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Ayhan Ulubelen, and Gülaçti Topcu

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NEW ABIETANE DITERPENOIDS FROM *SALVIA MONTBRETII*

AYHAN ULUBELEN*

Faculty of Pharmacy, University of Istanbul, Istanbul, Turkey

and GÜLAÇTI TOPCU

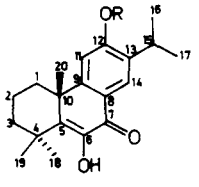
TUBITAK, Marmara Research Center, Department of Chemistry, P.O. Box 74, 41470 Gebze-Kocaeli, Turkey

ABSTRACT.—Five known compounds, ferruginol, ferruginyl 12-methyl ether, taxodione, hypargenin F, and demethylcryptojaponol, and three new abietane-type diterpenoids, montbretol (6,12-dihydroxyabieta-5,8,11,13-tetraen-7-one) [**1**], montbretyl 12-methyl ether (6-hydroxy-12-methoxyabieta-5,8,11,13-tetraen-7-one) [**2**], and 14-hydroxyferruginol [**3**], were isolated from the roots of *Salvia montbretii*. Structures were established by ir, uv, ms, and nmr spectral data.

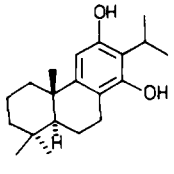
In continuation of our chemical investigations on the diterpenoid compounds from *Salvia* species, we now report on *Salvia montbretii* Benth. (Labiatae). Eight abietane-type diterpenoids have been isolated from the roots of this plant, five of which have been previously isolated from other *Salvia* species: namely ferruginol (1), ferruginyl 12-methyl ether (2), taxodione (2,3), hypargenin F (4), and demethylcryptojaponol (5). The other three are new compounds whose structures were established by spectral data as montbretol (6,12-dihydroxyabieta-5,8,11,13-tetraen-7-one) [**1**], montbretyl 12-methyl ether (6-hydroxy-12-methoxyabieta-5,8,11,13-tetraen-7-one) [**2**], and 14-hydroxyferruginol [**3**].

The hrms of montbretol [**1**] indicated a molecular formula $C_{20}H_{26}O_3$ (*m/z* 314.1854). The ^{13}C-nmr, SFORD, and APT experiments indicated the presence of five methyl quartets, three methylene triplets, three methine doublets and nine carbon singlets for **1**. Biogenetic consideration and the presence of an isopropyl group at δ 1.30 (3H, d, J = 7 Hz) and 1.32 (3H, d, J = 7 Hz) (H-16 and H-17), the methine proton at δ 3.17 (1H, septet, J = 7 Hz, H-15), and the three methyl signals at δ 1.68 (3H, s, H-20), 1.36 (3H, s), and 1.26 (3H, s) (H-18 and H-19) in the ^{1}H-nmr spectrum of **1** were reminiscent of an abietane skeleton (6,7). The ir spectrum of **1** showed a hydroxyl (3450 cm^{-1}), a conjugated carbonyl (1660 cm^{-1}), and aromatic signals (3040, 1605, 1560, 1505 cm^{-1}). The uv spectrum indicated the presence of a conjugated system (343 nm). In the ^{1}H-nmr spectrum there were two aromatic proton resonances at δ 6.45 (1H, s, H-11) and 7.71 (1H, s, H-14) as well as a hydroxyl signal at δ 6.01 (1H, br s, 6-OH) (D_2O exchangeable).

The oxo group was placed at C-7 for the following reasons. The chemical shift of one of the protons (δ 7.71) is only possible when it is in the vicinity of an oxo group, which suggested C-1 or C-7 as likely positions for this group. The H-1β signal was observed at δ 3.30 as shown by spin decoupling experiments. Considering these data, the oxo



1 R=H
2 R=Me



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group was placed at C-7. Spin decoupling experiments showed the presence of three sequential methylene groups, C-1 to C-3; when the signal at δ 3.30 (1H, dt, J = 3, 3, 13 Hz, H-1β) was irradiated, the signals at δ 1.96 (1H, ddd, J = 3, 12, 14 Hz, H-2β), 1.62 (1H, m, H-2α), and 1.49 (1H, ddd, J = 4.5, 13, 14 Hz, H-1α) were affected. When the signal at δ 2.34 (1H, br dd, J = 7 and 14 Hz, H-3β) was irradiated the signals at δ 1.96 (H-2β), 1.62 (H-2α), and 1.28 (1H, m, H-3α) were simplified, and when the signal at δ 1.96 (H-2β) was irradiated, the signals at 3.30 ppm (H-1β), 1.49 (H-1α), 1.62 (H-2α), and 2.34 (H-3β) were affected. Since one methyl signal appeared at δ 1.68 (H-20), the hydroxyl group was assigned to C-6 (7–9). Due to the lack of a proton signal geminal to the hydroxyl group, the double bond was placed between C-5 and C-6. This is in agreement with a uv maximum at 343 nm.

