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LUPENE DERIVATIVES FROM *SKIMMIA LAUREOLA*

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Key Word Index—*Skimmia laureola*; *Rutaceae*; triterpenoids; lupene derivatives.

Abstract—Three new lupenes, isolated from *Skimmia laureola*, have been characterized as 23-acetoxy-lup-20(29)-en-30-al-3-one, 3*β*,23-bisacetoxy-lup-20(29)-en-30-al and 23-acetoxy-lup-20(29)-en-30-ol-3-one.

INTRODUCTION

Following our earlier communications concerning the chemistry of oil [1,2] of *Skimmia laureola*, its chromones and coumarins [3], this paper reports the isolation and characterization of three new lupenes, designated as skimmianone (**1**), skimmial (**2**) and skimmiol (**3**) besides the previously reported [4] lupeol (**4**) and lupenone (**5**), from the ethyl acetate fraction of the defatted ethanol extract of the plant.

RESULTS AND DISCUSSION

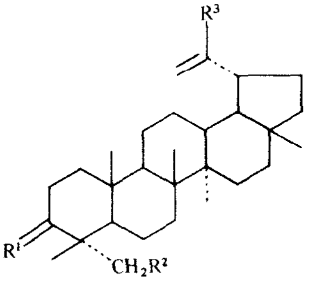
The compounds **1**–**3** responded positively to Liebermann–Burchard, TCA [5] and TNM tests for unsaturated triterpenoids. The resemblances in their spectral patterns suggested that the compounds were structurally related with differences in the nature or position of their functional groups.

The IR and ^1H NMR spectra of all the three compounds accounted for an acetoxyl, $\delta 2.03$–2.05 (3H, *s*). It was shown to be primary in nature, located at a non-hindered equatorial position [6,7] by a two proton AB*q*, $J = 9.7$ Hz, centered at $\delta 3.75$–3.82 and 3.80–3.91.

The compounds **1** and **2** absorbed at λ_{max} 225 and 230 nm but the compound **3** was transparent to UV light. This, together with the IR bands at ν_{max} 1725 and 1720 cm^{-1} and a single proton ^1H NMR signal at $\delta 9.55$ (1H, *s*), proved that the compounds **1** and **2** carried an α,β-unsaturated aldehyde function. Compound **3** was shown to possess an allylic primary hydroxyl [ν_{max} 3450 cm^{-1}; $\delta 4.25$ (1H, *br s*, exch. D_2O), 4.05 and 4.15 (1H each, AB*q*, $J = 7$ Hz).

Compounds **1** and **3** responded positively to the characteristic Zimmermann test for 3-ketotriterpenoids. This was substantiated by the two proton resonance signal at $\delta 2.42$ (2H, *m*), due to the adjacent methylene protons, in their ^1H NMR spectra. The ^1H NMR spectrum of the compound **2** contained resonance signal for another acetoxyl, $\delta 2.15$ (3H, *s*). It was found to be secondary and equatorial, at the usual C-3 position, by the axial carbinylic proton signal at $\delta 4.79$ (1H, *t*, $J = 9,7$ Hz) [8].

The ^1H NMR spectra of all the three compounds revealed the presence of an exocyclic disubstituted double bond. The spectra of compounds **1** and **2** exhibited two doublets, $J = 7$–8 Hz, at $\delta 5.86$, due to H-29′, and 6.26, due to H-29 [9]. The vinylic proton signal of compound **3** appeared as a multiplet at $\delta 5.30$ (2H, *m*). The UV absorptions, coupled with the downfield chemical shift of vinylic protons, in the ^1H NMR spectra of compounds **1** and **2**, was in agreement with the presence of the aldehyde function on the vinylic carbon. The facile loss of 55, 55 and 57 mass units from the molecular ions, in the mass spectrum of **1**, **2** and **3**, respectively, indicated the presence of an oxygenated isopropenyl side chain in these compounds. This, together with the presence of only five methyls and the multiplicity of the vinylic



	R¹	R²	R³
1	O	OAc	CHO
2	OAc H	OAc	CHO
3	O	OAc	CH_2OH
4	OH H	H	Me
5	O	H	Me
6	OH H	OH	CH_2OH
7	OAc H	OAc	CH_2OAc

protons, indicated that the compounds **1–3** were lup-20(29)-ene derivatives with two of the methyls transformed into oxygenated functions. Had the compounds been lup-22(29)-ene derivatives the vinylic protons should have appeared as a broad singlet [10].

