

## EUPHRATICOL AND EUPHRACAL, TWO NEW DITERPENES FROM *SALVIA EUPHRATICA*

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**ABSTRACT.**—Two new diterpenoids, euphraticol [**1**] and euphracal [**2**], were isolated from *Salvia euphratica*, together with the known compound cryptanol. The structures of the compounds were established by spectral data.

In continuation of our investigations into constituents of the roots of *Salvia* species (1–6), the roots of *Salvia euphratica* Montoret et Aucher ex Bentham var. *leiocalycina* (Rech. fil.) Hedge (Labiatae) were studied. The Me<sub>2</sub>CO extract of the plant yielded three diterpenoids. One of them was the known compound cryptanol (abietane-6,8,11,13-tetraene-11,12,14-triol) (**1**), and the other two were new and were named euphraticol (abietane-8,11,13-triene-2 $\alpha$ ,11,12-triol) [**1**] and euphracal (11,12,15-trihydroxyabietane-8,11,13-triene-20-al) [**2**]. The structures of the diterpenoids were established by spectral methods.

The mass spectrum of euphraticol [**1**] gave a molecular ion peak at  $m/z$  318, and this together with elemental analysis indicated a molecular formula C<sub>20</sub>H<sub>30</sub>O<sub>3</sub>. The uv maximum of **1** at 272 nm showed the presence of an aromatic ring without additional conjugation, and ir peaks at 3060, 1580, 1550, and 1520 cm<sup>-1</sup> supported the presence of an aromatic ring. The <sup>1</sup>H-nmr spectrum provided the most information and established an abietane structure for this compound. The signals at  $\delta$  0.90 (3H, s, H-18), 0.93 (3H, s, H-19), 1.15 (6H, d,  $J$  = 7 Hz, H-16 and H-17), 1.20 (3H, s, H-20) together

with the methine proton at  $\delta$  3.14 (1H, septet,  $J$  = 7 Hz, H-15) are common for the abietane skeleton (7–9). Other <sup>1</sup>H-nmr peaks of **1** showed one aromatic proton signal at  $\delta$  7.1 (1H, s, H-14) and aromatic hydroxyl peaks at  $\delta$  7.14 (1H, s, 12-OH), and 7.20 (1H, s, 11-OH) (D<sub>2</sub>O exchange). The presence of a third hydroxyl group was indicated by a signal at  $\delta$  3.70 (1H, dddd,  $J$  = 3 Hz and 7 Hz, H $\beta$ -2). If this group were on ring B there would be two possibilities for its position, C-6 and C-7. If it were at C-6 the methyl group at C-10 would be shifted at around 1.60–1.70 ppm (4, 8–10), and if it were at C-7 the chemical shift of the benzylic proton would be around 4.5–4.8 ppm (11). Since these shifts are not observed, and since the splitting pattern of the peak at  $\delta$  3.70 indicated that it must be between two methylene groups, it can only be located at C-2. The stereochemistry of the hydroxyl group at C-2 was assigned as  $\alpha$  by measuring the  $J$  values ( $J_{2a,1e} = J_{2a,3e} = 3$  Hz and  $J_{2a,1a} = J_{2a,3a} = 7$  Hz) and by studying a Dreiding model. The <sup>13</sup>C-nmr spectrum of **1** is in agreement with the suggested structure (Table 1). Because biogenetically related diterpenoids have the trans chair conformation, the A and B rings, the C-10 methyl group, and the C-5 proton must be trans axial to each other (12).

The second diterpenoid, euphracal [**2**], analyzed for C<sub>20</sub>H<sub>28</sub>O<sub>4</sub> ( $m/z$  332), and its ir spectrum showed the presence of an aldehyde (1708 cm<sup>-1</sup>) and an aromatic system (1590, 1560, 1520 cm<sup>-1</sup>). Its uv spectrum supported the

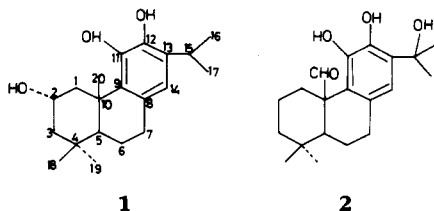


TABLE 1.  $^{13}\text{C}$ -nmr Data of Compounds 1 and 2.

Carbon	Compound	
	1	2
C-1	40.20	33.30
C-2	79.30	20.22
C-3	41.20	39.30
C-4	32.50	35.50
C-5	47.25	48.10
C-6	21.20	21.45
C-7	29.20	28.95
C-8	138.20	137.50 <sup>a</sup>
C-9	138.20	139.50 <sup>a</sup>
C-10	39.80	39.30
C-11	146.25	147.50
C-12	153.20	156.80
C-13	148.50	149.25
C-14	125.75	126.20
C-15	27.50	76.80
C-16	22.10 <sup>b</sup>	22.10 <sup>b</sup>
C-17	22.50 <sup>b</sup>	22.40 <sup>b</sup>
C-18	22.50 <sup>b</sup>	21.90 <sup>b</sup>
C-19	21.30 <sup>b</sup>	21.90 <sup>b</sup>
C-20	22.10 <sup>b</sup>	201.80

<sup>a,b</sup>Values in the same column with the same subscript may be interchanged.

