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A 3,4-SECO-TRITERPENE FROM *CARALLUMA BUCHARDII*

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Key Word Index—*Caralluma buchardii*; Asclepiadaceae; steroids; triterpenes; squalene; 3,4-seco-lup-20(29)-en-3-oic acid methyl ester; sitosterol acetate; lupeol acetate; guimarenol; lupenone; lupeol; sitosterol.

From *Caralluma buchardii* N E Brown, endemic to Fuerteventura, Canary Islands, squalene, sitosterol acetate, lupeol acetate, guimarenol [1], lupenone, lupeol sitosterol and the new natural triterpene 3,4-seco-lup-20(29)-en-3-oic acid methyl ester (**1**) were isolated [2]*. The structure of the latter was established from its spectral data and transformation to the product 3,4-seco-lupan-3-oic acid methyl ester (**2**), which could be synthesized from lupeol (**3**).

Compound **1**, $C_{31}H_{52}O_2$, M^+ at *m/e* 456, did not crystallize and from MS and ^{1}H NMR spectroscopy appeared to be a triterpene acid methyl ester with an isopropenyl group and an isopropyl group. The fragmentation pattern observed in its MS was characteristic [3] of the 3,4-seco-lupene series with an isopropyl group at C-5 (fragments [**a**] and [**b**]). Compound **1** is a natural 3,4-seco-triterpene which has an isopropyl group at C-5 where one would normally expect to find an isopropenyl group [4]. Its ^{1}H NMR spectrum showed four singlets for angular methyl groups and two superimposed methyl doublets (J = 7 Hz) in the region δ 0.72–1.02 as well as a broad singlet of 3H $W_{1/2}$ = 3 Hz at 1.68 and a multiplet 2H ($W_{1/2}$ = 18 Hz) at 4.65 corresponding to an isopropenyl grouping [5]. A methyl ester group was easily recognised from the ^{1}H NMR data by a singlet at 3.65 (3 H), and from the IR absorption at 1720 cm^{-1}. The ^{13}C NMR spectrum confirmed these findings with a methylene grouping at δ 150.7 (*s*, C-20) and 109.45 (*t*, C-29) and a carbomethoxy group at 174.7 (*s*, C-3) and 51.5 (*q*, MeO).

It was possible to transform **1** to the 20(29)-dihydro derivative **2**, (M^+ at *m/e* 458) which was also obtained from lupeol (**3**) by the following reaction sequence. Lupeol (**3**) reduction gave lupanol (**4a**) which was oxidized with Jones' reagent to lupanone (**4b**) and, by treatment with hydroxylamine chlorhydrate, the oxime **4c** was formed (IR absorptions at 3230 and 930 cm^{-1}). The oxime **4c** was treated with tosyl chloride in pyridine to obtain the expected 3,4-seco-lupan-3,4-lactam (**6**) as principal product and a small amount of **5** (M^+ at *m/e* 423), the result of an abnormal Beckmann reaction [6].

Compound **5** was unambiguously characterized by IR spectroscopy (absorptions at 2160 cm^{-1} for the group C≡N and at 1640 and 900 cm^{-1} for the methylene double bond) and by ^{1}H NMR which showed an isopropenyl group, confirming the cleavage of the bond at C-3/C-4, with signals at δ 4.78 (2 H, *m*, $W_{1/2}$ = 20 Hz) and 1.71 (3 H, *br s*, $W_{1/2}$ = 3 Hz). Hydrolysis catalysed by the base of **6**, followed by methylation of the acid **7a** thus produced led to the formation of **7b**, $C_{31}H_{52}O_2$, which, by hydrogenation, gave the same methyl ester (**2**) as that obtained by reducing the natural product **1**. As **1** and **7b** are different substances and the isopropenyl group in **7b**, sited by the series of reactions previously described is located at C-5, then **1** must have the structure 3,4-seco-lup-20(29)-en-oic acid methyl ester.

EXPERIMENTAL

Mps were determined of a Kofler hot-stage apparatus and are uncorr. Optical rotations were measured in $CHCl_3$ and ^{1}H NMR and ^{13}C NMR, at 60 and 20 MHz, respectively, were taken in $CDCl_3$ with TMS as internal reference. Column and dry column chromatography was performed on Si gel 0.2–0.5 and 0.063–0.2 mm, respectively.

