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# TERPENOIDS FROM *SALVIA TCHIHATCHEFFII*

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**Key Word Index**—*Salvia tchihatcheffii*; Lamiaceae; terpenoids; tchihatine; salvitchihatine; erithrodiol diacetate.

**Abstract**—From the roots of *Salvia tchihatcheffii*, two new hydroxyabieta-tetraenes diterpenes tchihatine and salvitchihatine, and a new triterpene, erithrodiol diacetate, were isolated in addition to known compounds. 

## INTRODUCTION

As a part of our continuing studies on *Salvia* species, we have investigated an endemic species in Turkey, *S. tchihatcheffii* (Fisch. & Mey.) Boiss., syn: *Dracocephalum tchihatcheffi* Fisch. & Mey. [1]. From this plant, we have isolated the known terpenoid compounds (+)-ledol [2], dehydroabietic acid [3], 6,7-dehydroroyleanone [4], 3-acetylerithrodiol [5], 28-acetylerithrodiol [6], the acetate of 3$\beta$-hydroxyolean-12-en-28-al [7], sitosterol and stigmasterol, and the flavone salvigenine. In addition, two new diterpenoids tchihatine (**1**) and salvitchihatine (**2**), and a new triterpene, erithrodiol diacetate (**3**), were isolated. To date, of the 40 *Salvia* species studied only three, *S. crypthanta*, *S. pisidica* [8] and *S. pomifera* [9], yielded erithrodiol derivatives.

## RESULTS AND DISCUSSION

According to the literature data, the identification of the three isomers ledol, globulol and viridiflorol is difficult, because their spectral data, particularly those of ledol and viridiflorol, are very similar. In order to identify the sesquiterpene isolated in this study, we carried out 2D NMR experiments (NOESY and HMBC) and found the sesquiterpene to be (+)-ledol. Based on the discussions given in a recent study [2], the structure of ledol is further proven (see Experimental).

Two of the new compounds were diterpenes. They were obtained as a mixture and separated by preparative TLC. Compound **1** was assigned the molecular formula of $C_{20}H_{28}O$ (HR mass spectrometry, $m/z = 284.2147$ $[M]^+$. The $^1H$ NMR spectrum of **1** showed two narrow doublets at $\delta$ 7.20 (1H, $J = 1.5$ Hz, H-12) and 6.20 (1H, $J = 1.5$ Hz, H-14), two broad singlets at $\delta$ 4.78 and 4.72 (each 1H, $CH_2$-16), a vinylic methyl at $\delta$ 1.85 (3H, *s*, Me-17) and three methyl signals as singlets at $\delta$ 0.96, 0.72 and 0.70 (Me-18, Me-19 and Me-20). Spin decoupling experiments showed that H-1$\beta$ ($\delta$ 3.16, *br d*, $J = 12$ Hz) was coupled with $H_2$-2 ($\delta$ 2.55, *m*), $H_2$-2 with H-3a ($\delta$ 2.25, *m*) and H-3b ($\delta$ 1.60, *m*), H-6a ($\delta$ 1.28, *m*) with H-7a ($\delta$ 2.25, *m*) and H-12 with H-14. The $^{13}C$ NMR (APT experiment) spectrum displayed 20 carbon atoms consisting of four methyl quartets, six methylene triplets, three methine doublets and seven carbon singlets. The assignments of the carbons and protons were made by means of a HETCOR experiment (Table 1). Since no hydrogen signal next to a hydroxyl group was present in the $^1H$ NMR spectrum, the hydroxyl group had to be tertiary and in the C ring at C-11; H-1$\beta$ at $\delta$ 3.16 (1H, *br d*, $J = 12$ Hz) confirmed the presence of a C-11 hydroxyl group [10]. The spectral data indicated the structure of **1** to be 11-hydroxyabieta-8,11,13,15-tetraene.

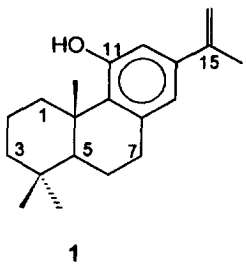
The second new diterpenoid **2** was assigned the molecular formula $C_{20}H_{28}O$. The $^1H$ NMR spectrum of **2** showed the presence of aromatic signals similar to those of **1** at $\delta$ 7.20 (1H, *d*, $J = 1.5$ Hz, H-11) and 6.21 (1H, *d*, $J = 1.5$ Hz, H-14) and an olefinic proton signal at $\delta$ 6.59 (1H, *t*, $J = 4$ Hz, H-6). An isopropyl side chain was observed at $\delta$ 2.88 (1H, *sept*, $J = 7$ Hz, H-15) and 1.14 (6H, *d*, $J = 7$ Hz, Me-16 and Me-17). Other methyl signals were at $\delta$ 1.1, 1.18, and 1.27 (Me-18, Me-19 and Me-20). Spin decoupling experiments showed the relationships between H-6 ($\delta$ 6.59), H-7a ($\delta$ 2.25, *m*) and H-7b ($\delta$ 3.6 *m*), between H-1$\beta$ ($\delta$ 3.10, *br d*, $J = 9$ Hz) and H-2 ($\delta$ 2.5, *m*) and between H-15, Me-16 and Me-17. The $^{13}C$ NMR (APT) spectrum as well as HETCOR experiments allowed the assignment of all of the protons and carbons (Table 1). The spectral data showed that the structure of **2**, which we have

