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A PENTACYCLIC TRITERPENE WITH ANTI-INFLAMMATORY AND ANALGESIC ACTIVITY FROM THE ROOTS OF *COMMIPHORA MERKERI*[1]

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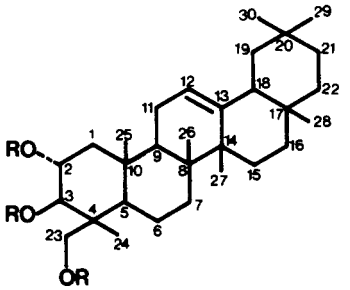
ABSTRACT.—A new pentacyclic triterpene [**1**] with anti-inflammatory activity was isolated from the roots of *Commiphora merkeri*. The structure was established on the basis of spectral data and conversion to its triacetate.

Species from the genus *Commiphora* (Burseraceae) are widely used (1–4) for the treatment of a variety of ailments. Our interest in *Commiphora merkeri* Engl. was aroused by its use in folk medicine against infections (2). The presence of volatile oils and monoterpenes and sesquiterpenes in the above genus has been reported (5). Triterpenes in the resin of *Commiphora gladulosa* were first reported by Thomas and Müller (6), while a crystalline steroidal fraction (7) with anti-inflammatory activity was isolated from the petroleum ether extract of *Commiphora mukul*.

In our general program (8) designed to locate the origin of the activity, 2α,3β,23-trihydroxyolean-12-ene [**1**] was discovered. We report the isolation, characterization, and biological activity of this new pentacyclic triterpene **1** from the roots of *C. merkeri*.

The structural assignment of **1** was based upon accurate mass determination, empirical formula ($C_{30}H_{50}O_3$), ir, ^{1}H- and ^{13}C-nmr spectral data, and conversion to the triacetate **2**. The mass spectrum ($[M]^+$ *m/z* 458) shows the typical *m/z* 218 fragment (RDA) for 12-oleanenes (9), indicating the absence of oxygen functions on rings D and E. The mass spectrum ($[M]^+$ *m/z* 584) of the acetate **2** indicates a total of three acetoxyls, which is evident in the ^{1}H-nmr spectrum of **2** (δ 1.97, 2.01, and 2.08); this was substantiated by the ir spectrum of **2**.



1 R=H
2 R=Ac

The ^{1}H-nmr spectrum of **1** shows a multiplet centered at δ 3.64 and a doublet at δ 3.40 (J = 10 Hz), assignable to the H-2 and H-3 anomeric protons, respectively. A downfield shift of the H-2 and H-3 protons (11) is observed in the ^{1}H-nmr spectrum of the triacetate at δ 5.20 (m) and 5.05 (d, $J_{2,3}$ = 10 Hz). The pair of doublets centered at δ 3.40 (J = 12 Hz) and δ 3.70 (J = 12 Hz) in the ^{1}H-nmr spectra of **1** and **2**, respectively, is indicative of a $-CH_2-O$ group and is in agreement with the resonances reported for similar C-23 hydroxyl terpenoids (11–13). Broad multiplets at δ 5.18 and δ 5.20 can be assigned to the C-12 vinyl proton in the ^{1}H-nmr spectra of **1** and **2**, respectively. Signals in the ^{13}C-nmr spectrum of **2**, attributed to C-2, C-3, C-12, C-13, and C-23 (δ 70.0, 78.7, 124.1, 145.4, and 65.5, respectively) are consistent with published data on 2α,3β,23-trihydroxyolean-12-enes (11,14,15).

[1]Part 9 in the series "Studies of South African Medicinal Plants." For Part 8, see Dekker *et al.*, *J. Nat. Prod.*, **51**, 584 (1988).

The triterpene **1** was tested orally for possible anti-inflammatory and analgesic activity (16). It was found to have a 28% inhibition (100 mg/kg dose) [phenylbutazone (reference) had 64% inhibition at 100 mg/kg dose] of the phlogistic response (carrageenan-induced edema) in the rat. At the same dose, compound **1** caused a 37% inhibition of the writhing response in the rat [aspirin (reference) had 85% inhibition at 100 mg/kg dose].

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—Melting points were determined using a Reichert hot stage microscope and are uncorrected. Ir spectra were obtained with a Unicam SP1050 spectrophotometer. Nmr spectra were recorded on Varian EM360 and Varian FT20 instruments using TMS as internal standard. Mass spectra were determined on an AEI MS-9 spectrometer. Preparative chromatography was carried out on a Waters/LC system 500, and Kieselgel 60 (70–230 mesh, Merck) was used for cc. Optical rotations were obtained from a Perkin-Elmer 141 polarimeter.

