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THOMANDERTRIOL, A TRITERPENOID FROM THE TWIGS OF *THOMANDERSIA LAURIFOLIA*

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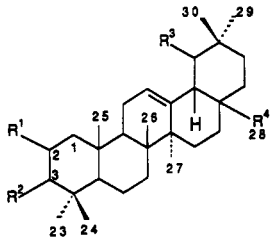
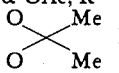
ABSTRACT.—Thomandertriol [**3**], a new pentacyclic triterpene, was isolated from the $CHCl_3$ extract of the twigs of *Thomandersia laurifolia*. Its structure was established as 2α,3α,19α-trihydroxyolean-12-ene using spectroscopic data and chemical correlation. Taraxeryl palmitate, 2α,3α-dihydroxyurs-12-en-28-oic acid, maslinic and epimaslinic acids were also isolated.

Thomandersia laurifolia (T. Anders ex Benth.) Baill. (Acanthaceae) is a small tree of the rainforest canopy occurring from Cameroon to Zaire (1). *T. laurifolia* and its sister species, *Thomandersia hensii*, are both extensively used in traditional medicine (1). A leaf decoction is used in Cameroon and Zaire as remedy for diarrhea and colic. The irritant sap is the treatment of choice for furuncles, abscesses, and syphilitic ulcers. A decoction of the roots and leafy twigs is used for urinogenital disorders and intestinal parasites and as a tonic in cases of debility and fatigue. Pulped roots are used to treat edema and rheumatism and sometimes ear and eye inflammations (1). Our interest in the systematic study of chemical constituents of Cameroonian medicinal plants has led to the investigation of twigs and leaves of *T. laurifolia*. We now report the isolation and structural elucidation of triterpenes from $CHCl_3$ extract of the twigs of this plant.

The $CHCl_3$ extracts of the finely powdered twigs of *T. laurifolia*, upon repeated cc, preparative tlc, and crystallizations, afforded a mixture of sterols, one carotenoid, zeaxanthin (2), and five triterpenoids. By means of spectroscopic data, published information, or comparison with authentic specimens, four of these triterpenes were identified as taraxeryl palmitate (3), maslinic acid [**1**] (4), and a mixture of epimaslinic acid [**2**] and 2α,3α-dihydroxyurs-12-en-28-oic acid (5,6). A new triterpenoid, tentatively named thomandertriol [**3**], was also fully characterized.

Compound **3**, obtained as a powder, gave a positive Liebermann-Burchard reaction indicative of a triterpene skeleton. It analyzed for $C_{30}H_{50}O_3$ from its eims and elementary analysis. The ir spectrum of **3** revealed absorption peaks at ν max 3400–3600 (hydroxyl groups) and 1630 (C=C). There was no peak due to a carbonyl group. The ^{1}H-nmr spectrum of **3** showed singlets due to eight tertiary methyl groups at δ 0.73, 0.85, 0.93, 0.96 (6H), 1.00, 1.12, and 1.20 ppm. The ^{13}C-nmr and DEPT spectra of **3** (see Experimental), which exhibited one trisubstituted double bond δC 143.1 (C), 124.2 (CH), three oxymethines δC (81.6, 78.6, 65.9), and eight tertiary methyl groups (15.9, 16.8, 21.5, 24.2, 24.6, 27.8, 28.1, 28.2), were in agreement with the molecular formula $C_{30}H_{50}O_3$. The appearance of a coarse triplet at δ 5.28–5.32 (for H-12) and signals in the region of δC 144 (s, C-13) and 122 (d, C-12) in the ^{1}H- and ^{13}C-nmr spectra were indicative of a Δ^{12} oleanene skeleton (7–10). This suggestion was confirmed by the mass spectrum of **3**, which revealed a very small parent ion but prominent peaks at *m/z* 234, 224, and 201 $[234-H_2O-Me]^+$. The former peaks corresponded to fragmentation through a retro-Diels-Alder reaction at



1 R^1=α-OH, R^2=β-OH, R^3=H, R^4=COOH
2 R^1=R^2=α-OH, R^3=H, R^4=COOH
3 R^1=R^2=R^3=α-OH, R^4=Me
4 R^1=R^2=α-OAc, R^3=α-OH, R^4=Me
5 R^1+R^2=  R^3=α-OH, R^4=Me

ring C. The mass of the peak at *m/z* 224 $[M-234]^+$ indicated that two of the three hydroxyl groups were located in the rings A and B. These two hydroxyl groups were assigned to ring A from examination of the acetylated product.

