Phytochemistry, Vol. 26, No. 12, pp. 3305–3308, 1987.
Printed in Great Britain.

0031-9422/87 $3.00 + 0.00
Pergamon Journals Ltd

TRITERPENOIDS FROM *SALVIA DESERTA*

GIUSEPPE SAVONA, MAURIZIO BRUNO, BENJAMÍN RODRÍGUEZ* and JOSÉ L. MARCO*

Istituto di Chimica Organica dell'Università, Archirafi 20, 90123 Palermo, Italy; *Instituto de Química Orgánica, CSIC, Juan de la Cierva 3, 28006 Madrid, Spain

(*Received* 10 *March* 1987)

Key Word Index—*Salvia deserta*; Labiatae; triterpenes; lupane and oleanane derivatives.

Abstract—From the aerial parts of *Salvia deserta* a new oleanane and two new lupane triterpenoids have been isolated, together with five already known ursane, oleanane and lupane derivatives. The structures of the new substances were established by spectroscopic means.

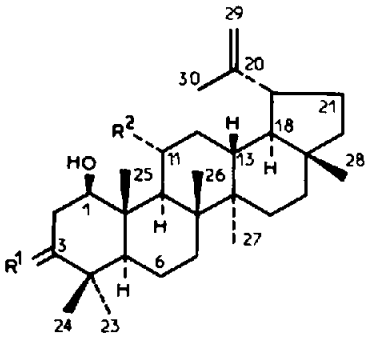
INTRODUCTION

In continuation of our studies on the triterpenoid compounds from *Salvia* species [1–3], we have now investigated the aerial parts of *S. deserta* Schang. From this material eight triterpene derivatives have been isolated, five of which are the previously known ursolic, oleanolic and 2α,3β-dihydroxyolean-12-en-28-oic acids [4], lup-20(29)-ene-1β,3β-diol (**1**) [5–7] and 11α,20-dihydroxylupan-3-one (**2**) [2]. The other three are new substances, whose structures were established as 1β,11α-dihydroxylup-20(29)-en-3-one (**3**), 1β,11α,20-trihydroxylupan-3-one (**4**) and 1β,11α-dihydroxyolean-18-en-3-one (**5**).

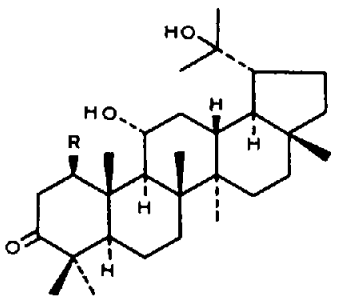
Although compound **1** is already known as a natural [5, 6] and synthetic [7] substance, its complete physical and spectroscopic data have not been reported in the literature [5–7] and they are included in Tables 1 and 2 and the experimental part of this communication.

RESULTS AND DISCUSSION

The first of the new triterpenoids (**3**) had a molecular formula $C_{30}H_{48}O_3$ and its IR spectrum showed hydroxyl (3300 cm^{-1}), ketone (1713 cm^{-1}) and vinylidene group (3070, 1640, 895 cm^{-1}) absorptions. Its ^1H NMR spec-



