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TWO 24-NOR-TRITERPENOID CARBOXYLIC ACIDS FROM *ACANTHOPANAX TRIFOLIATUS**

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Key Word Index—*Acanthopanax trifoliatus*; Araliaceae; 24-nor-triterpenes; 24-nor-3α,11α-dihydroxy-lup-20(29)-en-28-oic acid; 24-nor-11α-hydroxy-3-oxo-lup-20(29)-en-28-oic acid; ^{1}H NMR; ^{13}C NMR; X-ray analysis; biosynthesis.

Abstract—From *Acanthopanax trifoliatus* the new nor-triterpenes 24-nor-3α,11α-dihydroxy-lup-20(29)-en-28-oic acid and 24-nor-11α-hydroxy-3-oxo-lup-20(29)-en-28-oic acid were isolated. Their structures were determined on the basis of spectroscopic data, X-ray analysis and chemical transformations.

INTRODUCTION

Recently [1, 2] we reported the isolation and structures of some new triterpenes of the lupane series from *Acanthopanax trifoliatus* (L.) Merr. (Araliaceae), used in the folk medicine of south-east Asia [3, 4] as a drug with Ginseng-like activity. In this communication we describe the isolation and structures of two new 24-nor-lupanes from the same source. Based on spectroscopic data, X-ray analysis and chemical transformations the structures of the constituents were determined as 24-nor-3α,11α-dihydroxy-lup-20(29)-en-28-oic acid (**1**) and 24-nor-11α-hydroxy-3-oxo-lup-20(29)-en-28-oic acid (**2**).

RESULTS AND DISCUSSION

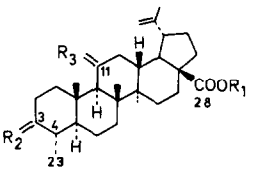
Extraction of dried leaves with methanol yielded, after silica gel CC the new 24-nor-triterpenoid carboxylic acids **1** (0.5%; $C_{29}H_{46}O_4$ $[M]^+$ at m/z 458.3419) and **2** (0.05%; $C_{29}H_{44}O_4$ $[M]^+$ at m/z 456.3218) as well as 3α,11α-dihydroxy-lup-20(29)-en-23,28-dioic acid (0.02%) isolated previously from the Araliaceae *Schefflera octophylla* [5]. The IR spectra of **1** and **2** showed absorptions assignable to hydroxyl, carbonyl and $>C=CH_2$ functions. The ORD spectrum of **2** showed a positive carbonyl Cotton effect at 286 nm (a + 19).

The formation of the monomethyl esters **3** and **4** indicated the presence of one carboxyl function. Acetylation of **3** or **4** gave the diacetate **5** and the monoacetate **6**, respectively. Oxidation of **3** or **4** with PDC afforded the same diketone **7** with a positive Cotton effect at 286 nm (a + 16).

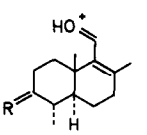
The mass spectra of **1**–**7** showed typical fragment ions derived from ring C cleavages similar to those found for other lupane carboxylic acids [5, 6]. In particular, a key ion A (m/z 223 and 221 for **1** and **2**, respectively) indicated the C-11 substitution [7] as well as the lack of a methyl group at ring A of the lupane skeleton.

The ^{1}H NMR spectrum of **1** confirmed the presence of four tertiary methyl groups (one of them shifted downfield to δ1.65), one secondary methyl group [δ1.08 (*d*, J = 6.5 Hz)], two secondary alcohol functions [δ3.88 (*m*, H-3β), δ4.10 (*dt*, $J = J' = 11.0$ Hz, $J'' = 5.0$ Hz, H-11β)] and two olefinic protons [δ4.60, 4.79 (2*m*)].