The position of the primary acetoxyl at C-4, in all the three compounds, was decided on the basis of the chemical shift and multiplicity of 23-methylene protons [6] and mass fragmentation. The mass spectra of compounds **1** and **2** contained strong peaks at *m/z* 263, due to the fragment carrying rings A/B; the corresponding peak was observed at *m/z* 307 in the mass spectrum of compound **3**. The mass spectral fragmentations of all the compounds were consistent with those of lup-20(29)-ene derivatives [11] and confirmed the lupene nature of the compounds. The structures were finally established by the ^{13}C NMR spectra and chemical interconversions.

The assignments of the ^{13}C NMR chemical shifts (Table 1) were made by comparison with the reported data of known lupene derivatives [12], the study of the off-resonance decoupled spectra and the known chemical shift rules [13]. The spectral data of the compounds **4** and **5** fitted well with the reported data for lupeol [12] and lupenone [12, 14]. The spectral data of the compounds **1–3** resembled that of lupenone and lypenyl acetate with predictable differences.

The ^{13}C NMR spectra of the compounds **1–3** accounted for the presence of an α,β-unsaturated oxygenated function which deshielded C-20 and C-29 by 12 and 10 ppm, in the case of the C-30 aldehyde, and 3 and 2 ppm, in the case of the C-30 hydroxyl, as compared to lupenone and lupenyl acetate, respectively. The C-12 signal was also deshielded by 3 ppm. An analysis of the molecular models revealed that this deshielding was due to the preferred conformation in which the C-30 oxygen function with its lone pair of electrons lies in close proximity to C-12. The 23-acetoxyl displays the A and B-ring carbon shifts significantly, in comparison to lupenone and lupenylacetate. It causes, by E-long range eclipsed interactions, a shielding effect; the effect being more pronounced (6 ppm) at C-5.

Compound **1** on reduction with lithium aluminium hydride gave a triol **6** which on acetylation formed the triacetate **7**. This compound was also obtained by similar

Table 1. ^{13}C NMR chemical shifts for compounds **1–5** (δ_C ppm, CDCl$_3$)

C	**1**	**2**	**3**	**4**	**5**
1	38.5	37.8	38.3	38.7	39.6
2	33.1	23.1	33.3	27.4	34.1
3	218.2	74.7	218.1	78.8	217.9
4	48.4	40.7	48.3	38.3	47.2
5	49.9	48.6	49.9	55.2	55.8
6	19.7	18.0	19.5	18.3	19.6
7	33.9	32.0	33.7	34.2	33.5
8	41.3	39.7	41.1	40.9	40.7
9	49.7	47.5	50.1	50.3	49.7
10	36.8	36.9	36.7	37.1	36.8
11	22.7	23.0	22.6	20.9	21.4
12	28.5	26.4	28.7	25.1	25.1
13	37.5	37.5	37.5	38.0	38.1
14	43.6	43.4	43.6	42.8	42.7
15	27.6	27.7	27.6	27.4	27.4
16	35.4	35.9	35.3	35.5	35.6
17	44.6	46.0	44.5	42.9	42.7
18	46.3	47.1	46.4	48.2	48.2
19	51.3	50.5	51.1	47.9	47.8
20	168.5	168.4	158.7	150.6	150.5
21	28.1	28.5	28.0	29.8	29.8
22	40.9	40.6	39.9	39.9	39.9
23	65.6	65.6	65.9	28.0	26.6
24	17.0	16.1	17.1	15.4	21.0
25	16.4	16.0	16.3	16.1	15.8
26	17.9	17.9	17.8	15.9	15.4
27	15.8	15.7	14.7	14.5	14.4
28	20.3	20.2	19.1	18.0	18.0
29	119.3	119.3	109.8	109.2	109.2
30	180.7	180.5	118.6	19.3	19.2
O$\underline{\text{C}}$OMe(23)	172.4	171.2	172.5	—	—
OCO$\underline{\text{Me}}$(23)	21.3	21.5	21.3	—	—
-O$\underline{\text{C}}$OMe(3)	—	170.5	—	—	—
		21.1	—	—	—

treatment of the compounds **2** and **3**. The Sarett oxidation of the compound **3** gave a product identical to **1**. The compounds **1–3** were thus identified as 23-acetoxy-lup-20(29)-en-30-al-3-one (**1**), 3β,23-bisacetoxy-lup-20(29)-en-30-al (**2**) and 23-acetoxy-lup-20(29)-en-30-ol-3-one (**3**), respectively. These compounds are new to the chemical literature.