Upon acetylation with Ac_2O in pyridine, **3** gave the diacetate **4**, δ_H (2.10, 1.94). The ^{1}H-nmr spectrum of **4** showed signals due to carbinylic protons at δ 4.94 (d, J=3.0 Hz, H-3) and 5.21 (ddd, J=12, 4, 3, Hz, H-2). The chemical shift and the coupling constant of the H-3 signal showed that the hydroxyl group at C-3 was axial. The magnitudes of the coupling constants associated with H-2 indicated that the proton had a trans-diaxial relationship with one H-1 proton, and therefore the hydroxyl group at C-2 was equatorial. These chemical shifts and spin coupling constants are almost superimposable with those published for hirsudiol diacetate [δ_H 5.26 (ddd, J=12.0, 4.5, 3.0 Hz, H-2) and 4.97 (d, J=2.4 Hz, H-3)] (11).

The diacetate **4** gave an hydroxyl absorption at ν max 3600 cm^{-1} in its ir spectrum. The fact that acetylation did not change the masses of the fragments *m/z* 234 and 201 served to locate this unreactive hydroxyl group in either ring D or E. It was finally fixed at C-19 in the α orientation because of the appearance in the ^{1}H-nmr spectrum of **4** of a signal at δ 3.32 (1H, d) with H-18/H-19 coupling constant J ax/eq=3.4 Hz, as all the remaining possible oxymethine positions possess at least two neighboring hydrogens. The non-acetylation of the C-19α hydroxyl group is most likely due to its neopentyl character and therefore steric hindrance (12). Moreover the acetylation of this C-19α hydroxyl group was not successful even under drastic conditions (heating) (13).

In the presence of Me_2CO and a catalytic amount of H_2SO_4, **3** formed the acetonide **5**. The above spectroscopic data and chemical correlations led to the assignment of 2α,3α,19α-trihydroxyolean-12-ene to thomandertriol [**3**]. From a biogenetic point of view it is important to note that oxidation at the C-2, C-3 and/or C-19 positions is a common feature of the ursane and oleanane triterpenoids isolated from *T. laurifolia*.

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—DEPT experiments were carried out with θ=45°, 90°, and 135°; the quaternary carbons were determined by subtraction of these spectra from the broad-band ^{13}C-nmr spectrum. Nmr spectra were measured at 200.13 MHz for ^{1}H and at 50.32 MHz for ^{13}C nmr. Chemical shifts are given at δ (ppm) with TMS as internal standard. Eims was obtained at 70 eV. Si gel 60 (70–230 mesh Merck) was used for cc. Preparative tlc was performed on Si gel GF 254.

PLANT MATERIAL.—The twigs of *T. laurifolia* were collected at Edea, Cameroon in April 1986 and identified at the National Herbarium in Yaoundé, where a voucher specimen (No. 9120) has been deposited.

EXTRACTION AND ISOLATION OF CONSTITUENTS.—The air-dried and powdered twigs of *T. laurifolia* (5 kg) were extracted with $CHCl_3$ in a Soxhlet apparatus. The extract was concentrated under reduced pressure, and the residue (40 g) was chromatographed over Si gel. Elution began with hexane and continued stepwise through hexane/EtOAc mixtures, EtOAc, and EtOAc/MeOH mixtures. Fractions were combined on the basis of tlc analysis. From the chromatographic separation above, and in some cases with the aid of successive preparative tlc, a total of five triterpenes and one carotenoid (zeaxanthin, 20 mg) were obtained along with a mixture of sterols (4 g). From the spectroscopic data, published information, or comparison with authentic specimens, four of these

triterpenoids were identified as the known taraxeryl palmitate (40 mg), maslinic acid [**1**] (50 mg), and a mixture of epimaslinic acid [**2**] and 2α,3α-dihydroxyurs-12-en-28-oic acid (2.5 g). The new triterpenoid **3** (35 mg) and its derivatives are described below.