Montbretyl 12-methyl ether [**2**] is a methyl ether of the first compound. The hrms of **2** indicated a molecular formula $C_{21}H_{28}O_3$ (*m/z* 328.2050). Its uv spectrum was quite similar to that of **1** (342 nm). The ir spectrum indicated an aromatic ring system (3050, 1620, 1597, 1560, 1505 cm^{-1}), a hydroxyl (3420 cm^{-1}), and a conjugated carbonyl (1665 cm^{-1}). The ^{13}C-nmr spectrum and SFORD and APT experiments indicated nine quarternary carbon singlets, three methine doublets, three methylene triplets, and six methyl quartets for **2** (Table 1). A detailed inspection of the ^{1}H-nmr spectrum of **2**, as well as the COSY spectrum and spin decoupling experiments, allowed unambigous assignment of the protons. The ^{1}H-nmr spectrum showed signals quite similar to those of compound **1** at δ 7.73 (1H, s, H-14), 6.48 (1H, s, H-11), 6.29 (1H, s, 6-OH) (D_2O exchangeable), 3.84 (3H, s, 12-OMe), 3.25 (1H, septet, J = 7 Hz, H-15), 1.28 (6H, d, J = 7 Hz) (H-16 and H-17), 1.67 (3H, s, H-20), 1.37 (3H, s), and 1.30 (3H, s) (H-18 and H-19). The COSY spectrum of **2** showed correlation between H-15 and H-16, H-17, while no correlation was seen between the signals at δ 7.73 and

TABLE 1. ^{13}C-nmr Data for Compounds **1**, **2**, and **3** ($CDCl_3$, TMS).

Carbon	Compound		
	1	**2**	**3**
C-1	31.70	31.73	37.84
C-2	18.24	18.12	17.08[a]
C-3	34.00	34.14	38.84
C-4	34.00	35.08	31.21
C-5	139.70	140.15	51.42
C-6	142.70	143.10	17.82[a]
C-7	185.20	185.39	30.44
C-8	121.50	123.20	114.36
C-9	149.20	148.80	133.46
C-10	41.30	41.70	38.84
C-11	108.70	107.60	109.15
C-12	149.20	152.30	141.75
C-13	131.90	130.78	121.51
C-14	115.82	117.70	143.17
C-15	25.32	25.40	26.50
C-16	21.70	21.85	22.22[b]
C-17	21.70	21.85	22.17[b]
C-18	31.70	31.76	31.21
C-19	24.20	24.30	21.80
C-20	27.60	27.80	23.78
C-21	—	57.50	—

[a,b]Interchangeable assignments.

6.48, indicating the para positions (H-11 and H-14). Spin decoupling experiments indicated three sequential methylene groups (C-1 to C-3). Due to reasons similar to those given for compound **1**, the hydroxyl and the carbonyl groups were placed at C-6 and C-7, respectively. Thus, the spectral data indicated that compound **2** is montbretyl 12-methyl ether.

Compound **3** had molecular formula $C_{20}H_{30}O_2$ (*m/z* 302.2260). Its uv spectrum indicated an aromatic ring without further conjugation (258 nm). The ir spectrum showed a strong signal for hydroxyl(s) at 3440 cm^{-1}, aromatic signals (3050, 1605, 1580, 1560, 1500 cm^{-1}), and no carbonyl signal. The ^{1}H-nmr spectrum of **3** showed methyl signals at δ 1.18 (3H, s), 1.20 (3H, s), 1.22 (3H, s) (H-18, H-19, H-20) and δ 1.25 (6H, d, J = 6.8 Hz) (H-16 and H-17), and a methine proton signal at δ 3.24 (1H, septet, J = 6.8 Hz, H-15). Since H-1β was observed at δ 2.4 (1H, br d, J = 13 Hz) the aromatic proton at δ 7.15 (1H, s) was assigned to H-11. Therefore the second hydroxyl group was placed at C-14. When the hydroxyl group is at C-11, the H-1β signal normally appears downfield below 3.40 ppm (5,10). No other signals were present between 3.24 and 7.15 ppm, so the hydroxyl groups are in ring C at the C-12 and C-14 positions. ^{13}C nmr and SFORD experiments showed five aromatic carbon singlets and only one doublet, no carbonyl, five methyl quartets, three methine doublets, five methylene triplets, and seven quarternary carbon singlets, consistent with the suggested structure for **3**.