The ^{1}H NMR spectrum of **2** accounts also for four tertiary methyl functions [δ1.06 (9H), 1.69], one secondary methyl group [δ1.04 (*d*, J = 6.5 Hz)] as well as a



	R_1	R_2	R_3
1	H	α-OH; β-H	α-OH; β-H
2	H	O	α-OH; β-H
3	CH_3	α-OH; β-H	α-OH; β-H
4	CH_3	O	α-OH; β-H
5	CH_3	α-OAc; β-H	α-OAc; β-H
6	CH_3	O	α-OAc; β-H
7	CH_3	O	O



A

*Part 14 in the series "Natural Products from Vietnamese Plants". For Part 13 see ref. [1].

secondary alcohol function [δ4.10 (*dt*, $J = J' = 10.5$ Hz, $J'' = 5.5$ Hz, H-11β)] and two olefinic protons [δ4.58, 4.78 (2*m*)].

In the ^{13}C NMR spectrum of **1** (Table 1) the assignments of the signals were made by comparison with the ^{13}C NMR data of 3α,11α-dihydroxy-lup-20(29)-en-28-oic acid [1] and by inspection of the signal multiplicities in the SFORD spectrum.

On the other hand, the shift values for C-11–C-22 and C-26–C-30 of both compounds were in a good agreement, indicating an identical C-, D- and E-ring partial structure. The observed highfield shifts of C-3 ($\Delta\delta - 4.4$), C-5 ($\Delta\delta - 4.0$) and C-23 ($\Delta\delta - 8.7$) as well as the downfield shift of C-2 ($\Delta\delta + 3.7$) suggested the absence of a Me-4β group in the lupane skeleton. Similarly, the highfield shift of C-25 ($\Delta\delta - 5.0$) can be interpreted in terms of the loss of 1,3-diaxial interactions between Me-4β and Me-10β.

The chemical shifts of the signals in the ^{13}C NMR spectrum of **2** were assigned by comparison with **1**.

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

Carbon No.	1	2
1	35.0*t	43.0t
2	30.7t	38.1‡t
3	70.9d	212.7s
4	36.6d	45.1d
5	45.6d	53.8†d
6	17.8t	22.3t
7	35.8*t	34.4t
8	42.7s	42.3s
9	54.1d	54.4†d
10	39.3s	38.6s
11	70.3d	70.0s
12	38.6t	38.3‡t
13	37.8d	37.7d
14	42.9s	42.8s
15	30.1t	30.2t
16	33.0t	32.9t
17	56.6s	56.6s
18	49.5d	49.4d
19	47.6d	47.5d
20	150.9s	150.9s
21	31.3t	31.3t
22	37.5t	37.4t
23	21.1q	12.4§q
24	—	—
25	13.6q	13.8§q
26	17.8q	17.5q
27	14.7q	14.7q
28	178.8s	178.8s
29	110.1t	110.1t
30	19.6q	19.6q

*,†,‡,§Assignments with similar symbols may be interchanged.

*A list of the refined co-ordinates is deposited at the Cambridge Crystallographic Centre, U.K.

Oxidation of the hydroxyl group in the 3α-position gave predictable changes in the chemical shifts of the neighbouring carbon atoms. Similarly as found for betulafolienetriol and betulafolienediol [8], downfield shifts of all A-ring carbon atoms and a highfield shift of the equatorial Me-4 group were observed.

From the above data the new 24-nor-triterpenoid carboxylic acids were considered to be 24-nor-3α,11α-dihydroxy-lup-20(29)-en-28-oic acid (**1**) and 24-nor-11α-hydroxy-3-oxo-lup-20(29)-en-28-oic acid (**2**), respectively.

The structure of **1** (especially regarding the configuration at C-4) was independently confirmed by X-ray analysis of its corresponding methyl ester, **3**, using the computer programs Multan [9] and Shelx 76 [10].

Crystal data: orthorhombic (from ether–*n*-hexane), space group $P2_12_12_1$; unit cell $a = 8.437(4)$ Å, $b = 22.340(8)$ Å, $c = 14.096(5)$ Å; $Z = 4$; $D_c = 1.179$ g/cm^{-1}; $R = 0.072$*. Figure 1 shows a stereo view of the molecule. The Me-23 group occupies the equatorial 4α-position.