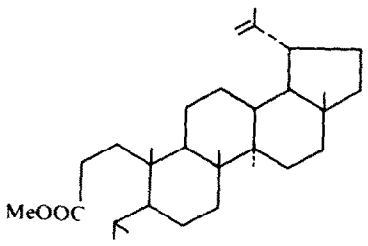
Extraction. The whole plant (10 kg) collected in July was ground, air-dried, extracted in a Soxhlet with EtOH and conc. *in vacuo*. The syrupy residue was dissolved in 50% aq. EtOH and thoroughly extracted with EtOAc. The conc extracts were chromatographed on Si gel (C_6H_6, C_6H_6–EtOAc and EtOAc).

3,4-Seco-lup-20(29)-en-3-oic acid methyl ester (**1**). Amorphous. (Found: C, 81.31; H, 11.53. $C_{31}H_{52}O_2$ requires: C, 81.52; H, 11.48%). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1720 (ester), 1640, 890 (C=CH$_2$); ^{1}H NMR: δ 0.77 (6 H, *d*, J = 7 Hz, C-23 and C-24), 0.78 (6 H, *s*, C-25 and C-28), 0.92 (3 H, *s*, C-27), 1.02 (3 H, *s*, C-26), 1.68 (3 H, *br s*, $W_{1/2}$ = 3 Hz, C-30), 3.65 (3 H, *s*, —COOMe), 4.65 (2 H, *m*, $W_{1/2}$ = 18 Hz, C-29); ^{13}C NMR, ppm (TMS = 0): 174.7, 150.7, 109.45, 51.5, 48.3, 48.0, 47.3, 43.2, 43.0, 40.8, 40'65, 40.0 (double), 38.2, 35.6, 33.0, 29.9, 29.7, 28.4, 27.5, 25.4, 25.3, 24.8, 21.6, 19.6, 19.4, 18.9, 18.3, 18.0, 16.0, 14.4; MS (70 eV) *m/e* (rel. int.): 456 (M^+, 100), 441 (M^+ − Me, 38), 413 (M^+ − *i* Pr, 19), 369 ([**a**] 38), 257 (28), 237 ([**b**] 9), 218 (23), 189 (43).

3,4-Seco-lupan-3-oic acid methyl ester (**2**) *from* **1**. A soln of **1** (60 mg) in EtOH (25 ml) was hydrogenated over 10% Pd/C (60 mg) at room temp. and atm pres. Usual work-up and dry column chromatography (petrol–C_6H_6, 3:1) gave **2** (50 mg); amorphous; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1725 (ester); ^{1}H NMR: δ 0.75 (3 H, *s*, C-28), 0.76 (6 H, *d*, J = 7 Hz, C-23 and C-24), 0.81 (3 H, *s*, C-25), 0.92 (3 H, *s*, C-27), 1.04 (3 H, *s*, C-26), 3.67 (3 H, *s*, —COOMe); MS (15 eV) *m/e* (rel. int.): 458 (M^+, 100), 443 (M^+ − Me, 27), 415 (M^+ − *i*Pr, 61), 371 (97), 259 (51), 191 (78).

Lupenone oxime (**4c**) *from lupeol* (**3**). A soln of **3** (655 mg) in EtOH (100 ml) was hydrogenated over 10% Pd/C (500 mg) as described above for the synthesis of **2**, and gave **4a** (640 mg). A

* Following submission of this paper Prof. Ourissen has informed us that this compound has been isolated from sediments deposited in the delta of the Mahakam River (Borneo) [2].



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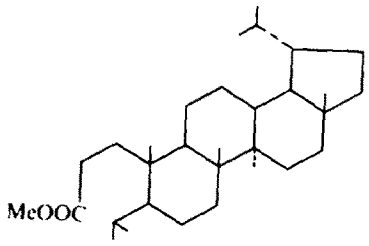

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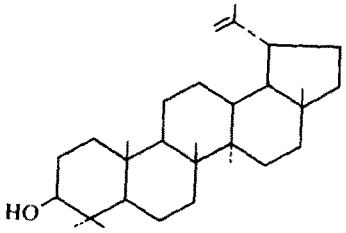

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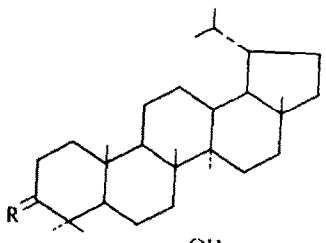
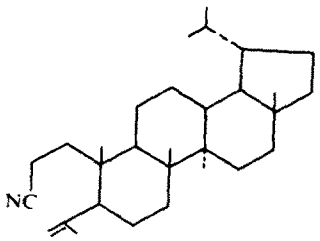