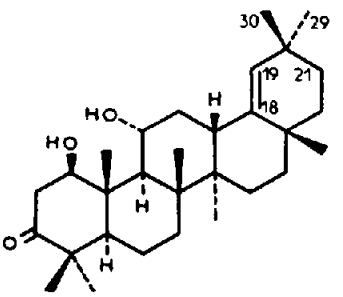
1 R^1 = αH, βOH; R^2 = H



2 R = H

3 R^1 = O; R^2 = OH

4 R = OH



5

Table 1. ^{1}H NMR data of compounds 1, 3–5 (TMS as int. standard)*

	1†	3†	4‡	5†
H-1α	3.43 *dd*	4.08 *dd*	4.44 *dd*	4.13 *dd*
H-2α	§	2.21 *dd*	2.59 *dd*	2.20 *dd*
H-2β	§	3.03 *dd*	3.25 *dd*	3.08 *dd*
H-3α	3.24 *dd*	—	—	—
H-9α	§	1.61 *d*	§	1.64 *d*
H-11β	§	3.89 *td*	4.10 *td*	3.94 *td*
H-12β	§	2.05 *ddd*	§	1.78 *ddd*
H-13β	2.38 *td*	2.40 *td*	§	2.48 *ddd*
H-19	2.16 *m*	§	§	4.87 *br s*‖
H_A-29	4.68 *d*	4.73 *d*	—	—
H_B-29	4.55 *dd*	4.60 *dd*	—	—
C(Me)	1.67 *br s* (Me-30)	1.70 *br s* (Me-30)	1.41 *s*	1.25 *s*
	1.04 *s*	1.08 *s*	1.29 *s*	1.09 *s*
	0.95 *s*	1.07 *s*	1.20 *s*	1.09 *s*
	0.95 *s*	1.05 *s*	1.15 *s*	1.08 *s*
	0.90 *s*	1.01 *s*	1.11 *s*	1.03 *s*
	0.79 *s*	0.89 *s*	1.06 *s*	0.96 *s*
	0.75 *s*	0.80 *s*	1,06 *s*	0.94 *s*
	—	—	0.84 *s*	0.79 *s*
J (Hz)				
1α,2α	4.7	2.0	1.8	1.2
1α,2β	11.3	8.5	8.8	8.7
2α,2β	§	13.4	13.4	13.6
2α,3α	4.4	—	—	—
2β,3α	12.1	—	—	—
9α,11β	§	10.7	10,6	10.9
11β,12α	§	10.7	10.6	10.9
11β,12β	§	5.3	5.2	4.5
12α,12β	§	11.9	§	12.7
12α,13β	10.8	10.8	§	12.9
12β,13β	5.8	5.8	§	3.6
13β,18α	10.8	10.8	§	—
13β,19	§	§	§	2.0
19β,29B	1.4	1.2	—	—
29A,29B	2.4	2.1	—	—

*All these assignments have been confirmed by double resonance experiments.
†In $CDCl_3$.
‡In pyridine-d_5.
§Overlapped signal.
‖$W_{1/2}$ = 3.5 Hz.

trum (Table 1) showed signals for six C-Me singlets, an allylic methyl group, a vinylidene grouping, an equatorial hydroxyl group (geminal proton at δ3.89, *td*) placed between a methylene and a methine groups ($J_{aa'}$ = $J_{aa''}$ = 10.7 Hz; $J_{ae'}$ = 5.3 Hz), and another hydroxymethine group (δ4.08, *dd*, $J_{aa'}$ = 8.5 Hz, $J_{ae'}$ = 2.0 Hz) which must also be equatorial and placed between a tetrasubstituted sp^3 carbon atom and a methylene grouping. The protons of this last methylene appeared at δ3.03 (*dd*) and 2.21 (*dd*, J_{gem} = 13.4 Hz), thus establishing a partial structure such as (C)-CH_2-CHOH-(C), in which one of the fully substituted carbons may be the ketone function revealed by the IR spectrum of 3.

All the above data can be accommodated only on a lup-20(29)-ene triterpenoid structure with a hydroxyl group at the C-11α position [2, 8] and a 1β-hydroxy-3-keto or 1-keto-3β-hydroxy structural moiety.

The ^{13}C NMR spectrum of 3 (Table 2) was in complete agreement with a 1β,11α-dihydroxylup-20(29)-en-3-one structure (3) [8, 9–11], since the carbon atom chemical shifts (3, Table 2) were identical with those calculated from lupeol [11] taking into account the introduction of two hydroxyl groups at the C-1β [10, 13, 14] and C-11α [8–10] positions and the existence of a C-3 keto group [11, 15] instead of the C-3β hydroxyl group of lupeol. In particular, the C-4, C-23 and C-24 carbon atom resonances (δ47.3, 28.7 and 19.6, respectively, Table 2) were in agreement with a 1β-hydroxy-3-keto partial structure (3) and not with the isomeric 1-keto-3β-hydroxy moiety, in which the expected chemical shift values for these carbons

Table 2. ^{13}C NMR chemical shifts of compounds 1, 3–5 (TMS as int. standard)