In addition to the new 24-nor-lupane derivatives **1** and **2**, described in this report, 3α,11α-dihydroxy-lup-20(29)-en-23,28-dioic acid, 3α,11α-dihydroxy-lup-20(29)-en-28-oic acid and its 23-dihydroxylated derivative [2], as well as the corresponding 23-oxo compound [1] have been found recently in leaves of *Acanthopanax trifoliatus*. Thus, this series of compounds seems to reflect the biosynthetic demethylation pathway of 4,4-dimethylated lupanes to 24-nor compounds like **1** and **2**.

EXPERIMENTAL

An EA-mass spectrometer of the Research Institute 'Manfred von Ardenne', Dresden, was used to record the positive ion MS (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.

Acanthopanax trifoliatus (L.) Merr. was identified by Dr. P. V. Nguyen, Institute of Biology, National Research Centre of the S.R.V. Hanoi; a voucher specimen has been deposited.

Isolation of compounds **1** *and* **2**. Dried and powdered leaves (200 g), collected near Hanoi in April 1981, were deffated with petrol and, subsequently, extracted with MeOH for 6 hr under reflux. Evaporation of the solvent and CC (silica gel) of the residue (40 g) yielded **2** (0.1 g, 0.05% yield, elution with petrol–$CHCl_3$, 3:7) and **1** (1 g, 0.5% yield, elution with petrol–$CHCl_3$, 1:9).

Compound **1**: mp 227–228° (Me_2CO–petrol); $[\alpha]_D^{25}$ +18.2° (EtOH; *c* 0.52); IR ν_{max}^{Nujol} cm^{-1}: 1645, 3070 (>C=CH$_2$), 1700 (COOH), 3475 (br, OH); MS *m/z* (rel. int.): 458.3419, $C_{29}H_{46}O_4$ calc. 458.3396 [M]$^+$ (4), 440 (30), 285 (7), 264 (9), 246 (40), 234 (100), 223 (65, A), 220 (38), 205 (53), 201 (52), 189 (82), 175 (85), 161 (59), 152 (36); ^{1}H NMR (pyridine-d_5–TMS): δ0.98, 1.05, 1.11 (3*s*, H_3-25, H_3-26, H_3-27), 1.08 (*d*, $J = 6.5$ Hz, H_3-23), 1.65 (*s*, H_3-30), 3.88 (*m*, H-3β), 4.10 (*dt*, $J = J' = 11.0$ Hz, $J'' = 5.0$ Hz, H-11β), 4.60, 4.79 (2*m*, H_2-29).

Compound **2**: mp 186–188° (Me_2CO–petrol); $[\alpha]_D^{25}$ +22.0° (EtOH; *c* 0.38); ORD: $[\phi]_{268}$ −680, $[\phi]_{304}$ +1210, $a = +19$; IR ν_{max}^{Nujol} cm^{-1}: 1640, 3070 (>C=CH$_2$), 1690 (COOH), 1730 (>C=O), 3450 (*br*, OH); MS *m/z* (rel. int.): 456.3218, $C_{29}H_{44}O_4$ calc. 456.3239 [M]$^+$ (10), 438 (30), 423 (9), 410 (5), 392 (10), 264 (14), 246 (57), 234 (56), 221 (63, A), 219 (42), 204 (74), 191 (67), 189 (100), 175 (74), 163 (50), 154 (36), 152 (30); ^{1}H NMR (pyridine-d_5–TMS): δ1.06 (9H, *s*, H_3-25, H_3-26, H_3-27), 1.04 (*d*, $J = 6.5$ Hz, H_3-23), 1.69 (*s*, H_3-30), 4.10 (*dt*, $J = J' = 10.5$ Hz, $J'' = 5.5$ Hz, H-11β), 4.58, 4.78 (2m, H_2-29). Further elution with

