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Phytochemistry, Vol. 28, No. 8, pp. 2206–2208, 1989.
Printed in Great Britain.

0031-9422/89 $3.00+0.00
Pergamon Press plc.

A LUPEOL DERIVATIVE FROM *SALVIA PRATENSIS*

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(*Received in revised form* 30 *January* 1989)

Key Word Index—*Salvia pratensis*; Labiatae; triterpenoids; lupeol derivative; 7β-hydroxylup-20(29)-en-3-one.

Abstract—The aerial parts of *Salvia pratensis* afforded, in addition to the known triterpenoids β-amyrin, germanicol, lupeol and loranthol, a new related lupenol, 7β-hydroxylup-20(29)-en-3-one, whose structure was elucidated by spectroscopic methods and chemical transformations.

INTRODUCTION

A reinvestigation of the chemical constituents of *Salvia pratensis* L. [1, 2] has led to the isolation of one new derivative of lupeol, 7β-hydroxylup-20(29)-en-3-one (**1**). Furthermore the known compounds β-amyrin, germanicol, lupeol [3] and loranthol [4] were isolated.

RESULTS AND DISCUSSION

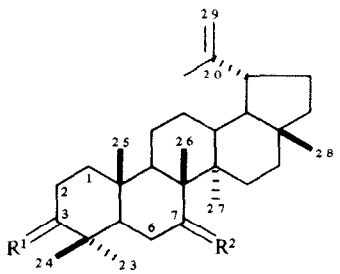
Chromatography of the neutral fraction from an extract of *Salvia pratensis* afforded a crystalline dextrorotatory material, which was identified as a mixture of β-amyrin, germanicol and lupeol by ^{13}C NMR spectral analysis which gave data coincident with those described by Bhattacharyya *et al.* [3].

Mass spectroscopy (M^+ at *m/z* 440) established the molecular formula of compound **1** as $C_{30}H_{48}O_2$. Its IR spectrum indicated a hydroxyl group (3.450 cm^{-1}), a carbonyl group (1.705 cm^{-1}) and an exocyclic methylene (1.645 and 885 cm^{-1}).

The ^1H NMR spectrum (Table 1) of **1** showed signals for six tertiary methyl groups, a vinylic methyl (δ1.64) which was shown to be coupled to two vinylic protons (δ4.65 and 4.53), thus indicating the presence of an isopropenyl group and also signals for a hydroxymethine group (δ3.83, 1H, *dd*, $J_1=6.8$ Hz, $J_2=8.8$ Hz) which must be axial and placed between a tetrasubtituted sp^3 carbon atom and a methylene grouping.

These data suggest a 20(29)-lupene structure with one β-hydroxy group and one keto group for the triterpenoid **1**. The functional groups were confirmed by the following reactions of this compound: the acetylation afforded a monoacetyl derivative **1a** and the Sarett oxidation gave the diketone **3**.

The carbonyl group of the compound **1** may be in any position with the exclusion of ring E (owing to its IR absorption), but it was located in position C-3 (the most likely on biosynthetic grounds) by comparison of the ^1H NMR data for H-3 in lupeol and acetoxylupeol at δ3.20 and 4.60, respectively [5, 6], with the ^1H NMR



	R^1	R^2
1	O	α-H; β-OH
1a	O	α-H; β-OAc
2	α-H; β-OH	α-H; β-OH
2a	α-H; β-OAc	α-H; β-OAc
3	O	O

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signals corresponding to the hydroxymethine group at δ3.83 for **1** and to the acetoxymethine group at δ5.20 in the compound **1a**.

The ^{13}C NMR spectrum (Table 2) of **1** was in complete agreement with the existence of a C-3 ketone [7, 8] instead of the C-3β hydroxyl group; in particular the C-1, C-2, C-4, C-23 and C-24 carbon atom resonances (δ39.5, 34.1, 46.8, 26.6 and 21.0, respectively) were in agreement with a 3-keto partial structure and not with those of a 3β-hydroxy moiety [7].

