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3α,11α-DIHYDROXYLUP-20(29)-ENE-23,28-DIOIC ACID FROM *SCHEFFLERA OCTOPHYLLA**

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Key Word Index—*Schefflera octophylla*; Araliaceae; triterpenes; 3α,11α-dihydroxylup-20(29)-ene-23,28-dioic acid.

Abstract—The structure of 3α,11α-dihydroxylup-20(29)-ene-23,28-dioic acid, a new triterpene isolated from *Schefflera octophylla*, has been determined by spectroscopic methods.

INTRODUCTION

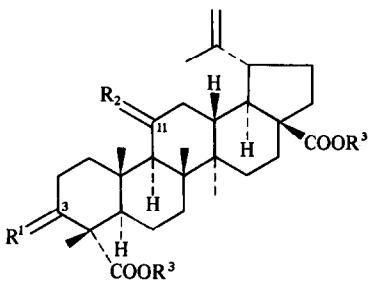
In an earlier communication [1] we described the isolation and structure of 3α-hydroxylup-20(29)-ene-23,28-dioic acid (**1**), the main triterpene of *Schefflera octophylla* which is used in Vietnamese folk medicine as a tonic drug, an antirheumatic agent and for liver diseases [2]. We now report on a further new pentacyclic triterpene from dried leaves of this plant. Based on spectroscopic data and chemical transformations the structure of this constituent is shown to be 3α,11α-dihydroxylup-20(29)-ene-23,28-dioic acid (**2**).

RESULTS AND DISCUSSION

The dried leaves were extracted with petrol followed by methanol. Evaporation of the latter extract and column chromatography on silica gel yielded the main triterpene **1** [1] and 1.6% of the more polar constituent **2** ($C_{30}H_{46}O_6$ M^+ at *m/z* 502; mp 213–214°). The IR spectrum (nujol) showed absorptions at 3400, 3075, 1700 and 1640 cm^{-1} assignable to hydroxyl, carboxyl and >C=CH_2 functions, respectively.

The formation of the dimethyl ester **3** ($C_{32}H_{50}O_6$ M^+ at *m/z* 530.3565, calc. 530.3607) and its diacetyl derivative **4** indicated the presence of two carboxylic functions and two hydroxyl groups. Oxidation of **3** with PDC gave the diketo diester **5** with a negative Cotton effect at 296 nm ($a = -64$).

The mass spectral fragmentation of the derivatives **2–5** is mainly characterized by bond cleavages of ring C allowing an assignment of the functional groups to the rings AB and DE, respectively (Scheme 1) [3]. The appearance of an intense *a*-type ion is evidence for substitution at C-11 [4]. This is supported by an ion of type *d* at *m/z* 317 in **5** appearing similar as found for 11-oxo-olean-12-enes [5]. Furthermore, ion *e* locates one carboxylic group of **2** at C-17 (i.e. C-28) [1, 3].

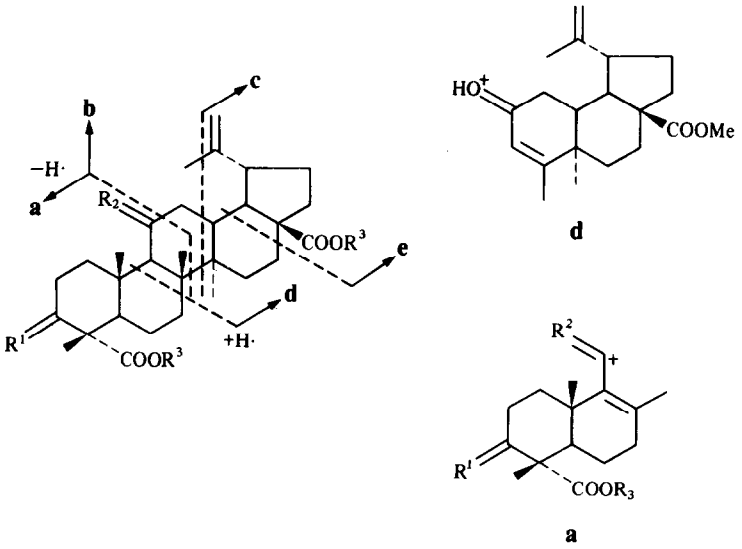


1 $R^1 = \alpha\text{-OH}, \beta\text{-H}$; $R^2 = H_2$; $R_3 = H$
2 $R^1 = \alpha\text{-OH}, \beta\text{-H}$; $R^2 = \alpha\text{-OH}, \beta\text{-H}$; $R^3 = H$
3 $R^1 = \alpha\text{-OH}, \beta\text{-H}$; $R^2 = \alpha\text{-OH}, \beta\text{-H}$; $R^3 = Me$
4 $R^1 = \alpha\text{-OAc}, \beta\text{-H}$; $R^2 = \alpha\text{-OAc}, \beta\text{-H}$; $R^3 = Me$
5 $R^1 = R^2 = O$; $R^3 = Me$

The ^1H NMR spectrum of **2** showed two olefinic protons at δ4.60 and 4.75, five tertiary methyl groups (one of them low-field shifted to 1.72) and two protons for secondary hydroxyl groups. The triplet-like signal centred at 3.73 ($\Sigma J_{AX} + J_{BX} = 5.4$ Hz) indicated that one hydroxyl group was present at the 3α-position [1]. The other signal appeared as a six line pattern centered at δ3.93 with two diaxial ($J = 11$ Hz) and one axial-equatorial ($J' = 5$ Hz) coupling which agrees with a 11α-position of the second hydroxyl.

