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J. Nat. Prod., **1991**, 54 (2), 579-581 • DOI:
10.1021/np50074a036 • Publication Date (Web): 01 July 2004

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DC 20036

A NEW β -AGAROFURAN SESQUITERPENE DIBENZOATE FROM *SALVIA PALAEFOLIA*

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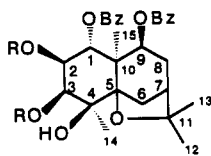
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ABSTRACT.—The aerial part of *Salvia palaeifolia* has already yielded squalene, lupeol, taraxerol, taraxerone, β -amyrin, olean-12-en-3-one, oleanonic, oleanolic and ursolic acids, 5-hydroxy-7,6,8,4'-tetramethoxyflavone, caryophyllene oxide, and an enantiomer of glechomafuran. More polar fractions of the same extract have now afforded a new β -agarofuran sesquiterpene, 1 α ,9 β -dibenzoyloxy-2 β ,3 β ,4 β -trihydroxydihydro- β -agarofuran [**1**].

As part of our continuing search for biologically active substances from the medicinal plants of South America, *Salvia palaeifolia* H.B.K. (Labiatae) (1) was analyzed. *S. palaeifolia* is an Andean species collected in Colombia and is extensively used there as an antihypertensive agent (2). An extract of the aerial part of the plant has been shown to yield the known triterpenes squalene, lupeol, taraxerol, taraxerone, β -amyrin, olean-12-en-3-one, oleanonic, oleanolic and ursolic acids, the flavonoid 5-hydroxy-7,6,8,4'-tetramethoxyflavone, and the sesquiterpenes caryophyllene oxide and an enantiomer of glechomafuran. The absolute configuration of glechomafuran was established (3) by X-ray diffraction analysis. From the more polar fractions of the same extract we have now obtained a new β -agarofuran sesquiterpene, the structure and absolute configuration of which have been established as 1 α ,9 β -dibenzoyloxy-2 β ,3 β ,4 β -trihydroxydihydro- β -agarofuran [**1**].

The molecular formula for **1** was established as C₂₉H₃₄O₈ by hrms. Intense

bands were obtained in the ir spectrum for alcohol aromatic and ester groups. ¹H-nmr signals were evident for four angular methyls and ten aromatic protons between δ 7.20 and 7.90 assignable to two benzoate groups. These were confirmed by ms fragments at *m/z* 388 and *m/z* 266, corresponding to the loss of one and two benzoic acid molecules, respectively. Two doublets, at δ 3.47 and 2.81, and a singlet at δ 3.33 disappeared when the ¹H-nmr spectrum was taken in D₂O, indicating the presence of three alcohol groups, two secondary and one tertiary, in the molecule. The sixth oxygen atom should belong to an ether bridge. The characteristic β -agarofuran skeleton H-7 (4) is to be seen as a dq centered at δ 2.48, revealing the absence of functional groups on C-6 and C-8. Double resonance experiments together with the coupling constant values enabled the positions and relative configurations of the alcohol groups and the benzoates to be established. Acetylation of **1** gave a diacetate **2**. The absolute configuration of compound **1** was determined by application of the cd exciton chirality method (5). Its 1,9-dibenzoate system exhibits positive first and negative second Cotton effects, λ ext 236.5 nm, $\Delta\epsilon$ 21.1 and λ ext 221.3 nm, $\Delta\epsilon$ -9.7, in the region of the $\pi \rightarrow \pi^*$ intramolecular charge transfer or 'La transition, λ max 229.0 nm, ϵ 25000. The sign of the ex-



- 1** R=H
2 R=Ac

citon Cotton effects gives the absolute configuration shown with positive chirality (6).

β -Agarofuran sesquiterpenes are omnipresent in the Celastraceae, especially in the genera *Maytenus*, but, to the best of our knowledge, this is the first time that one has been isolated from a *Salvia*.

EXPERIMENTAL

PLANT MATERIAL.—The plant material was collected in Cundinamarca (Bogotá plain), Colombia in December 1987. A voucher specimen (No. 293387) is on file in the Herbario Nacional Colombiano and was identified by Dr. Clara Iris Orozco of the Instituto de Ciencias Naturales of the Universidad Nacional de Colombia. Another voucher specimen has been lodged with the Department of Botany of the Universidad de La Laguna where its identification was confirmed.