Table 1. $^1H$ and $^{13}C$ NMR data for compounds **1** and **2**

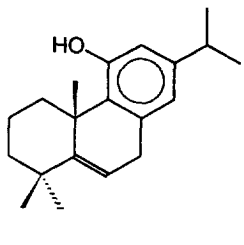
| Position | 1 | | 2 | |
|---|---|---|---|---|
| | $^1H$ | $^{13}C$ | $^1H$ | $^{13}C$ |
| 1 | 3.16 *br d*, 1.6 *m* | 38.7 | 3.10 *br d*, 1.80 *m* | 40.3 |
| 2 | 2.55 *m* | 18.6 | 2.5 *m* | 20.2 |
| 3 | 2.25 *m*, 1.60 *m* | 41.2 | 2.30 *m*, 1.80 *m* | 40.8 |
| 4 | — | 31.6 | — | 33.0 |
| 5 | 2.60 *t* | 46.2 | — | 147.1 |
| 6 | 1.58 *m*, 1.28 *m* | 20.2 | 6.59 *t* | 135.2 |
| 7 | 3.60 *m*, 2.25 *m* | 31.8 | 2.25 *m* | 34.6 |
| 8 | — | 126.1 | — | 126.5 |
| 9 | — | 147.0 | — | 146.5 |
| 10 | — | 38.8 | — | 36.4 |
| 11 | — | 151.2 | — | 150.9 |
| 12 | 7.20 *d* | 140.9 | 7.20 *d* | 140.9 |
| 13 | — | 131.4 | — | 130.8 |
| 14 | 6.20 *d* | 106.1 | 6.21 *d* | 106.3 |
| 15 | — | 144.2 | 2.88 *sept* | 28.6 |
| 16 | 4.72 *br s*, 4.78 *br s* | 110.3 | 1.14 *d* | 23.6 |
| 17 | 1.85 *s* | 16.1 | 1.14 *d* | 23.6 |
| 18 | 0.72 *s* | 33.4 | 1.10 *s* | 32.1 |
| 19 | 0.70 *s* | 23.5 | 1.18 *s* | 24.0 |
| 20 | 0.96 *s* | 24.5 | 1.27 *s* | 24.6 |

named salvitchihatine is 11-hydroxyabieta-5,8,11,13-tetraene.

The HREI mass spectrum of the third new compound indicated the molecular formula $C_{34}H_{54}O_4$. Its IR spectrum exhibited acetyl absorbances at 1737 and 1242 $cm^{-1}$. The $^1H$ NMR spectrum showed similarities to that of erithrodiol, displaying the signals for an olefinic proton at $\delta$ 5.19 (*t*, $J = 3$ Hz, H-12) and the C-28 methylene protons at $\delta$ 3.70 and 4.03 (each 1H, *d*, $J = 11$ Hz); these were shifted downfield compared to erithrodiol, indicating the presence of an acetyl group at C-28. H-3 was also shifted downfield to $\delta$ 4.5 (*dd*, $J = 7$ and 10 Hz), indicating the second acetyl group at C-3$\beta$. Seven methyl signals were observed as singlets at $\delta$ 0.86, 0.87, 0.89, 0.93, 0.95, 1.16 and 1.27. The two acetyl methyls gave rise to a singlet at $\delta$ 2.07. The mass fragmentation pattern of **3** indicated an olean type structure with RDA degradation peaks at *m/z* 276 and 203. Acetylation of erithrodiol as well as both 3- and 28-acetylerithrodiol yielded the same compound **3**. The $^1H$ NMR spectra of each acetylated compounds were exactly the same, further verifying the structure of **3** to be 3,28-diacetylerithrodiol.




**1**




**2**

## EXPERIMENTAL

*General.* IR: $CHCl_3$; NMR: 200 MHz ($^1H$) and 50.32 MHz ($^{13}C$), $CDCl_3$; TLC; Kieselgel 60 $F_{254}$ precoated plates; CC: silica gel (60–200 mesh) and Sephadex LH-20

*Plant material. Salvia tchihatcheffii* was collected from central Turkey (Mürted-Kazan, Ankara) in July and identified by Prof. Dr Semra Kurucu. A voucher specimen (AEF 19570) is deposited at the Herbarium of the Faculty of Pharmacy, University of Ankara.

