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THE DITERPENOID CONSTITUENTS OF *SALVIA FULGENS* AND *SALVIA MICROPHYLLA*

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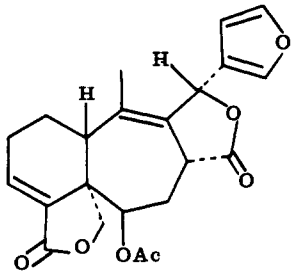
In continuing our studies on Mexican Salvias from which neo-clerodane- (1-6) and abietane- (7) type diterpenoids have been isolated, in this paper we describe the diterpenoid components of *Salvia fulgens* Cav. and *Salvia microphylla* var. *microphylla* Kunt. (Labiatae). These species constitute the folk medicine known as "mirto," used in our country for some stomach ailments.

In previous work (4) on *S. fulgens*, we described the structure of salvigenolide [**1**], a novel diterpenoid with a rearranged neo-clerodane skeleton. In a reinvestigation of this species, in addition to **1** and β-sitosterol, we isolated sandaracopimaric acid [**2a**]. This is to our knowledge the first report on the presence of a pimarane-type diterpenoid from a *Salvia* species.

From the Me_2CO extract of the leaves and stems of *S. microphylla*, after extensive chromatographic purification, several diterpenoids were isolated. The most abundant compound was 7α-hydroxysandaracopimaric acid [**2b**], which was purified and identified as the methyl ester derivative **2c**. Compound **2b** was previously isolated from *Juniperus communis* (8). Reduction of **2c** with $LiAlH_4$ afforded 8(14),15-sandaracopimaradien-7α,18-diol, which is identical to the antimicrobial and antispasmodic principle isolated from *Iboza riparia* Kunt. (Labiatae) (9). Oxidation of **2c** with MnO_2 yielded the corresponding α,β unsaturated ketone derivative **3a**, which was also detected in the methylated crude fraction from which **2c** was purified (see Experimental section). Hence, the parent compound, 7-oxo-sandaracopimaric acid [**3b**], is also present in the plant. Compound **3b** has not been described previously in the literature; however, a related compound has been described from *Aralia cordata* (10).

The most polar constituents of *S. microphylla* were 7,15-isopimaradien-14α,18-diol and 7α-hydroxy-neoclerodane-3,13-diene-18,19: 15,16-diolide [**4**]. The former was recently isolated from *Lepechinia glomerata* (Labiatae) (11) and compound **4**, originally isolated



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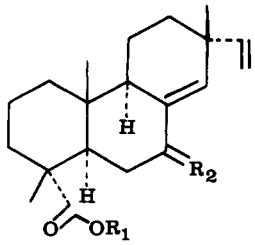
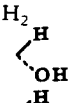
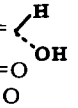
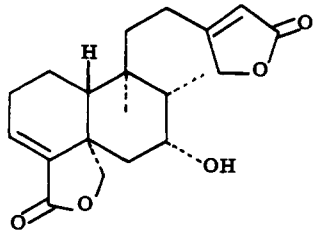


2a R_1=H, R_2=H_2
2b R_1=H, R_2= 
2c R_1=Me, R_2= 
3a R_1=Me, R_2=O
3b R_1=H, R_2=O



4

from *Baccharis trimera* (Asteraceae) (12), has been found recently in *Salvia semiatrata* Zucc. (3) and *Salvia melissodora* Lag.[1]

S. fulgens constitutes the first species of the *Salvia* genus from which a pimarane-type diterpenoid has been isolated. This fact, together with the coexistence of clerodanes, could be of taxonomic importance. *S. microphylla* shares the same chemical character. It is interesting to note that both species are located in *Salvia* Section Fulgentes (Epling) (13).

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—Melting points were determined in a Fisher-Johns apparatus and are uncorrected. Column chromatography was carried out by using Merck Si gel 60. Ir and uv spectra were determined on Nicolet FT 5X and Perkin-Elmer 552 spectrometers, respectively. ^{1}H-nmr spectra were recorded at 80 MHz in $CDCl_3$, with TMS as internal standard, in a Varian FT80A apparatus. Mass spectra were obtained at 70 eV on a Hewlett-Packard 5985-B spectrometer. Hplc analysis was carried out in a Varian 8500 apparatus.

PLANT MATERIAL.—*S. fulgens* was collected in November 1983, in Huitzilac, Morelos, México, (voucher MEXU 379095), and *S. microphylla* var. *microphylla* was collected in the valley of Mexico in July 1984 (voucher MEXU 379090).