The location of the hydroxyl group was limited to position C-7, 15, or 16 by the following considerations. Absorption maxima in the IR and UV spectra of the diketone **3** (ν_{max} 1.705 cm^{-1}; λ_{max}=290 nm) excluded the hydroxyl group from the E-ring or a 1,3-diketone. Position C-16 can similarly be excluded by comparison of the ^{13}C NMR data of the known lup-20(29)-ene-3β,16β-diol [7] with loranthol (Table 2). In the Sarett oxidation of loranthol and oxidation of **1**, the same crystalline product was obtained, mp and MS (Experimental) and ^{1}H NMR (Table 1) were identical with the known 3,7-lupendione (**3**), the ^{13}C NMR data are shown in Table 2. All these data give evidence that the structure of **1** is 7β-hydroxylup-20(29)-en-3-one.

EXPERIMENTAL

Mps: uncorr. Optical rotations: MeOH. UV: EtOH. IR: KBr. ^{1}H NMR: 200 MHz, $CDCl_3$, TMS as int. standard. ^{13}C NMR: 50.3 MHz. MS: 70 eV. Analytical TLC: Silica gel G. Prep. TLC: Silica gel PF$^{234-236}$. CC: Silica gel 60 (0.063–0.2 mm).

Extraction and separation of compounds. Salvia pratensis L. collected in Valgañon (La Rioja, Spain) in July 1987, voucher specimens are deposited in the Botany Department (register number SALA No. 7320). Air-dried plant material (1.4 kg), was extracted with hexane in a Soxhlet for 15 hr. and yielded 82 g of extract (5.85%). The neutral fraction (5.1 g) of the MeOH–urea (1:4) soluble extract was chromatographed over silica gel developed with hexane and hexane–Et_2O mixtures of increasing

Table 2. ^{13}C NMR spectral data of compound **1**, **1a**, **2**, **2a** and **3**

C	1	1a	2	2a	3
1	39.5	39.3	38.7	38.3	39.2
2	34.1	34.0	27.5	23.7	34.0
3	217.0	216.4	78.9	80.6	215.8
4	46.8	47.0	37.3	38.1	47.4
5	52.4	51.8	52.5	52.2	53.8
6	30.0	26.6	27.5	23.7	27.8
7	74.1	76.5	74.7	77.1	213.7
8	44.5	45.6	46.9	45.6	43.7
9	50.0	50.0	50.5	49.8	52.0
10	37.0	36.9	37.3	36.6	37.3
11	21.6	21.5	20.9	20.5	21.8
12	25.4	25.3	25.3	25.1	25.8
13	38.8	38.8	38.7	37.2	39.9
14	42.8	44.4	42.8	44.2	43.3
15	30.5	29.8	29.4	29.9	27.7
16	36.1	36.2	36.1	37.1	35.8
17	42.8	42.8	42.8	42.7	42.7
18	48.2	48.3	48.3	50.3	48.0
19	46.8	48.3	48.2	48.3	47.8
20	150.9	150.9	151.0	150.8	150.9
21	30.0	30.1	30.0	30.0	30.0
22	40.2	40.2	40.2	40.1	40.3
23	26.6	26.7	28.0	25.2	26.0
24	21.0	22.0	15.4	15.8	20.9
25	15.6	15.8	15.1	15.6	15.6
26	10.0	11.3	10.2	11.5	15.6
27	14.9	15.0	15.8	14.9	15.6
28	18.0	18.1	17.9	18.0	18.3
29	109.4	109.6	109.4	109.4	109.6
30	19.5	19.5	19.4	19.4	19.6
OAc	—	170.5	—	170.7	—
OAc	—	—	—	170.4	—
OAc	—	21.0	—	21.2	—
OAc	—	—	—	20.7	—