PLANT MATERIAL.—The roots (9.5 kg) of *C. merkeri* were collected on 14 October 1977 at Louis Trichardt, Northern Transvaal. A voucher specimen is deposited in the Botanical Research Institute, Pretoria.

EXTRACTION AND ISOLATION.—Plant material was extracted in accordance with our normal procedures (8). Air-dried milled roots of *C. merkeri* (9.5 kg) were successively extracted with C_6H_6 (29 g extract), EtOAc (29 g extract) and MeOH (110 g extract) at room temperature for 48 h. The EtOAc extract was found to exhibit anti-inflammatory activity (35% inhibition). Compound **1** was isolated by means of open cc and preparative hplc using C_6H_6-EtOAc (9:1) as the mobile phase.

2α,3β,23-TRIHYDROXYOLEAN-12-ENE [**1**].—Crystallization from EtOH yielded **1** as fine white needles (1.9 g, 0.9% of total extract): mp 256°; $[\alpha]^{22}D$ +48° (*c* = 1.8, dioxane) and $[\alpha]^{22}D$ +122° (*c* = 1.2, $CHCl_3$); ir ν max (KBr) 3450, 2950, 2880, 1460, 1380, 1050 cm^{-1}; ^1H nmr ($CDCl_3$/CD_3OD) δ 0.77 (3H, s, H-26), 0.83 (3H, s, H-28), 0.88 (3H, s, H-29), 1.05 (3H, s, H-25), 1.05 (3H, s, H-30), 1.08 (3H, s, H-27), 1.12 (3H, s, H-24), 3.30 (1H, d, *J* = 12 Hz, H-23), 3.50 (1H, d, *J* = 12 Hz, H-23), 3.30–3.98 (1H, m, H-2β), 3.40 (1H, d, *J* = 10 Hz, H-3α), 5.18 (1H, m, H-12); hrms *m/z* calcd for $C_{30}H_{50}O_3$, 458.7312, found 458.7307.

2α,3β,23-TRIACETOXYOLEAN-12-ENE [**2**].—Acetylation of **1** with Ac_2O/pyridine yielded the triacetate **2** as a colorless oil: $[\alpha]^{22}D$ +40° (*c* = 2.2 in $CHCl_3$); ir ν max ($CHCl_3$) 2950, 1755, 1460, 1370, 1250, 1040 cm^{-1}; ^1H nmr ($CDCl_3$) δ 0.80 (3H, s, H-26), 0.86 (3H, s, H-28), 0.90 (6H, s, H-29, H-30), 1.01 (3H, s, H-25), 1.06 (3H, s, H-27), 1.13 (3H, s, H-24), 1.97 (3H, s, OAc), 2.01 (3H, s, OAc), 2.08 (3H, s, OAc), 3.50 (1H, d, *J* = 12 Hz, H-23), 3.90 (1H, d, *J* = 12 Hz, H-23), 5.05 (1H, d, *J* = 10 Hz, H-2β), 5.10 (1H, m, H-3α), 5.20 (1H, m, H-12); ^{13}C nmr ($CDCl_3$) δ 16.9 (q, C-26), 17.2 (q, C-25), 18.1 (t, C-6), 20.6 (q, $OCOCH_3$), 20.7 (q, $OCOCH_3$), 21.0 (q, $OCOCH_3$), 21.7 (q, C-28), 23.2 (t, C-11), 23.5 (t, C-16), 23.6 (q, C-29), 22.1 (q, C-24), 25.8 (t, C-27), 28.2 (t, C-15), 31.1 (s, C-20), 31.3 (t, C-21), 32.3 (t, C-7), 32.6 (t, C-22), 33.1 (q, C-30), 33.8 (s, C-10), 37.9 (t, C-1), 39.7 (s, C-8), 40.2 (s, C-4), 41.7 (s, C-14), 41.9 (d, C-18), 44.2 (t, C-19), 47.4 (s, C-17), 47.8 (d, C-5), 47.9 (d, C-9), 65.5 (t, C-23), 70.0 (d, C-2), 78.7 (d, C-3), 124.1 (d, C-12), 145.4 (s, C-13), 170.6, 170.3, 170.2 (3×s, OCOMe); hrms *m/z* calcd for $C_{36}H_{56}O_6$, 584.8044, found 584.8069.

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