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A REARRANGED ABIETANE DITERPENOID FROM THE ROOT OF *SALVIA AETHIOPIS*

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Key Word Index—*Salvia aethiopis*; Labiatae; diterpenoids; 12-hydroxy-4,5-seco-5,10-*friedo*-4(18),5(10),6,8,12-abietapentaene-11,14-dione; salvipisone; aethiopinone; royleanone.

Abstract—From the root of *Salvia aethiopis* a new diterpenoid, salvipisone, has been isolated. Its structure, 12-hydroxy-4,5-seco-5,10-*friedo*-4(18),5(10),6,8,12-abietapentaen-11,14-dione, was established by spectroscopic means and by partial synthesis from aethiopinone. The previously known diterpenoids aethiopinone and royleanone were also found in the same source.

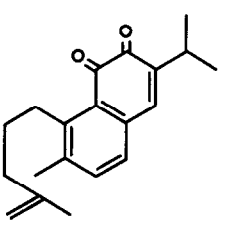
In continuation of our studies on the diterpenoids from *Salvia* spp. [1–4], we have now investigated the root of *S. aethiopis*, a plant material from which the rearranged abietane diterpenoid aethiopinone (**1**) has been previously isolated [5]. Now, a careful study of the acetone extract of the root of this plant allowed the isolation of aethiopinone (**1**) [5] as the major constituent, besides minor quantities of two other diterpenoids, one of which was the known compound royleanone [2, 6] and the other one was a new substance, named salvipisone (**2**).

The new diterpenoid (salvipisone, **2**), $C_{20}H_{24}O_3$, had an IR spectrum which showed absorptions of terminal methylene (3080, 890 cm^{-1}), aromatic (3030, 3010, 1575 cm^{-1}) and hydrogen-bonded 2-hydroxy-1,4-benzoquinone (3350, 1665, 1650 cm^{-1}) groupings. The presence of a 2-hydroxy-1,4-naphthaquinone moiety in salvipisone (**2**) was revealed by its UV absorption at λ_{max} 256, 282, 288 and 356 nm [7] and also confirmed by its UV spectra obtained after addition of base, aluminium chloride and aluminium chloride plus hydrochloric acid, which showed (Table 1) characteristic band shifts of this chromophore [8].

The ^1H NMR spectrum of salvipisone was consistent with the 2-hydroxy-1,4-naphthaquinone moiety and the substitution pattern depicted in formula **2**, showing signals of an isopropyl group attached to the quinone ring (δ3.37, 1H, *septet*, J = 7.1 Hz, H-15, and δ1.30, 6H, *d*, J = 7.1 Hz, Me-16 and Me-17), two *ortho* aromatic protons (δ7.95, *d*, J = 8 Hz, $W_{1/2}$ = 0.9 Hz, and δ7.50, *br d*, J = 8 Hz, $W_{1/2}$ = 1.8 Hz, H-7 and H-6, respectively), one of which (δ7.50) was also coupled with a methyl group (δ2.43, 3H, *d*, ^4J = 0.8 Hz, Me-20), and a 2-methyl-1-penten-5-yl side-chain (δ4.74, 2H, five lines, J = 1 Hz, 2H-18; δ3.13, 2H, *m*, C-1 benzylic protons; δ2.24, 2H, *br t*, J = 7.6 Hz, allylic C-3 protons; δ1.79, 3H, *t*, J = 1 Hz, Me-19; and δ1.61, 2H, *m*, C-2 methylene protons). The signal of the hydrogen-bonded hydroxyl proton appeared at δ7.77 as a sharp singlet and it disappeared after addition of D_2O. Extensive decoupling experiments confirmed all the above assignments.

Furthermore, the ^{13}C NMR spectrum of salvipisone (Table 2) was also in complete agreement [5, 9] with a structure such as **2** for this new diterpenoid.