presence of an aromatic ring without conjugation (272 nm). Its  $^1\text{H}$ -nmr spectrum showed methyl singlets at  $\delta$  1.42 (6H, s, H-16 and H-17), 0.94 (3H, s, H-18), and 1.01 (3H, s, H-19), which are characteristic for an abietane skeleton (4). The lack of an isopropyl methine proton (H-15) at ca. 3.00 ppm indicated that one of the hydroxyl groups must be at C-15.  $^1\text{H}$ -nmr peaks were at  $\delta$  3.07 (1H, br s, 15-OH) ( $\text{D}_2\text{O}$  exchange), 6.97 (1H, s, H-14), 7.14 (1H, s, 12-OH) and 7.22 (1H, s, 11-OH) ( $\text{D}_2\text{O}$  exchange), 9.75 (1H, s, CHO). The aldehyde group could be situated either at C-4 or at C-10. If the aldehyde were at C-4 and equatorial, the chemical shift of its proton would be at 9.17–9.25 ppm (13–15). In various examples (13, 15–17) it was observed that an aldehyde group at C-4 causes an upfield shift of the C-10 Me group to ca. 0.84–0.85 ppm. A  $^{13}\text{C}$ -nmr study with a group of triterpenes indicated that a C-4 position with an aldehyde (or other groups) gives

a doublet instead of a singlet when the off-resonance decoupling technique is applied (18). The same situation was observed by Gao *et al.* (13). Neither this doublet nor the upfield shift of the C-10 Me group was found in the present case. The chemical shifts of 2 were quite similar to those of pisiferal (9.79, 1H, s, CHO, 6.81 for H-14) (19).  $^{13}\text{C}$  nmr showed the aldehyde peak at 201.8 ppm, and other peaks are in agreement with the suggested structure (Table 1).

## EXPERIMENTAL

**GENERAL EXPERIMENTAL PROCEDURES.**—Uv spectra were recorded on a Varian Techtron model 635 instrument in  $\text{Et}_2\text{O}$ , ir on a Perkin-Elmer 577 in  $\text{CHCl}_3$ ,  $^1\text{H}$  nmr on a Bruker FT 200 and 400 MHz in  $\text{CDCl}_3$ ,  $^{13}\text{C}$  nmr on FT 50.323 MHz instruments; ms on a Varian MAT 711. Kieselgel 60 F 254 (E. Merck) tlc plates were used for preparative separation.

**PLANT MATERIAL.**—The roots of *S. euphratica* were collected from southeastern Turkey (Refahiye) in July 1987, and identified by Dr. E. Tuzlaci, University of Marmara. A voucher specimen, MARE 860, is deposited in the Herbarium of the Faculty of Pharmacy, University of Marmara, Istanbul.

**EXTRACTION AND FRACTIONATION.**—Dried and powdered roots of the plant (500 g) were extracted with  $\text{Me}_2\text{CO}$  in a Soxhlet. After filtration and evaporation in vacuo, 18 g of a residue was obtained and used for the isolation of the compounds.

**SEPARATION AND ISOLATION OF THE COMPOUNDS.**—The  $\text{Me}_2\text{CO}$  concentrate (18 g) was fractionated in a Si gel column (5 × 60 cm), eluting with petroleum ether, and a gradient of EtOAc was added up to 100%. Fractions were further cleaned and/or separated on preparative plates. The compounds were obtained in the following order: cryptanol (20 mg), euphraticol (10 mg), euphracal (12 mg).

**EUPHRATICOL [1].**— $[\alpha]^{26}_D + 48.7^\circ$  ( $c = 0.1$ , MeOH); uv  $\lambda$  max 272 (log  $\epsilon$  3.7), 228 (log  $\epsilon$  4.0); ir  $\nu$  max 3470, 3060, 2950, 2870, 1580, 1550, 1520, 1450, 1400, 1380, 1330, 1270, 1100, 960, 900, 810, 780, 730  $\text{cm}^{-1}$ ;  $^1\text{H}$  nmr see text;  $^{13}\text{C}$  nmr see Table 1; eims  $m/z$  (rel. int.)  $[\text{M}]^+$  318 ( $\text{C}_{20}\text{H}_{30}\text{O}_3$ ) (20),  $[\text{M} - \text{Me}]^+$  303 (2), 300  $[\text{M} - \text{H}_2\text{O}]^+$  (5), 274  $[\text{M} - 44]^+$  (14), 259 (10), 207 (18), 69 (77). Found C 75.80, H 9.27; calcd for  $\text{C}_{20}\text{H}_{30}\text{O}_3$ , C 75.47, H 9.43%.

**EUPHRACAL [2].**— $[\alpha]^{26}_D + 158^\circ$  ( $c = 0.1$ ,

MeOH); uv  $\lambda$  max 272 (log  $\epsilon$  3.5), 236 (log  $\epsilon$  4.6); ir  $\nu$  max 3500, 3350, 3050, 2980, 2850, 1708, 1590, 1560, 1520, 1460, 1380, 1320, 1250, 1150, 950, 910, 800  $\text{cm}^{-1}$ ;  $^1\text{H}$  nmr see text;  $^{13}\text{C}$  nmr see Table 1; eims  $m/z$  (rel. int.)  $[\text{M}]^+$  332 ( $\text{C}_{20}\text{H}_{28}\text{O}_4$ ) (1),  $[\text{M} - \text{Me}]^+$  317 (2), 228 (2), 220 (30), 205 (100). Found C 72.32, H 8.44; calcd for  $\text{C}_{20}\text{H}_{28}\text{O}_4$ , C 72.28, H 8.44%.

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