C	1*	3*	4†	5*
1	79.0 *d*‡	78.6 *d*	79.4 *d*	78.9 *d*
2	37.5 *t*	43.0 *t*	44.2 *t*	43.1 *t*
3	75.7 *d*	216.4 *s*	216.3 *s*	216.5 *s*
4	38.9 *s*	47.3 *s*	47.3 *s*	47.2 *s*
5	53.1 *d*	50.8 *d*	50.6 *d*[a]	50.9 *d*
6	18.0 *t*	19.5 *t*	19.9 *t*	19.4 *t*
7	34.1 *t*	33.6 *t*	34.2 *t*	33.2 *t*
8	41.3 *s*	42.4 *s*[a]	43.6 *s*[b]	42.6 *s*[a]
9	51.4 *d*	55.2 *d*	56.1 *d*	55.9 *d*
10	43.5 *s*	43.9 *s*[a]	44.6 *s*[b]	43.9 *s*[a]
11	23.8 *t*	69.4 *d*	69.3 *d*	70.0 *d*
12	25.0 *t*	36.3 *t*	35.9 *t*	37.1 *t*
13	38.0 *d*	36.7 *d*	36.9 *d*	37.3 *d*
14	42.8 *s*	42.6 *s*[a]	43.8 *s*[b]	42.9 *s*[a]
15	27.4 *t*	27.4 *t*	28.0 *t*	27.4 *t*
16	35.5 *t*	35.3 *t*	39.9 *t*	37.2 *t*
17	42.9 *s*	42.9 *s*	42.9 *s*	34.3 *s*
18	48.3 *d*	47.6 *d*[b]	48.4 *d*	141.2 *s*
19	47.9 *d*	47.7 *d*[b]	50.5 *d*[a]	130.1 *d*
20	150.8 *s*	150.2 *s*	72.1 *s*	32.4 *s*
21	29.7 *t*	29.7 *t*	28.6 *t*	33.9 *t*
22	39.9 *t*	39.7 *t*	40.2 *t*	37.4 *t*
23	27.8 *q*	28.7 *q*	28.8 *q*	28.9 *q*
24	14.9 *q*	19.6 *q*	19.6 *q*	19.3 *q*
25	11.9 *q*	13.5 *q*	14.9 *q*	14.1 *q*[b]
26	16.2 *q*	17.0 *q*	17.3 *q*	17.4 *q*
27	14.4 *q*	14.3 *q*	14.2 *q*	14.2 *q*[b]
28	18.0 *q*	18.0 *q*	20.0 *q*	25.2 *q*
29	109.4 *t*	110.1 *t*	25.3 *q*	31.3 *q*
30	19.2 *q*	19.3 *q*	32.5 *q*	29.1 *q*

*In $CDCl_3$.
†In pyridine-d_5.
‡SFORD multiplicity.
[a,b]Assignments bearing the same sign may be interchanged.

[11] are δ 38.8, 28.0 and 15.0, respectively, as in compound 1 (see Table 2).

Another of the new triterpenoids isolated from *S. deserta* had a molecular formula $C_{30}H_{50}O_4$ and its ^{1}H NMR spectrum (4, Table 1) showed signals for two secondary hydroxyl groups at the C-1β and C-11α positions identical with those found in compound 3. In addition, triterpenoid 4 also possessed a ketone function (ν_{CO} 1708 cm^{-1}, δ_{CO} 216.3, *s*) and the isopropenyl side chain of compound 3 was replaced in 4 by a 2-hydroxypropan-2-yl moiety [^{1}H NMR: no signals of olefinic protons; eight C-Me singlets (Table 1); ^{13}C NMR δ 72.1, *s*, C-20, eight methyl groups (Table 2)]. This conclusion was in complete agreement with the ^{13}C NMR spectrum of 4, which showed C-1–C-17 and C-22–C-27 carbon atom resonances identical with those of 3, whereas the chemical shift differences in the C-18 C-21 and C-28–C-30 carbons (Table 2) clearly showed that triterpenoid 4 was the 20(29)-dihydro-20-hydroxy derivative of 3.

The last triterpenoid (5) isolated from *S. deserta* had a molecular formula $C_{30}H_{48}O_3$ and its IR spectrum showed ketone (1710 cm^{-1}) and hydroxyl (3460, 3390 cm^{-1}) absorptions. Its ^{1}H NMR spectrum (Table 1) showed signals for an 11α-hydroxyl group and a 1β-hydroxy-3-keto structural moiety, all identical with those found in compounds 3 and 4. In addition, triterpenoid 5 possessed a trisubstituted olefinic double bond (olefinic proton at δ4.87, *br s*) and eight methyl groups attached to fully substituted sp^3 carbon atoms (see Table 1). These data suggested that 5 was 1β,11α-dihydroxyolean-18-en-3-one, which was confirmed by the fact that the ^{13}C NMR spectrum of 5 showed C-1–C-13 and C-23–C-26 carbon atom resonances identical with those of compounds 3 and 4 (Table 2), and the C-14–C-22 and C-27–C-30 chemical shifts were the same that those reported for 3β-acetoxyolean-18-ene (germanicol acetate) [16].

From a biogenetic point of view, it is important to note that, apart the C-3β hydroxyl (or ketone) group, oxidation at the C-1 and C-11 positions is a common feature in the oleanane and lupane triterpenoids isolated from plants belonging to the *Salvia* genus [2, 3, 17]. Furthermore, olean-18-ene derivatives such as 5 have been previously found in *Salvia* species [18] and in other genera of Labiatae [19].