4a R = OH, H
4b R = O
4c R = N—OH

Scheme 1



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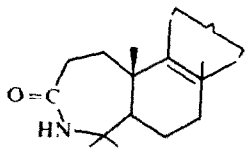

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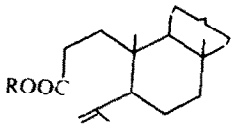
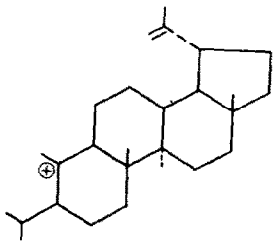
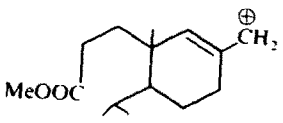


7a R = H
7b R = Me



[a]



[b]

Scheme 2.

soln of **4a** (640 mg) in Me_2CO (125 ml) was treated at 0° with Jones' reagent until the reaction was completed. The usual work-up gave a residue consisting mainly of **4b** (607 mg) which without being purified was dissolved in pyridine (10 ml). $H_2NOH \cdot HCl$ (1 g) in MeOH (150 ml) was added and the soln refluxed for 3.5 hr, then poured into H_2O and extracted with $CHCl_3$. Dry column chromatography of the residue gave **4c**: mp 286–288° ($CHCl_3$–MeOH), $[\alpha]_D$-48° (*c*, 0.301); IR ν_{max}^{KBr} cm^{-1}: 3230 (OH), 930 (N—O); ^1H NMR: δ 0.75 (3 H, *s*, C-28), 0.91 (3 H, *s*, C-27), 1.02 (3 H, *s*, C-26).

Compounds **5** *and* **6** *from* **4c**. Tosyl chloride (750 mg) was added to a soln of **4c** (325 mg) in pyridine (25 ml) and the mixture was left at room temp. for 12 hr. The usual work-up and chromatographic separation (C_6H_6 and EtOAc) yielded **5** and **6**. Compound **5**: amorphous; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 2160 (C≡N), 1640, 900(C=CH_2): ^1H NMR: δ 0.74 (3 H, *s*, C-28), 0.75 (6 H, *d*, J = 7 Hz, C-29 and C-30), 0.83 (3 H, *s*, C-25), 0.92 (3 H, *s*, C-27), 1.07 (3 H, *s*, C-26), 1.71 (3 H, *br s*, $W_{1/2}$ = 3 Hz, C-24), 6.67 and 6.88 (2 H, *mm*, $W_{1/2}$ = 4 Hz, C-23); MS (15 eV) *m/e* (rel. int.): 423 (M^+, 61), 408 (M^+ – Me, 46), 380 (M^+ – *i*Pr, 100), 339 (23), 231 (46), 191 (92). Compound **6**: mp 307–309° ($CHCl_3$–MeOH), $[\alpha]_D$ – 11° (*c* 0.297); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3370 (NH), 1640 (NHCO); ^1H NMR: δ 0.74 (3 H, *s*, C-28), 0.90 (3 H, *s*, C-27), 1.05 (3 H, *s*, C-26).

3,4-*Seco-lup*-4(23)-*en*-3-*oic acid methyl ester* (**7b**). A soln of **6** (33 mg) in 20% KOH–MeOH was refluxed for 3 hr, then poured into H_2O, acidified with dil HCl and extracted with $CHCl_3$. The residue was dissolved in Et_2O, treated with an excess of CH_2N_2 in Et_2O and the dried product was chromatographed (petrol–C_6H_6, 3:1). Compound **7b** (25 mg): amorphous: IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1718 (ester), 1635, 890 (C=CH_2); ^1H NMR: δ 0.72 (3 H, *s*, *C*-28), 0.75 (6 H, *d*, J = 7 Hz, C-29 and C-30), 0.79 (3 H, *s*, *C*-25), 0.89 (3 H, *s*, C-27), 1.72 (3 H, *s*, C-24), 3.65 (3 H, *s*, COOMe), 6.67 and 6.86 (2 H, *mm*, $W_{1/2}$ = 4 Hz, C-23).

Compound **2** from **7b**. A soln of **7b** (21 mg) in EtOH was hydrogenated as described for the synthesis of **2** from **1**. Chromatography (petrol–C_6H_6, 3:1) gave a compound which was identical with **2**: (M^+ at *m/e* 458, TLC, superimposable IR and ^1H NMR spectra).

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