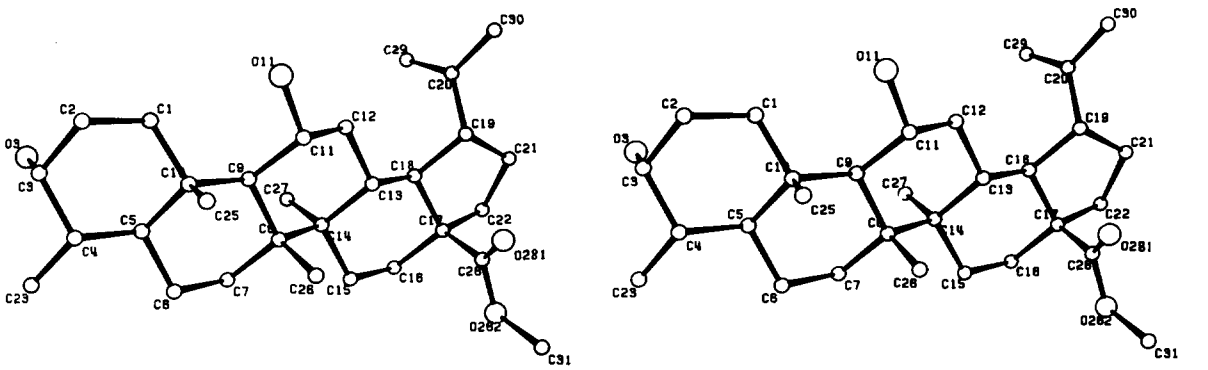


Fig. 1. Stereo view of the methyl ester 3.

$CHCl_3$–HOAc (7:3) yielded 40 mg (0.02%) 3α,11α-dihydroxy-lup-20(29)-en-23,28-dioic acid of mp 213–214° [5].

Methyl esters 3 *and* 4. Obtained from 1 or 2 by treatment with CH_2N_2 in MeOH.

Compound 3: mp 140–142° (Me_2CO–petrol); $[\alpha]_D$ +11.8° (EtOH; *c* 0.40); IR ν_{max}^{Nujol} cm^{-1}: 1640 (>C=CH_2), 1720 (COOMe), 3300, 3465, 3600 (OH); MS *m/z* (rel. int.): 472.3523, $C_{30}H_{48}O_4$ calc. 472.3552 $[M]^+$ (41), 454 (57), 436 (27), 412 (41), 299 (10), 278 (47), 260 (46), 248 (84), 234 (51), 223 (68), 201 (51), 189 (100), 175 (93), 168 (71), 166 (49), 161 (68); ^1H NMR ($CDCl_3$–TMS): δ0.98, 1.02, 1.04 (3*s*, H_3-25, H_3-26, H_3-27), 0.93 (*d*, *J* = 6.5 Hz, H_3-23), 1.72 (*s*, H_3-30), 3.66 (*s*, COOMe), 3.72 (*m*, H-3β), 3.96 (*dt*, *J* = *J'* = 11.0 Hz, *J''* = 5.0 Hz, H-11β), 4.63, 4.77 (2*m*, H_2-29).

Compound 4: mp 171–173° (Et_2O–petrol); $[\alpha]_D^{25}$ +20.3° (EtOH; *c* 0.40); IR ν_{max}^{Nujol} cm^{-1}: 1645, 3070 (>C=CH_2), 1720 (COOMe), 3420, 3520 (br, OH); MS: *m/z* (rel. int.): 470.3422, $C_{30}H_{46}O_4$ calc. 470.3396 $[M]^+$ (44), 452 (49), 437 (29), 410 (64), 393 (38), 299 (16), 278 (68), 260 (67), 250 (95), 234 (75), 221 (75), 201 (95), 189 (100), 175 (80), 168 (99); ^1H NMR ($CDCl_3$–TMS): δ1.02 (9H, *s*, H_3-25, H_3-26, H_3-27), 1.01 (*d*, *J* = 6.5 Hz, H_3-23), 1.71 (*s*, H_3-30), 3.66 (*s*, COOMe), 4.05 (*dt*, *J* = *J'* = 10.5 Hz, *J''* = 5.0 Hz, H-11β), 4.62, 4.76 (2*m*, H_2-29).