The ^{13}C NMR spectrum of **2** (Table 1) established the presence of two carboxylic groups (*s*, 178.8 and *s*, 179.7), one 1,1-disubstituted double bond (*s*, 150.9 and *t*, 110.1) and two secondary hydroxyls (*d*, 69.9 and *d*, 72.8). The assignment of all thirty carbon atoms was achieved by means of the SFORD and APT techniques and correlation of the shift values for **1** [1; Preiss, A., Budecisky, M., Lischewski, M., Ty, Ph.D. and Adam, G., unpublished] with the substituent effects of a hydroxyl group at the 11α-position on the steroidal skeleton [6]. Besides the expected large downfield shifts for the signals corresponding to C-11, C-9 and C-12 and C-1 signal was also significantly displaced downfield due to the 11α-configuration of this

*Part 8 in the series "Natural Products from Vietnamese Plants". For Part 7 see Schmidt, J., Lien, N. T., Khoi, N. H. and Adam, G. (1983) *Phytochemistry* **22**, 1032.



Scheme 1. Main skeleton fragmentation of the lupane derivatives **2**–**5**.

Table 1. ^{13}C NMR chemical shifts of **2** (50.3 MHz, δ values are downfield from TMS: δ (TMS) = $\delta(C_5D_5N) + 135.5$

Carbon		Carbon	
1	35.4*	16	32.9
2	26.6	17	56.6
3	72.8	18	49.5
4	52.8	19	47.6
5	45.2	20	150.9
6	22.1	21	31.3
7	35.9*	22	37.5
8	42.9	23	179.7
9	56.6	24	18.1
10	39.6	25†	18.3
11	69.9	26†	17.2
12	38.5	27	14.8
13	37.7	28	178.8
14	43.4	29	110.1
15	30.2	30	19.6

*†Assignments may be interchanged.

hydroxyl group. Similar hydroxylation shifts were found recently for rigidenol [7] and nepetecin [4]*.

From the above data the new triterpene acid is considered to be 3α,11α-dihydroxylup-20(29)-ene-23,28-dioic acid (**2**). Other lupane triterpenes with the scarce 11-hydroxy substitution are nepeticin from *Nepeta hindostana* [4], rigidenol from *Maitenus rigida* [7] and some lupenes from *Salvia phlomoides* [8].

*In the data for nepetecin the chemical shift value cited for C-12 is apparently incorrect.

EXPERIMENTAL

An EA-mass spectrometer of the Research Institute 'Manfred von Ardenne', Dresden, was used to record the positive ion mass spectra (10–16 eV, duoplasmatron ion source, plasma gas Ar, direct inlet system). Exact mass measurements were obtained from a JEOL JMS D-100 instrument operating at 75 eV.

Schefflera octophylla (Lour.) Harms was identified by Dr. Ph. V. Nguyen, Institute of Biology, National Research Centre of the SRV, Hanoi, and a voucher specimen is kept there.

Isolation of 3α,11α-dihydroxylup-20(29)-ene-23,28-dioic acid (**2**). Dried and powdered leaves (100 g), collected near Hanoi (Nov. 1981), were defatted with petrol and subsequently extracted with MeOH for 8 hr under reflux. Evaporation of the solvent from the filtered extract yielded after CC (silica gel) **1** (7 g, elution with $CHCl_3$–EtOAc, 9:1) and **2** (1.6 g ~ 1.6% yield, elution with $CHCl_3$–EtOAc, 7:3): mp 213–214° (EtOAc–petrol); $[\alpha]_D^{29}$ −2.0° (*c* 0.40, EtOH); MS *m/z* (rel. int.): 502 $[M]^+$ (3), 484.3162 $C_{30}H_{44}O_5$ calc. 484.3189 $[M-H_2O]^+$ (13), 466 (14), 440 $[M-H_2O-CO_2]^+$ (19), 438 (15), 422 (30), 411 (13), 407 (18), 385 (19), 367 (16), 304 (19), 285 (21), 267 [**a**] (29), 249 (37), 246 (36), 234 [**b**] (85), 221 (59), 220 [**c**] (60), 219 [**c** − H] (62), 203 (70), 201 (68), 189 (90), 175 (93), 161 (80), 152 [**e**] (60), 147 (90), 133 (92), 121 (98), 107 (100). ^1H NMR (Me_2CO-d_6–TMS): δ1.00, 1.09, 1.12, 1.20 (4 × *s*, 24-H_3, 25-H_3, 26-H_3, 27-H_3), 1.72 (*s*, 30-H_3), 3.73 (*t*, $\Sigma J_{AX} + J_{BX}$ = 5.4 Hz, H-3β), 3.93 (six line pattern, J = 11 Hz, J' = 5 Hz, H-11β), 4.60 and 4.75 (2 × *m*, 29-H_2).