Final proof that salvipisone has the structure depicted in formula **2** was obtained by partial synthesis from



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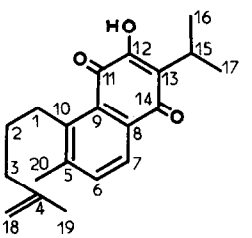

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Table 1. UV spectra of compound **2** [λ_{max} nm (log ε)]

MeOH	+NaOMe	+$AlCl_3$	+$AlCl_3$–HCl
250 sh (4.23)	223 (4.32)	258 (4.23)	258 (4.21)
256 (4.29)	277 (4.33)	264 sh (4.19)	265 sh (4.18)
282 (4.09)	289 sh (4.18)	271 sh (4.13)	273 sh (4.13)
288 (4.08)	347 (3.31)	314 (3.89)	313 (3.81)
356 (3.53)	472 (3.13)	394 (3.61)	390 (3.53)

Table 2. ^{13}C NMR chemical shifts ($CDCl_3$, in δ values from internal TMS) of compound **2**

C-1	27.1 *t**	C-11	183.4 *s*
C-2	30.0 *t*	C-12	153.2 *s*
C-3	38.5 *t*	C-13	123.8 *s*†
C-4	145.5 *s*	C-14	184.5 *s*
C-5	143.0 *s*	C-15	24.6 *d*
C-6	136.3 *d*	C-16	19.9 *q*
C-7	125.5 *d*	C-17	19.9 *q*
C-8	133.5 *s*	C-18	110.3 *t*
C-9	126.5 *s*†	C-19	22.4 *q*
C-10	144.8 *s*	C-20	20.2 *q*

*SFORD multiplicity.

†These assignments may be interchanged.

aethiopinone (**1**) [5]. Oxidation of compound **1** with hydrogen peroxide in acetic acid with sulphuric acid as catalyst gave, in poor yield, a substance identical in all respects (mp, mmp, TLC, IR, UV, ^1H NMR and mass spectra) with natural salvipisone (**2**).

Up to now aethiopinone (**1**) and salvipisone (**2**) are the only 4,5-seco-5,10-*friedo*-abietane derivatives isolated from natural sources and they must be biogenetically derived from an abietane structure.

EXPERIMENTAL

Mps are uncorr. Plant materials were collected in June 1983, near Luzón (Guadalajara, Spain), and voucher specimens were deposited in the Herbarium of the Faculty of Pharmacy (Madrid 'Complutense' University).

Extraction and isolation of the diterpenoids. Dried and finely powdered *S. aethiopis* L. roots (450 g) were extracted with Me_2CO (4 l.) at room temp. for 1 week. After filtration, the solvent was evaporated yielding a red gum (10.5 g) which was subjected to dry CC over silica gel (500 g, Merck No. 7734, deactivated with 10% H_2O). Elution with *n*-hexane–EtOAc (49:1) yielded, in order of elution, royleanone (12-hydroxy-8,12-abietadiene-11,14-dione, 17 mg) [2, 6], salvipisone (**2**, 76 mg) and aethiopinone (**1**, 2.6 g) [5]. The previously known diterpenoids were identified by their physical (mp, $[\alpha]_D$) and spectroscopic (IR, UV, ^1H NMR, MS) data and by comparison (mmp, TLC) with authentic samples.

Salvipisone (**2**). Mp 81–83° (from MeOH); $[\alpha]_D^{23}$ 0° ($CHCl_3$; *c* 0.66); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3350, 3080, 3030, 3010, 2970, 2940, 2880, 1665, 1650, 1575, 1470, 1460, 1380, 1290, 1165, 1120, 1005, 890, 850; UV: see Table 1; ^1H NMR (300 MHz, $CDCl_3$): see the text; ^{13}C NMR (20.15 MHz, $CDCl_3$): see Table 2; EIMS (direct inlet) 75 eV, *m/z* (rel. int.): 312 $[M]^+$ (85), 297 (8), 294 (21), 279 (8), 269 (22), 256 (31), 251 (12), 244 (100), 243 (78), 241 (36), 225 (15), 215 (12), 201 (13), 197 (12), 187 (8), 173 (9), 128 (14), 115 (13), 103 (8), 91 (6), 83 (7), 69 (32), 41 (23). (Found: C, 76.60; H, 7.86. $C_{20}H_{24}O_3$ requires: C, 76.89; H, 7.74%.)

Salvipisone (**2**) *from aethiopinone* (**1**). To a soln of aethiopinone (**1**, 650 mg) in 8 ml HOAc a drop of conc. H_2SO_4 was added followed by addition of 2 ml 30% H_2O_2. The reaction mixture was stirred at room temp. for 4 hr. Work-up in the usual manner yielded a complex mixture (TLC) of compounds from which 40 mg of pure **2** were isolated by prep. TLC (silica gel plates, *n*-hexane–EtOAc, 19:1 as eluent), identical in all respects (mp, mmp, TLC, IR, UV, ^1H NMR, MS) with the natural compound.

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