EXTRACTION AND ISOLATION OF COMPOUNDS FROM *S. FULGENS*.—The Me_2CO extract (50 g) of the dried aerial parts of *S. fulgens* (2 kg) was chromatographed over Si gel (1.2 kg) and eluted with petrol/EtOAc mixtures affording, in order of elution, β-sitosterol (300 mg), sandaracopimaric acid [**2a**] (400 mg), and salvigenolide [**1**] (500 mg). Known components were identified by comparing the spectroscopic data with those of authentic material. Compound **2a** was identified by comparison with literature data (ir, ^{1}H nmr, ^{13}C nmr, eims, and mp) (14-16).

EXTRACTION AND ISOLATION OF DITERPENOIDS OF *S. MICROPHYLLA* VAR. *MICROPHYLLA*.—Dried aerial parts of *S. microphylla* (3 kg) were extracted with Me_2CO (15 l) for 1 week. Evaporation of the solvent yielded 170 g of gummy extract which was chromatographed over Si gel and eluted with petrol/EtOAc. The fractions eluted with petrol-EtOAc (6:4) were combined (14 g) and treated with etheral CH_2N_2. The reaction mixture obtained was chromatographed over 700 g of Si gel, using petrol/EtOAc mixtures as eluents, affording in order of elution: methyl 7-oxo-sandaracopimarate [**3a**] (5 mg), methyl 7α-hydroxysandaracopimarate [**2c**] (1.5 g), 7α-hydroxy-neo-clerodane-3,13-diene-18, 19: 15,16 diolide [**4**] (50 mg), and 7,15-isopimaradien-14α,18 diol (80 mg). The latter compound as well as **2c** were identified by comparison of physical data with literature data (8, 11). Compound **4** was identified by comparison with an authentic sample, and **3a** was identical with the MnO_2 oxidation product of **2c** by hplc analysis. [Column Si-10 of 25 cm, uv detector at 270 nm, hexane-CH_2Cl_2 (8:2) as eluent at 40 ml/h].

METHYL-7-OXO-SANDARACOPIMARATE [**3a**].—Mp 87-90° (petrol/EtOAc); uv λ max (MeOH) (ε)=245 (7800), $[\alpha]^{20}$ −40 (589 nm), −40 (578 nm), −46.7 (546 nm), −113.7 (435 nm), −186.7 (405 nm), (*c* 0.15 $CHCl_3$); ir ($CHCl_3$) ν cm^{-1} 1720, 1680, 1634, 1607, 996, 920; ^{1}H nmr ($CDCl_3$) δ 0.85 (s, 3H-20), 1.10 (s, 3H-17), 1.20 (s, 3H-19), 3.60 (s, 3H-COO*Me*), 4.95 (dd, H-16, *J*=10 and 1 Hz), 4.89 (dd, H-16, *J*=18 and 1 Hz), 5.80 (dd, H-15, *J*=18 and 10 Hz), 6.70 (d, H-14, *J*=2 Hz); eims *m/z* (rel. int.) 330 (M^+, 82), 315 (20), 271 (40), 270 (20), 255 (30), 237 (20), 181 (70), 162 (60), 149 (60), 133 (60), 105 (80), 91 (100), 79 (60), 77 (50), 50 (40).

REDUCTION OF **2c** WITH $LiAlH_4$.—A solution of **2c** (200 mg) in THF (5 ml) was treated with $LiAlH_4$ (100 mg) under argon with stirring (6 h). After usual work up, 151 mg of a crystalline solid (mp 75-79°, Me_2CO) was obtained. It was identified as 8(14),15-sandaracopimaradien-7α, 18 diol previously isolated (9) from *I. riparia* (mp 76-81° from Me_2CO).

MnO_2 OXIDATION OF METHYL 7α-HYDROXYSANDARACOPIMARATE [**2c**].—Compound **2c** (500 mg) in CH_2Cl_2 (10 ml) was treated with MnO_2 (5 g). The resultant mixture was stirred 48 h at room temperature. Usual work up yielded 473 mg of crude product that was purified by column chromatography to afford methyl 7-oxo-sandaracopimarate [**3a**] identical to the product present in the esterified plant extract (hplc, Si-10 analysis).

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[1]J. Cárdenas and R. Gaviño, unpublished results.

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