EXPERIMENTAL

Mps are uncorr. For general details on methods, see refs [1–3]. Plant materials were collected in June 1986, in the Botanic Garden of Palermo (Italy) and voucher specimens were deposited in the Herbarium of this Centre.

Extraction and isolation of the triterpenoids. Dried and finely powdered *S. deserta* aerial parts (600 g) were extracted with Me_2CO (5 l) at room temp. for a week. The extract was evapd to dryness yielding a residue (10 g) which was chromatographed on a silica gel (Merck, No. 7734, deactivated with 15% H_2O, 200 g) column. Elution with *n*-hexane–EtOAc mixtures gave the following compounds in order of elution: oleanolic acid (30 mg), ursolic acid (40 mg), 1β,11α-dihydroxylup-20(29)-en-3-one (3, 7 mg), 1β,11α-dihydroxyolean-18-en-3-one (5, 5 mg), lup-20(29)-ene-1β,3β-diol (1, 6 mg) [5–7], 2α,3β-dihydroxyolean-12-en-28-oic acid (30 mg) [4], 11α,20-dihydroxylupan-3-one (2, 50 mg) [2] and 1β,11α,20-trihydroxylupan-3-one (4, 20 mg). The previously known compounds were identified by their physical (mp, $[\alpha]_D$) and spectroscopic (^{1}H NMR, IR, MS) data and by comparison (mmp, TLC) with authentic samples.

Lup-20(29)-ene-1β,3β-diol (1). Mp 249–251° (EtOAc–*n*-hexane); $[\alpha]_D^{19}$ +11° ($CHCl_3$ *c*0.311); IR ν_{max}^{KBr} cm^{-1}: 3350 (OH), 3080, 1645, 883 (isopropenyl double bond), 2960, 2930, 2860, 1470, 1460, 1380, 1040, 990; ^{1}H NMR (300 MHz, $CDCl_3$): see Table 1; ^{13}C NMR (75.4 MHz, $CDCl_3$): see Table 2; EIMS (70 eV, direct inlet) *m/z* (rel. int.): 442 $[M]^+$ (9), 427 (4), 424 (24), 409 (5), 406 (7), 391 (5), 257 (14), 231 (11), 229 (25), 219 (15), 204 (31), 193 (81), 189 (44), 177 (58), 121 (61), 109 (60); 95 (67), 81 (54), 69 (60), 55 (73), 43 (100). (Found: C, 81.50; H, 11.19. Calc. for $C_{30}H_{50}O_2$: C, 81.39; H, 11.38%.) (Lit. [5]: mp 251–252°, IR ν_{max}^{KBr} cm^{-1}: 3400, 3050, 1650, 880).

1β,11α-Dihydroxylup-20(29)-en-3-one (3). Mp 234–237° (MeOH); $[\alpha]_D^{18}$ +108° ($CHCl_3$; *c*0.084); IR ν_{max}^{KBr} cm^{-1}: 3300 (OH), 3070, 1640, 895 (isopropenyl double bond), 1713 (ketone), 2960, 2900, 2860, 1460, 1385, 1370, 1035, 985; ^{1}H NMR (300 MHz, $CDCl_3$); see Table 1; ^{13}C NMR (75.4 MHz, $CDCl_3$): see Table 2; EIMS (70 eV, direct inlet) *m/z* (rel. int.): 456 $[M]^+$ (0.5), 438 (16), 423 (11), 420 (40), 405 (6), 324 (100), 309 (16), 229 (14), 203 (24), 135 (45), 121 (62), 119 (33), 109 (53), 107 (62), 95 (72), 81 (45), 69 (55), 55 (46). (Found: C, 79.03; H, 10.49. $C_{30}H_{48}O_3$ requires: C, 78.89; H, 10.59%.)

1β,11α,20-*Trihydroxylupan-3-one* (**4**). Mp 260–264° (MeOH); $[\alpha]_D^{18}$ +69° ($CHCl_3$; *c*0.121); IR ν_{max}^{KBr} cm^{-1}: 3470, 3360, 3240 (OH), 1708 (ketone), 2960, 2900, 1460, 1380, 1320, 1175, 1120, 1040, 990; ^1H NMR (300 MHz, pyridine-d_5): see Table 1; ^{13}C NMR (75.4 MHz, pyridine-d_5): see Table 2; EIMS (70 eV, direct inlet) *m/z* (rel. int.): $[M]^+$ absent, 456 $[M-18]^+$ (2), 441 (9), 438 (19), 421 (18), 342 (100), 324 (96), 309 (21), 203 (25), 189 (24), 163 (26), 149 (29), 132 (52), 121 (59), 107 (55), 95 (78), 81 (52), 69 (58), 59 (69), 55 (42). (Found: C, 76.05; H, 10.57. $C_{30}H_{50}O_4$ requires: C, 75.90; H, 10.62%.)