EXPERIMENTAL

Mps: uncorr. IR were recorded in KBr discs, UV in EtOH; ^{1}H NMR in $CDCl_3$ and CD_3OD at 90 and 250 MHz with TMS as int. standard; ^{13}C NMR at 62.89 MHz and high resolution MS at 70 eV.

The extraction of plant material has been described elsewhere [3]. The EtOAc fraction recovered from the crude column after successive development with petrol (bp 60–80°) and benzene afforded a mixture (7 g) which on further cc and development of the column with graded petrol–benzene and benzene–EtOAc systems afforded six mixtures containing coumarins and triterpenoids. From these mixtures the compound **1–5** were recovered by repeated chromatography on silica gel and purified by prep. TLC and crystallizations. The C_6H_6–EtOAc (7:3) fraction afforded the compounds **1** (0.07 g) **2** (0.056 g) and **5** (0.032 g). The C_6H_6–EtOAc (1:1) fraction afforded the compounds **3** (0.08 g) and **4** (0.031 g).

Skimmianone, *23-acetoxy-lup-*20(29)*-en-*30*-Ol-*3*-one* (**1**) Colourless needles from MeOH–petrol, mp 187–188°, $[\alpha]_D^{25}$ (EtOH)+33.2° (c, 1.05), M$^+$ at *m/z* 496.7216 (Calc. for $C_{32}H_{48}O_4$, 496.7369); UV λ_{max}^{EtOH} nm: 225; IR: $\nu_{max}\text{cm}^{-1}$: 1725, 1740, 1715, 1685; ^{1}H NMR ($CDCl_3$): δ0.83 (3H, *s*), 0.93 (3H, *s*), 1.00 (3H, *s*), 1.03 (3H, *s*), 1.08 (3H, *s*), 2.03 (3H, *s*), 2.42 (2H, *m*, H-2), 3.85 and 3.80 (1H each AB*q*, *J* = 9.7 Hz, *H*-23), 5.86 and 6.26 (1H each, ABq, *J* = 8 Hz, H-29, H-29′), 9.55 (1H, *s*,H-30): MS *m/z*: 496, 481, 436, 464, 441, 390, 279, 205 (100%), 203, 191, 189 and 149.

Skimmial, *3β-23-bisacetoxy-lup-*20(29)*-en-*30*-al* (**2**) Colourless needles from petrol–benzene, mp 218–220°; $[\alpha]_D^{25}$ (EtOH) +23.8 (c, 2.0), M$^+$ at *m/z* 540.7802 (Calc. for $C_{34}H_{52}O_5$, 540.7905); UV λ_{max}^{EtOH} nm: 230; IR $\nu_{max}\text{cm}^{-1}$: 1760, 1720, 1710, 1680, 1245; ^{1}H NMR ($CDCl_3$): δ0.77 (3H, *s*), 0.87(3H, *s*), 1.03 (3H, *s*), 1.07 (3H, *s*), 1.09 (3H, *s*), 2.03 (3H, *s*), 2.15 (3H, *s*,OAc), 3.75 and 3.89 (1H each, ABq *J* = 9.7 Hz, H-23), 4.79 (1H, *t*, *J* = 9.7 Hz, H-3), 5.86 and 6.26 (1H each, *d*, *J* = 7.5 Hz, H-29, H-29′), 9.55 (1H, *s*,H-30); MS *m/z*: 540, 525, 507, 485, 480, 453, 420, 331, 205 (100%), 203, 201, 189.

