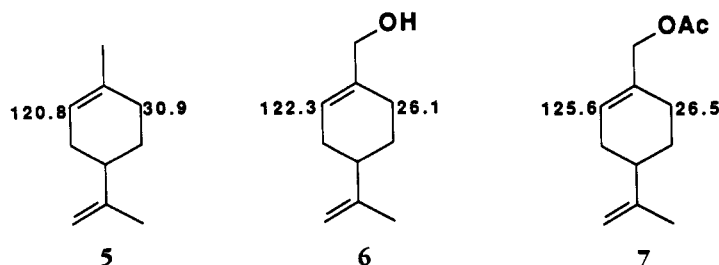
^bRecorded at 20 MHz in CDCl₃.

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—Spectra were recorded with the following instruments: ir, Perkin-Elmer 720; ¹H nmr, Varian EM-360 (60 MHz); ¹³C nmr, Varian XL-300 and Varian FT-80; ms, HP 5995 gc-ms system. Optical rotations were determined on a Carl Zeiss Jena polarimeter.

PLANT MATERIAL.—*V. arborea* was collected in October 1984 at Araripe National Forest, in Ceará, Brazil. A voucher specimen is deposited in the Herbarium Prisco Bezerra of the Universidade Federal do Ceará (No. 12862).

EXTRACTION AND ISOLATION.—Ground



¹Personal information from Dr. K.L. Loening, Director of Nomenclature, Chemical Abstract Service, Columbus, Ohio (1986).

trunk wood of *V. arborea* (6.5 kg) was steam distilled giving 6 ml of volatile constituents as a clear oil. Gc-ms computer analysis (2) allowed the identification of estragol, β -elemene, methyl

eugenol, β -cubebene, β -himachalene, β -maaliene, δ -guaiene, β -bisabolene, elemicin, α -cadinol, and α -bisabolol as major constituents.

After steam distillation, the residual marc was extracted with hexane followed by EtOH, and the solvents were evaporated.

The hexane-soluble portion (20 g) was chromatographed on SiO₂ with hexane, hexane/EtOAc mixtures, EtOAc, EtOAc/MeOH mixtures, and MeOH. A total of 30 fractions (250 ml each) were collected. From fractions 3–5 eluted with hexane-EtOAc (94:4) α -bisabolol (1 g) was obtained.

The EtOH-soluble portion (300 g) was chromatographed on SiO₂ with hexane, hexane/CHCl₃ mixtures, CHCl₃, CHCl₃/EtOH mixtures, and EtOH. A total of 60 fractions (250 ml each) were collected. From fractions 9 and 10 eluted with hexane-CHCl₃ (1:1), compound **2** was obtained.

(-)- α -BISABOLOL [**1**].—Compound **1** (1 g) was isolated as a colorless oil; [α]_D²⁵ -48.9° (1.06, EtOH) [lit. (3) -55.7]; ms and ¹H nmr (3); ¹³C nmr see Table 1.

(S)- α^4 -METHYL- α^4 -(4-METHYL-3-PENTENYL)-1-CYCLOHEXENE-1,4-DIMETHANOL [**2**].—Compound **2** (350 mg) was obtained as a colorless oil; ir γ max (film) 3360, 2960, 2910, 1670, 1443, 1430, 1370, 1290, 1150, 810 cm⁻¹; ¹H nmr (60 MHz, CDCl₃) δ 5.60 (1H, br, H-3'), 5.09 (1H, t, H-5), 3.89 (2H, br, H-7'), 1.68 (3H, s, H-7), 1.62 (3H, s, H-8), 1.10 (3H, s, H-1); ms *m/z* (%) 220 (20), 205 (5), 202 (8), 187 (7), 137 (6), 135 (67), 133 (12), 109 (100), 69 (48).

ACETYLATION OF **2**.—Compound **2** (250 mg) was acetylated (Ac₂O/pyridine) and chromatographed on a Si gel column with hexane-EtOAc (9:1) to give **3** as an oil (200 mg): [α]_D²⁵ -48.6° (1.08, EtOH); ir γ max (film) 2970, 2930, 1730, 1450, 1440, 1378, 1030, 968, 925, 818 cm⁻¹; ¹H nmr (60 MHz, CDCl₃) δ 5.64 (1H, br, H-3'), 5.09 (1H, t, H-5), 4.38

(2H, br, H-7'), 2.02 (3H, s, OCOCH₃), 1.66 (3H, s, H-7), 1.60 (3H, s, H-8), 1.10 (3H, s, H-1); ms *m/z* (%) 262 (19), 220 (15), 202 (78), 187 (44), 179 (2), 177 (64), 159 (41), 133 (17), 109 (100), 69 (49), 43 (67).

HYDROGENATION OF **3**.—To compound **3** (100 mg) dissolved in EtOH (20 ml) was added Pd/C (20 mg). Hydrogenation under pressure was carried out for 5 h, and usual work-up provided 70 mg of **4** as an oil: ir γ max (film) 3440, 2940, 2910, 1440, 1378, 1365, 920; ¹H nmr (60 MHz, CDCl₃) δ 1.10 (3H, s, H-1), 0.80–0.90 (9H, br, H-7, H-7', H-8); ms *m/z* (%) 211 (4), 208 (23), 151 (4), 141 (48), 138 (17), 137 (24), 129 (76), 124 (93), 123 (100), 111 (52), 95 (75), 81 (80), 69 (63).

ACKNOWLEDGMENTS

We are indebted to Professor Afrânio Fernandes for the botanical identification and to Professors J. Welch, State University of New York at Albany, and Delby Fernandes Medeiros and Emidio Cunha, Laboratório de Tecnologia Farmacêutica da Universidade Federal da Paraíba, for ¹H-nmr and ¹³C-nmr spectra.

LITERATURE CITED

1. J.B. Harborne and C.A. Williams, in: "The Biology and Chemistry of the Compositae." Ed. by V.H. Heywood, J.B. Harborne, and B.L. Turner, Vol. 1, Academic Press, London, 1977, pp. 503–537.
2. A.A. Craveiro, A.S. Rodrigues, C.H.S. Andrade, F.J.A. Matos, J.W. Alencar, and M.I.L. Machado, *J. Nat. Prod.*, **44**, 602 (1981).
3. M.A. Schwartz and G.C. Swanson, *J. Org. Chem.*, **44**, 953 (1979).
4. E. Flaskamp, G. Nonnenmacher, and O. Isaac, *Z. Naturforsch.*, **36b**, 114 (1981).
5. F. Bohlmann, R. Zeisberg, and E. Klein, *Org. Magn. Reson.*, **7**, 426 (1975).

Received 14 September 1987