Dimethyl ester **3**. Obtained from **2** by treatment with CH_2N_2 in MeOH. Amorphous; $[\alpha]_D^{25}$ −2.8° (*c* 0.36, EtOH); IR ν_{max}^{nujol} cm^{-1}: 1645 (>C=CH_2), 1730 (COOMe), 3075 (>C=CH_2), 3425 (*br*, OH); MS *m/z* (rel. int.): 530.3565 $C_{32}H_{50}O_6$ calc. 530.3607 $[M]^+$ (23), 512 (25), 499 (26), 495 (31), 480 (31), 470 (29), 452 (36), 438 $[M-HCO_2Me-MeOH]^+$ (62), 421 (42), 399 (44), 386 (42), 381 (35), 318 (38), 299 (41), 281 [**a**] (53), 278 (52), 263 (53), 250 (86), 248 [**b**] (85), 234 [**c**] (66), 233 (62), 218 (66), 201 (86), 189 [**b** − CO_2Me] (100), 175 (97), 168 [**e** + 2H] (94), 147 (84), 133 (88), 119 (99), 107 (98). ^1H NMR ($CDCl_3$–TMS): δ0.95, 1.05, 1.10, 1.21 (4 × *s*, 24-H_3, 25-H_3, 26-H_3, 27-H_3), 1.70 (*s*, 30-H_3), 3.64 and 3.68 (2 × *s*, COOMe), 3.70 (*m*, H-3β), 3.95 (six line pattern, J = 11 Hz, J' = 5 Hz, H-11β), 4.60 and 4.76 (2 × *m*, 29-H_2).

Acetate **4**. Acetylation of **3** with Ac_2O–pyridine (12 hr at 20°) gave after CC the diacetate **4**: amorphous; $[\alpha]_D^{25}$ −10.4° (*c* 0.35, EtOH); IR ν_{max}^{nujol} cm^{-1}: 1240 (OAc), 1645 (>C=CH_2), 1740 (ester), 3070 (>C=CH_2); MS *m/z* (rel. int.): 614 $[M]^+$ (7), 554 $[M-HOAc]^+$ (57), 495 (43), 494 $[M-2HOAc]^+$ (48), 479 (18), 472 (14), 462 (6), 451 (6), 435 (26), 419 (14), 365 [**a**] (68), 323 (31), 320 (20), 299 (27), 263 (81), 260 (68), 255 (50), 247 [**b** − H] (85), 234 [**c**] (66), 233 [**c** − H] (73), 213 (48), 201 (88), 187 (100), 175 (84), 167 [**e** + H] (36), 159 (62), 145 (65), 133 (70), 119 (83), 107 (84). ^1H NMR ($CDCl_3$–TMS): δ0.99, 1.02, 1.10, 1.22 (4 × *s*, 24-H_3, 25-H_3, 26-H_3, 27-H_3), 1.68 (*s*, 30-H_3), 1.95 and 2.02 (2 × *s*, acetate), 3.59 and 3.67 (2 × *s*, COOMe), 4.60 and 4.76 (2 × *m*, 29-H_2), 4.90 (*t*, $\Sigma J_{AX} + J_{BX}$ = 5.4 Hz, H-3β), 5.23 (six line pattern, *J* = 11 Hz, *J'* = 5 Hz, H-11β).

Oxidation of **3** *to the diketone* **5**. To PDC (108 mg) in DMF (2 ml) dialcohol **3** (38 mg) was added and the soln stirred at 20° for 6 hr. Standard work-up followed by CC (silica gel) by elution with petrol–$CHCl_3$ (7:3) gave the diketone **5** (13 mg): mp 231–233° (Me_2CO–petrol); $[\alpha]_D^{25}$ +2.0° (*c* 0.5, EtOH); IR ν_{max}^{KBr} cm^{-1}: 1645 (>C=CH_2), 1710 (C=O), 1730 (COOMe), 3075 (>C=CH_2); MS *m/z* (rel. int.): 526 $[M]^+$ (27), 508 (10), 498 (8), 483 (8), 467 $[M-CO_2Me]^+$ (17), 466 (13), 449 (7), 444 (6), 383 (6), 317 [**d**] (13), 277 [**a**] (100), 251 (22), 248 [**b**] (37), 247 [**b** − H] (43), 234 [**c**] (27), 233 (25), 217 (64), 189 (74), 175 (74), 161 (31), 147 (40), 133 (52), 119 (62), 107 (55). ^1H NMR (Me_2CO-d_6–TMS): δ0.94, 1.30, 1.30, 1.39 (4 × *s*, 24-H_3, 25-H_3, 26-H_3, 27-H_3), 1.70 (*s*, 30-H_3), 3.64 and 3.66 (2 × *s*, COOMe), 4.63 and 4.77 (2 × *m*, 29-H_2).

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