GENERAL TECHNIQUES.—Mp's were determined on a Kofler-type block and are uncorrected. Uv spectra were obtained on a Perkin-Elmer 550 SE. Cd were recorded on a Jasco J-600 spectropolarimeter and ir on a Perkin-Elmer 681 spectrometer. High and low resolution ms were taken on a VG-Micromass ZAB-2F spectrometer at 15 or 70 eV. ^1H -nmr spectra were run on a Bruker AC 80 WP-200 SY spectrometer and ^{13}C -nmr spectra on a Bruker WP-200 SY. Chemical shifts are given in δ . Merck (0.2–0.5 mm) and type G Si gel were used for wet cc and the same Si gel (0.2–0.063 mm) for dry cc. Tlc was carried out on type G Si gel plates. A Harrison Research Chromatotron apparatus, model 7924T, was used for Chromatotron chromatography.

PLANT EXTRACTION.—The leaves of *S. palaefolia* were shredded and extracted with cold Me_2CO , giving 105 g of extract which was dry-column chromatographed with C_6H_{14} and differing mixtures of $\text{C}_6\text{H}_{14}/\text{EtOAc}$ as eluents. This yielded squalene (2.8 g), taraxerone (1.5 g), olean-12-en-3-one (1 g), β -amyirin (0.5 g), caryophyllene oxide (2.3 g), lupeol (1 g), taraxerol (0.8 g), (–)-glechomafuran (2.5 g), ursolic acid (4 g), oleanonic acid (1 g), oleanolic acid (0.5 g), 5-hydroxy-7,6,8,4'-tetramethoxyflavone (2 g), 1β , 10α , 4α , 5β -diepoxy-8 β -hydroxyglechoman-8 α , 12-olide (0.15 g), 1α -acetoxy-8 α -hydroxy-2-oxoeudesma-3,7(11)-dien-8,12-olide (0.2 g), 1α , 8 α -dihydroxy-2-oxo-eudesma-3,7(11)-dien-8,12-olide (3 mg), and 1α ,9 β -dibenzoyloxy-2 β ,3 β ,4 β -trihydroxydihydro- β -agarofuran [1] (4.8 mg).

1α ,9 β -DIBENZOYLOXY-2 β ,3 β ,4 β -TRIHYDROXYDIHYDRO- β -AGAROFURAN [1].—Compound 1 (4.8 mg): ir ν max (CHCl_3) cm^{-1} 3420, 3020, 2960, 2880, 2820, 1695, 1688, 1575, 1555, 1425, 1390, 1360, 1255, 1150, 1115, 1090, 1045, 1000, 980, 870, 835, 813, 730, 685; uv (MeCN) λ max nm 229 (ϵ 25000); ^1H nmr (200 MHz, CDCl_3) δ 1.37 (6H, s, Me-12, Me-13), 1.45 (3H, s, Me-15), 1.46 (3H, s, Me-14), 1.88 (1H, d, $J = 12.2$ Hz, H-6 β), 2.04 (1H, dd, $J = 12.2, 2.8$ Hz, H-6 α), 2.16 (2H, m, H-2), 2.48 (1H, dq, H-7), 2.81 (1H, d, $J = 11.0$ Hz, 3-OH), 3.33 (1H, br s, 4-OH), 3.47 (1H, d, $J = 10.0$ Hz, 2-OH), 3.84 (2H, m, H-2 and H-3), 5.08 (1H, br d, $J = 5.2$ Hz, H-9), 5.94 (1H, d, $J = 10.8$ Hz, H-1), 7.20–7.90 (10H, m, H-Ar); ^1H nmr (200 MHz, $\text{CDCl}_3 + \text{D}_2\text{O}$) δ 1.37 (6H, s, Me-12, Me-13), 1.45 (3H, s, Me-15), 1.46 (3H, s, Me-14), 1.88 (1H, d, $J = 12.0$ Hz, H-6 β), 2.04 (1H, dd, $J = 12.0, 2.8$ Hz, H-6 α), 2.16 (2H, m, 2H-8),