*Extraction and isolation.* Dried and powdered roots (3.5 kg) were macerated with $Me_2CO$, and the solvent evapd *in vacuo* to yield a residue (52 g) which was fractionated by CC on silica gel (5 × 80 cm). The column was eluted with petrol, and a gradient of EtOAc was added up to 100%, followed by EtOH. The following compounds were isolated: **1** (10 mg); ledol (29 mg); 3-acetylerithrodiol (18 mg); dehydroabietic acid (7 mg); **2** (12 mg); **3** (20 mg); 28-acetylerithrodiol (10 mg); 6,7-dehydroroyleanone (15 mg); acetate of 3$\beta$-hydroxyolean-12-en-28-al (12 mg); salvigenine (45 mg); sitosterol (18 mg); stigmasterol (17 mg).

*Tchihatine* (**1**). Amorphous, UV $\lambda_{max}^{MeOH}$ nm (log $\varepsilon$): 284 (3.5), 225 (4.0); IR $\nu_{max}^{CHCl_3}$ $cm^{-1}$: 3470, 2960, 2840, 1680, 1590, 1520, 1460, 1380, 1150, 1040, 980, 880, 760; $^1H$ and $^{13}C$ NMR ($CDCl_3$): Table 1; HREIMS *m/z* (rel. int.): 284.2147, calc. 284.2140 $[M]^+$ (10), 248 (7), 221 (8), 191 (10), 126 (25), 113 (50), 83 (55), 70 (65), 59 (85).

*Salvitchihatine* (**2**). Amorphous, UV $\lambda_{max}^{MeOH}$ nm (log $\varepsilon$): 274 (3.6), 226 (4.1); IR $\nu_{max}^{CHCl_3}$ $cm^{-1}$: 3450, 2980, 2860, 1605, 1590, 1525, 1480, 1380, 1140, 1050, 980, 770; $^1H$ and $^{13}C$ NMR ($CDCl_3$): Table 1; HREIMS *m/z* (rel. int.) 284.2143, calc. 284.2140 $[M]^+$ (15), 261

(8), 243 (10), 221 (10), 191 (12), 163 (10), 141 (15), 125 (30), 113 (45), 70 (65), 57 (85).

*Erithrodiol diacetate* (**3**). $[\alpha]_D^{20}$ +65° (*c* 0.1, $CHCl_3$), mp 190°. IR $\nu_{max}^{CHCl_3}$ $cm^{-1}$: 2960, 2940, 2860, 1737, 1460, 1380, 1370, 1242, 1030, 760; $^1H$ NMR ($CDCl_3$): see text; HREIMS *m/z* (rel. int.): 526.4034, calc. 526.4023 $[M]^+$ (10), 484 $[M-Ac]^+$ (55), 424 $[484-HOAc]^+$ (93), 409 $[424-Me]^+$ (35), 276 [C+D rings]$^+$ (10), 203 $[276-CH_2OAc]^+$ (100), 189 (30), 119 (30), 15 (28), 69 (40).

(+)-*Ledol*. $[\alpha]_D^{20}$ +8.9 (*c* 0.1, $CHCl_3$). IR $\nu_{max}^{CHCl_3}$ $cm^{-1}$: 3422, 1465, 1385, 1175; $^1H$ NMR ($CDCl_3$): $\delta$ 0.11 (1H, *t*, $J = 9.2$ Hz, H-7), 0.61 (1H, *ddd*, $J = 12$, 9.2, 6 Hz, H-6), 0.91 (3H, *d*, $J = 7$ Hz, H-15), 0.98 and 1.01 (each 3H, *s*, H-12, H-13), 1.14 (3H, *s*, H-14); EIMS *m/z* (rel. int.): 222 $[M]^+$ (10), 204 $[M-H_2O]^+$ (70), 189 $[M-H_2O-Me]^+$ (55), 176 (14), 161 (100), 147 (31), 135 (30), 121 (49), 109 (92), 93 (52), 81 (53), 69 (72); $^{13}C$ NMR ($CDCl_3$): 16.10 (C-12), 16.31 (C-15), 18.39 (C-11), 18.80 (C-8), 22.28 (C-6), 25.76 (C-2), 28.54 (C-13), 28.66 (C-7), 29.07 (C-3), 32.10 (C-14), 37.76 (C-9), 38.44 (C-4), 39.71 (C-5), 58.20 (C-1), 74.95 (C-10).

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