Skimmiol, *23-acetoxy-lup-*20(29)*-en-*30*-ol-*3*-one* (**3**). Colourless amorphous compound, mp 192–193°, $[\alpha]_D^{25}$ (EtOH)+30.2° (*c*, 1.2), M$^+$ at *m/z* 498.8015 (Calc. for $C_{32}H_{50}O_4$, 498.8214); IR $\nu_{max}\text{cm}^{-1}$: 3450, 1750, 1705, 1680, 1240, 820; ^{1}H NMR: δ0.80 (3H, *s*); 0.97 (3H, *s*), 1.00 (3H, *s*), 1.05 (3H, *s*), 1.08 (3H, *s*), 2.05 (3H, *s*), 2.42 (2H, *m*, H-2), 3.82 and 3.91 (1H each, ABq, *J* = 9.7 Hz, H-23), 4.5 and 4.15 (1H each, ABq, *J* = 7 Hz, H-30), 4.25 (1H, *br*, *s*, exch.D_2O); 5.30 (2H, *m*, H-29 and H-29′); MS *m/z*: 498, 483, 480, 465, 450, 441, 381, 213, 205 (100%), 202, 191, 189, 148.

Lupeol (**4**). mp 212°; $[\alpha]_D^{25}$ (EtOH)+23° (c.0.5); IR $\nu_{max}\text{cm}^{-1}$: 3510, 1680, 810; ^{1}H NMR: δ0.78 (3H, *s*), 0.83 (3H, *s*), 0.95 (3H, *s*), 0.98 (3H, *s*), 1.03 (3H, *s*), 1.06 (3H, *s*), 1.70 (3H, *s*), 3.25 (1H, *q*, *J* = 9,6 Hz, H-3), 4.62 (2H, *d*, *J′* = 6 Hz, H-29, H-29′). Acetylation with Ac_2O–pyridine at room temp., gave the monoacetate, mp 214–215°; IR $\nu_{max}\text{cm}^{-1}$: 1720, 1640, 1240, 890; ^{1}H NMR: δ0.80 (3H, *s*), 0.82 (3H, *s*), 0.93 (6H, *s*), 1.03 (3H, *s*), 1.70 (3H, *s*), 2.02 (3H, *s*) 4.23 (1H, *t*, *J* = 9.7 Hz), 4.62 (2H, *d*, *J* = 6 Hz), MS *m/z*: 468, 473, 424, 413, 409, 381, 218, 205 (100%), 189. On Sarett oxidation gave compound **5** identical by Co-TLC.

Lupenone (**5**). mp 170°; IR $\nu_{max}\text{cm}^{-1}$: 1705, 1680, 810; ^{1}H NMR: δ0.83 (3H, *s*), 0.93 (6H, *s*), 1.00 (3H, *s*), 1.03 (3H, *s*), 1.08 (3H, *s*), 1.70 (3H, *s*), 2.56 (2H, *d*, *J* = 5 Hz), 5.86 (2H, *d*, *J* = 6 Hz, H-29, H-29′); MS *m/z*: 424, 409, 381, 262, 233, 207, 191, 189 (100%).

Reduction and acetylation of **1** and **2**. 0.03 and 0.02 g of the Compound **1** and **2** were refluxed with 0.40 and 0.30 g of $LiAlH_4$ in dry Et_2O (80 ml) for 6 hr. After usual work-up the respective alcohols were recovered and subjected as such to acetylation, with Ac_2O–pyridine at room temp. for 96 hr. The triacetate (**7**) was recovered by the usual method and purified by CC, colourless needles mp 192–193°; M$^+$ at *m/z* 584.8403 (calc. for $C_{36}H_{56}O_6$ 584.8441); IR $\nu_{max}\text{cm}^{-1}$: 1760, 1750, 1755, 1680, 880; ^{1}H NMR: δ0.79, 0.80, 0.93 (3H each, *s*), 1.00 (3H, *s*), 1.07 (3H, *s*), 2.03, 2.05, 2.06 (3H each, *s*, 3 × Ac), 3.75 and 3.89 (1H, each, ABq, *J* = 8 Hz, H-23), 4.60 and 5.32 (1H each, ABq, *J* = 9 Hz, H-30), 4.73 (1H, *t*, *J* = 7, 9 Hz, H-3), 5.88 and 6.20 (1H, each, *d*, *J* = 7 Hz, H-29, H-29′); MS *m/z*: 584, 569, 509, 484, 449, 420, 331, 205 (100%), 203, 201, 189.

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