TABLE 1. ^{13}C -nmr Data for Compound 2 (200 MHz, CDCl_3 as Solvent).^a

Carbon		Carbon	
C-1	73.36	Acetate Methyls	24.01
C-2	69.01		24.47
C-3	70.02	Benzoate Ring Carbons	2 × 127.85 (d)
C-4	68.12		2 × 128.15 (d)
C-5	89.89		2 × 129.14 (d)
C-6	30.30		2 × 130.20 (d)
C-7	42.97		132.70 (d)
C-8	32.75		132.80 (d)
C-9	75.95		128.79 (s)
C-10	47.96		129.24 (s)
C-11	84.11		
C-12	19.92	Acetate Carboxyls	164.69
C-13	20.46		165.38
C-14	29.99	Benzoate Carboxyls	2 × 170.30
C-15	20.93		

^a δ values based on DEPT experiments and correlations.

2.48 (1H, dq, H-7), 3.80 (1H, d, $J = 2.9$ Hz, H-3), 3.86 (1H, dd, $J = 10.8, 2.9$ Hz, H-2), 5.08 (1H, br d, $J = 5.2$ Hz, H-9), 5.94 (1H, d, $J = 10.8$ Hz, H-1), 7.20–7.90 (10H, m, H-Ar); ms m/z (rel. int. %) $[M]^+$ 510 (6), 495 (1), 492 (1), 477 (4), 459 (1), 388 (6), 370 (1), 266 (4), 248 (5), 233 (1), 202 (2), 173 (1), 140 (8), 122 (5), 105 (100). Calcd for $C_{29}H_{34}O_8$, 510.2239; found 510.2246 (hrms).

¹ $1\alpha, 9\beta$ -DIBENZOYLOXY- $2\beta, 3\beta$ -DIACETOXY- 4β -HYDROXYDIHYDRO- β -AGAROFURAN [2].—Treatment of **1** (4.5 mg) with Ac_2O in pyridine gave **2** (4 mg) after preparative tlc: $[\alpha]^{20}_D 83.9^\circ$ ($c = 0.6$, $CHCl_3$); 1H nmr (200 MHz, $CDCl_3$) δ 1.37 (3H, s, Me-12), 1.44 (3H, s, Me-13), 1.48 (6H, s, Me-14 and Me-15), 1.73 (3H, s, 2-OCOMe), 1.93 (1H, d, $J = 12.3$ Hz, H-6 β), 2.04 (1H, dd, $J = 12.3, 2.7$ Hz, H-6 α), 2.29 (3H, s, 3-OCOMe), 2.43 (1H, dq, H-7), 3.44 (1H, br s, 4-OH), 5.03 (1H, d, $J = 5.8$ Hz, H-9), 5.27 (1H, d, $J = 2.8$ Hz, overlapping 5.30, H-3), 5.30 (1H, dd, $J = 10.9, 2.8$ Hz, H-2), 6.27 (1H, d, $J = 10.9$ Hz, H-1), 7.24–8.02 (10H, m, Ar-H); ^{13}C nmr see Table 1; ms m/z (rel. int. %) $[M]^+$ 594 (2), 579 (14), 534 (1), 457 (14), 412 (3), 370 (14), 248 (15), 105 (100).

ACKNOWLEDGMENTS

This project has been subsidized by the National Program of Pharmaceutical Research & Development, No. FAR88-0501, AIETI, and the CICYT Project PB88-0420.

LITERATURE CITED

1. V. Vareschi, "Flora de los Páramos de Venezuela," Universidad de Los Andes, Ediciones del Rectorado, Mérida, 1970, p. 360.
2. H. García Barriga, "Flora Medicinal de Colombia," Imprenta Nacional, Bogotá, 1975, Vol. III, p. 33.
3. A.G. González, T.A. Grillo, A.G. Ravelo, J.G. Luis, M.L. Rodríguez, J. Calle, and A. Rivera, *J. Nat. Prod.*, **52**, 1307 (1989).
4. A.G. González, J.A. Jiménez, A.G. Ravelo, J.G. Luis, and I.L. Bazzocchi, *Phytochemistry*, **28**, 173 (1989).
5. N. Harada and K. Nakanishi, "Circular Dichroic Spectroscopy—Exciton Coupling in Organic Stereochemistry," University Science Books, Mill Valley, CA, 1983.
6. N. Harada and K. Nakanishi, *J. Am. Chem. Soc.*, **91**, 3989 (1969).

Received 3 May 1990