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—Spectra were recorded with the following instruments: ^{1}H nmr and ^{13}C nmr on Bruker AC 200 L; ir on Perkin-Elmer 983; uv on Varian Techtron 635; hrms Kratos MS-30 with D-55 data system.

PLANT MATERIAL.—Roots of *S. montbretii* were collected from southeast Turkey, Gaziantep, in June 1989 and identified by Dr. K. Alpinar, Istanbul. A voucher specimen (ISTE 42443) is deposited in the Herbarium of the Faculty of Pharmacy, University of Istanbul.

ISOLATION OF THE COMPOUNDS.—Powdered roots of the plant (437 g) were extracted with petroleum ether and then Me_2CO. Since both extracts showed the same tlc spots, they were combined (11 g) and fractionated on a Si gel column (5 × 60 cm). Further separation was done on Sephadex LH-20 columns and, when necessary, on preparative tlc plates. The following compounds were obtained: taxodione (50 mg), ferruginyl 12-methyl ether (9 mg), montbretyl 12-methyl ether (8 mg), 14-hydroxyferruginol (9 mg), ferruginol (13 mg), hypargenin F (12 mg), demethylcryptojaponol (8 mg), and montbretol (8 mg).

Montbretol [**1**].—Yellow, amorphous compound: uv λ max (MeOH) 343 (log ε 3.6), 250 (log ε 4.0) nm; ir ν max ($CHCl_3$) see text; ^{1}H nmr ($CDCl_3$) see text; ^{13}C nmr see Table 1; hrms *m/z* (rel. int. %) $[M]^+$ 314.1854 ($C_{20}H_{26}O_3$, calcd 314.1881) (25), $[M-Me]^+$ 299 (23), 244 (50), 229 (15), 129 (15), 115 (20), 91 (33), 73 (15), 71 (40), 57 (38).

Montbretyl 12-methyl ether [**2**].—Yellow, amorphous compound: uv λ max (MeOH) 342 (log ε 3.6), 248 (log ε 4.2) nm; ir ν max ($CHCl_3$) see text; ^{1}H nmr see text; ^{13}C nmr see Table 1; hrms *m/z* (rel. int. %) $[M]^+$ 328.2050 ($C_{21}H_{28}O_3$, calcd 328.2038) (10), $[M-Me]^+$ 313 (7), 278 (14), 257 (10), 217 (5), 113 (15), 71 (30), 57 (50).

14-Hydroxyferruginol [**3**].—Colorless compound: uv λ max (MeOH) 258 (log ε 3.4), 224 (log ε 4.3) nm; ir ν max ($CHCl_3$) see text; ^{1}H nmr ($CDCl_3$) see text; ^{13}C nmr see Table 1; hrms (rel. int. %) $[M]^+$ 302.2260 ($C_{20}H_{30}O_2$, calcd 302.2245) (12), $[M-Me]^+$ 287 (3), 260 (20), 245 (15), 235 (28), 219 (43), 205 (13), 115 (15), 95 (14), 71 (15), 58 (100), 57 (38).

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LITERATURE CITED

1. T. Nakanishi, H. Miyasaka, M. Nasu, H. Hashimoto, and K. Yoneda, *Phytochemistry*, **22**, 721 (1983).

2. A. Ulubelen and E. Tuzlacı, *J. Nat. Prod.*, **53**, 1597 (1990).
3. S.M. Kupchan, A. Karım, and C. Marcks, *J. Am. Chem. Soc.*, **90**, 5923 (1968).
4. A. Ulubelen, N. Evren, E. Tuzlacı, and C. Johansson, *J. Nat. Prod.*, **51**, 1178 (1988).
5. J.A. Hueso-Rodrıguez, M.L. Jimeno, B. Rodrıguez, G. Savona, and M. Bruno, *Phytochemistry*, **22**, 2005 (1983).
6. P. Rüedi, *Helv. Chim. Acta*, **67**, 1116 (1984).
7. T. Miyase, P. Rüedi, and C.H. Eugster, *Helv. Chim. Acta*, **60**, 2770 (1977).
8. M. Moir, P. Rüedi, and C.H. Eugster, *Helv. Chim. Acta*, **56**, 2539 (1973).
9. M. Hensch, P. Rüedi, and C.H. Eugster, *Helv. Chim. Acta*, **58**, 1921 (1975).
10. R.V. Stevens and G.S. Bisacchi, *J. Org. Chem.*, **47**, 2396 (1982).

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