Acetates 5 *and* 6. Acetylation of 3 or 4 with Ac_2O–pyridine (12 hr at 20°) gave, after CC, 5 and 6.

Compound 5: amorphous, $[\alpha]_D^{25}$ +9.8° (EtOH; *c* 0.38); IR ν_{max}^{Nujol} cm^{-1}: 1240, 1740 (acetate), 1645, 3075 (>C=CH_2); MS *m/z* (rel. int.): 556 $[M]^+$ (8), 496 (53), 436 (51), 377 (17), 320 (14), 307 (59), 299 (25), 260 (43), 247 (65), 234 (34), 215 (39), 205 (100), 201 (70), 187 (94), 175 (89), 165 (16), 161 (48); ^1H NMR ($CDCl_3$–TMS): δ0.90, 0.99, 1.06 (3*s*, H_3-25, H_3-26, H_3-27), 0.82 (*d*, *J* = 6.5 Hz, H_3-23), 1.67 (*s*, H_3-30), 1.94, 2.07 (2*s*, acetates), 3.66 (*s*, COOMe), 4.58, 4.73 (2*m*, H_2-29), 4.84 (*m*, H-3β), 5.21 (*dt*, *J* = *J'* = 11.0 Hz, *J''* = 5.0 Hz, H-11β).

Compound 6: mp 193–195° (Me_2CO–petrol); $[\alpha]_D^{25}$ +16° (EtOH; *c* 0.40); IR ν_{max}^{Nujol} cm^{-1}: 1645, 3070 (>C=CH_2), 1240, 1740 (acetate); MS *m/z* (rel. int.): 512 $[M]^+$ (15), 466 (10), 452 (80), 393 (78), 320 (10), 299 (14), 263 (71), 260 (47), 247 (73), 234 (32), 221 (100), 201 (83), 187 (95), 175 (78), 166 (24), 161 (46); ^1H NMR ($CDCl_3$–TMS): δ1.02, 1.05, 1.10 (3*s*, H_3-25, H_3-26, H_3-27), 1.01 (*d*, *J* = 6.5 Hz, H_3-23), 1.68 (*s*, H_3-30), 1.96 (*s*, acetate), 3.68 (*s*, COOMe), 4.60, 4.74 (2*m*, H_2-29), 5.24 (*dt*, *J* = *J'* = 11.0 Hz, *J''* = 5.0 Hz, H-11β).

Oxidation of 3 *or* 4 *to the diketone* 7. To compounds 3 (30 mg) or 4 (32 mg) in DMF (2 ml) PDC (85 mg) was added and the soln stirred at 20° for 6 hr. Standard work-up followed by CC by elution with petrol–$CHCl_3$ (1:1) gave the diketone 7 (21 mg): mp 237–242° (Me_2CO–petrol); $[\alpha]_D^{25}$ +20.3° (dioxane; *c* 0.36); ORD: $[\phi]_{268}$ −93.6, $[\phi]_{303}$ +1540, *a* = +16; UV: λ nm: (ε) 231 (290), 296 (56); IR ν_{max}^{Nujol} cm^{-1}: 1640, 3075 (>C=CH_2), 1690–1730 (br. ketone and ester); MS: *m/z* (rel. int.): 468 $[M]^+$ (40), 450 (12), 408 (24), 276 (30), 248 (31), 233 (36), 219 (100), 205 (24), 189 (62), 175 (67), 166 (16); ^1H NMR (Me_2CO-d_6–TMS): 0.93, 1.28, 1.39 (3*s*, H_3-25, H_3-26, H_3-27), 0.90 (*d*, *J* = 6.5 Hz, H_3-23), 1.70 (*s*, H_3-30), 3.65 (*s*, COOMe), 4.63, 4.77 (2*m*, H_2-29).

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