2α,3α,19α-Trihydroxyolean-12-ene [**3**].—Colorless powder: mp 289–291°; $[\alpha]_D$ −48° (c=0.33, $CHCl_3$); ir ν max (KBr) cm^{-1} 3400–3600 (OH), 1630 (C=C), 1450, 1350, 1380, 1040; ^1H nmr (CD_3OD) δ 0.73 (3H, s), 0.85 (3H, s), 0.93 (3H, s), 0.96 (6H, s), 1.00 (3H, s), 1.12 (3H, s), 1.20 (3H, s), 2.3 (1H, br s), 3.27 (1H, d J=3 Hz, H-19), 3.80–4.20 (m, H-2α, H-3α), 5.30 (m, H-12); ^{13}C nmr (CD_3OD) 143.1 (s, C-13), 124.2 (d, C-12), 81.6 (d, C-19), 78.6 (d, C-3), 65.9 (d, C-2), 49.8 (d, C-18), 47.8 (d, C-5), 47.3 (d, C-9), 41.2 (t, C-1), 41.1 (s, C-14), 40.8 (s, C-8), 39.4 (s, C-10), 38.1 (s, C-4), 38.0 (s, C-20), 37.8 (t, C-22), 34.4 (s, C-17), 32.8 (t, C-7), 29.5 (t, C-21), 28.2 (q, C-23), 28.1 (q, C-28), 28.0 (t, C-15), 27.8 (q, C-29), 27.5 (t, C-16), 24.6 (q, C-27), 24.2 (q, C-30), 23.5 (t, C-11), 21.5 (q, C-24), 17.9 (t, C-6), 16.8 (q, C-26), 15.9 (q, C-25); eims m/z (rel. int.) $[M]^+$ 458 (0.5), 234 (42), 230 (24), 224 (35), 219 (16), 205 (15), 202 (20), 201 (100), 200 (17), 191 (12), 189 (18), 187 (24), 185 (37), 133 (30), 131 (46), 119 (50), 107 (34), 105 (45), 91 (39), 80 (41), 69 (52), 55 (77), 43 (98). Found C 78.52, H 10.58 ($C_{30}H_{50}O_3$ requires C 78.60, H 10.48).

Acetylation of **3**.—Treatment of compound **3** (15 mg) with Ac_2O (12 ml) in pyridine (2 ml) at room temperature overnight gave the diacetate **4** as a yellow oil: ir ν max ($CHCl_3$) 3640 (OH) 1730 (br band, carbonyl groups), 1640 (C=C), 1460, 1370, 1260, 1240, 1040; ^1H nmr ($CDCl_3$) 0.68 (3H, s), 0.83 (3H, s), 0.94 (3H, s), 0.95 (6H, s), 0.98 (3H, s), 1.27 (3H, s), 1.28 (3H, s), 1.94 (3H, s, Ac), 2.10 (3H, s, Ac), 2.40 (1H, brs, H-18β), 3.32 (1H, d, J=3.4 Hz, H-19β), 4.94 (1H, d, J=3.0 Hz, H-3), 5.21 (1H, ddd, J=12, 4, 3 Hz, H-2), 5.42 (1H, t-like, H-12); eims m/z (rel. int.) $[M]^+$ 542 (absent), 234 (40), 228 (12), 213 (10), 201 (51), 167 (14), 149 (37), 97 (11), 87 (18), 85 (29), 83 (39), 74 (19), 71 (21), 69 (20), 57 (38), 43 (100), 41 (40).

Acetonide of **3**.—Compound **3** (10 mg) was dissolved in analytical grade Me_2CO (4 ml), 2 drops of concentrated H_2SO_4 were added, and the reaction mixture was stirred for 3 h at room temperature. Solid K_2CO_3 was then added and the mixture filtered. Removal of the solvent from the filtrate yielded the acetonide **5** as an oil: ^1H nmr ($CDCl_3$) δ 0.69 (3H, s, Me), 0.83 (3H, s, 6H, 2×Me), 0.87, 0.90, 1.00, 1.02, 1.16 each (3H, s, Me), 1.26 (6H, s, 2×methyls of acetonide).

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