1β,11α-*Dihydroxyolean-18-en-3-one* (**5**). Mp 229–233° (MeOH); $[\alpha]_D^{20}$ +54° ($CHCl_3$; *c*0.140); IR ν_{max}^{KBr} cm^{-1}: 3460, 3390 (OH), 1710 (ketone), 2960, 2930, 2860, 1460, 1385, 1120, 1015, 990; ^1H NMR (300 MHz, $CDCl_3$): see Table 1; ^{13}C NMR (75.4 MHz, $CDCl_3$): see Table 2; EIMS (70 eV, direct inlet) *m/z* (rel. int.): 456 $[M]^+$ (1.3), 441 (0.8), 438 (4.4), 423 (8), 405 (1), 324 (100), 309 (26), 243 (16), 175 (17), 121 (25), 107 (17), 95 (25), 81 (16), 69 (20), 55 (20). (Found: C, 78.79; H, 10.66. $C_{30}H_{48}O_3$ requires: C, 78.89; H, 10.59%.)

Acknowledgements—We thank the Palermo Botanical Garden Office for the facilities given for the collection of plant materials. This work was supported by the Spanish 'Comisión Asesora de Investigación Cientifica y Técnica' and by funds from 'Ricerca Scientifica M. P. I.' (Rome).

REFERENCES

1. Savona, G. and Rodríguez, B. (1980) *An. Quím.* **76C**, 187.
2. García-Alvarez, M. C., Savona, G. and Rodríguez, B. (1981) *Phytochemistry* **20**, 481.
3. Bruno, M., Savona, G., Hueso-Rodríguez, J. A., Pascual, C. and Rodríguez, B. (1987) *Phytochemistry* **26**, 497.
4. Cheung, H. T. and Feng, M. C. (1968) *J. Chem. Soc. C* 1047.
5. Hui, W.-H. and Li, M.-M. (1978) *Phytochemistry* **17**, 156.
6. Hui, W.-H., Lee, W. K., Ng, K. K. and Chan, C. K. (1970) *Phtochemistry* **9**, 1099.
7. Talapatra, S. K., Bhattacharya, S., Maiti, B. C. and Talapatra, B. (1973) *Chem. Ind. (London)* 1033.
8. Ahmad, V. U. and Mohammad, F. V. (1986) *J. Nat. Prod. (Lloydia)* **49**, 524.
9. Ahmad, V. U., Bano, S., Voelter, W. and Fuchs, W. (1981) *Tetrahedron Letters* **22**, 1715.
10. Eggert, H., Van Antwerp, C. L., Bhacca, N. S. and Djerassi, C. (1976) *J. Org. Chem.* **41**, 71.
11. Wenkert, E., Baddeley, G. V., Burfitt, I. R. and Moreno, L. N. (1978) *Org. Magn. Reson.* **11**, 337.
12. Patra, A., Mitra, A. K., Chatterjee, T. K. and Barua, A. K. (1981) *Org. Magn. Reson.* **17**, 148.
13. González, A. G., Arteaga, J. M., Bretón, J. L. and Fraga, B. M. (1977) *Phytochemistry* **16**, 107.
14. von Carstenn-Lichterfelde, C., Pascual, C., Rabanal, R. M., Rodríguez, B. and Valverde, S. (1977) *Tetrahedron* **33**, 1989.
15. Wehrli, F. W. and Nishida, T. (1979) *Fortsch. Chem. Org. Naturst.* **36**, 1.
16. Patra, A., Mukhopadhyay, A. K. and Mitra, A. K. (1981) *Org. Magn. Reson.* **17**, 166.
17. Ulubelen, A. and Topcu, G. (1984) *Phytochemistry* **23**, 133.
18. González, A. G., Bretón, J. L. and Fraga, B. M. (1971) *J. Chem. Soc. Chem. Commun.* 567.
19. Mazumdar, P. L., Maiti, R. N., Panda, S. K., Mal, D., Raju, M. S. and Wenkert, E. (1979) *J. Org. Chem.* **44**, 2811.