Table 1. ^{1}H NMR data of compounds **1**, **2a** and **3**

H	1	1a	2a	3
H-3			4.45 *dd* (4, 11.5)	
H-7	3.83 *dd* (6.8, 8.8)	5.20 *dd* (7.0, 8.9)	5.00 *dd* (6.0, 12.0)	
H-29	4.65 *dd* (2.2, 0.7)	4.68 *dd* (2.1, 0.7)	4.70 *dd* (2.0, 0.7)	4.68 *br s* ($W_{1/2}$ 4.6)
H-29	4.53 *br s* ($W_{1/2}$ 3.7)	4.58 *br s* ($W_{1/2}$ 3.7)	4.60 *dd* ($W_{1/2}$ 3.7)	4.58 *br s* ($W_{1/2}$ 3.6)
C(Me30)	1.64 *d* (0.7)	1.67 *d* (0.7)	1.64 *d* (0.7)	1.68 *d* (0.7)
	1.06 *s*	1.28 *s*	1.13 *s*	1.33 *s*
	1.04 *s*	1.20 *s*	0.98 *s*	1.15 *s*
	1.01 *s*	1.07 *s*	0.83 *s*	1.06 *s*
	0.99 *s*	1.02 *s*	0.83 *s*	1.03 *s*
	0.89 *s*	0.92 *s*	0.79 *s*	1.03 *s*
	0.77 *s*	0.80 *s*	0.76 *s*	0.80 *s*
OAc		2.00 *s*	2.03 *s*	
			1.97 *s*	

polarity to give a crystalline mixture of β-amyrin, germanicol and lupeol (710 mg, hexane–Et_2O, 9:1); **1** (1.05 g, hexane–Et_2O, 4:1) and loranthol (**2**) (431 mg, hexane–Et_2O, 7:3). The different components were purified by crystallization.

7β-Hydroxylup-20(29)-en-3-one (**1**). Colourless crystals, mp 217 219° (MeOH). IR ν_{max} cm^{-1}: 3450, 3060, 1705, 1645 and 885. ^1H and ^{13}C NMR in Tables 1 and 2. MS *m/z* (rel. int.): 440 (21), 425 (14), 399 (8), 384 (12), 371 (12), 303 (10), 387 (9), 257 (8), 235 (23), 205 (11), 183 (25), 155 (22), 137 (10), 69 (100), 41 (23).

λ	589	578	546	436	
[α]	+10.9	+12.3	+13.6	+26.5	(*c* 0.8).

Acetylation of compound **1**. Treatment of a crystalline sample of compound **1** with Ac_2O pyridine in the usual way afforded the monoacetate **1a**. IR ν_{max} cm^{-1}: 3060, 1730, 1705, 1645, 1220 and 885. ^1H and ^{13}C NMR in Tables 1 and 2.

Oxidation of compound **1**. A mixture 40 mg of **1** was dissolved in pyridine (0.2 ml) and added to a soln of CrO_3 (32 mg) in pyridine (0.2 ml) and CH_2Cl_2 (1 ml). The mixture was stirred for 4 hr in an ice water bath under N_2. The oxidation product was chromatographed over silica gel. Elution with hexane–Et_2O (19:1) afforded 32 mg of lup-20(29)-en-3,7-dione (**3**). Colourless crystals, mp 203–205° (MeOH). MS *m/z* (rel. int.): 438 (78), 423 (14), 370 (12), 327 (59), 247 (56), 234 (100), 205 (62), 130 (36), 109 (54), 95 (49), 41 (26).

Loranthol (**2**). Colourless crystals, mp 223–225° (MeOH). MS *m/z* (rel. int.): 442 (100), 427 (30), 409 (10), 391 (8), 386 (12), 332 (51), 331 (62), 249 (33), 236 (63), 223 (22), 217 (56), 203 (4), 195 (13), 189 (8), 175 (9), 139 (11).

λ	589	578	546	436	
[α]	+12	+14	+16.5	+32.5	(*c* 0.4).

Acetylation of Loranthol (**2**) afforded the diacetate **2a**. Colourless crystals mp 216° (CH_2Cl_2–hexane). IR ν_{max} cm^{-1}: 3065, 1740, 1730, 1650, 1225, 890. ^1H and ^{13}C NMR in Tables 1 and 2.

λ	589	578	546	436	
[α]	+21	+22.3	+25.7	+44.8	(*c* 0.4)

Oxidation of loranthol (**2**). Sarett oxidation of **2** afforded lup-20(29)-en-3,7-dione (**3**).

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