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STRUCTURES OF TWO NEW PHENOLIC 24-NOR-D:A-FRIEDO-OLEANANES RELATED TO ZEYLASTERONE: A PARTIAL SYNTHESIS OF TRIMETHYLZEYLASTERONE

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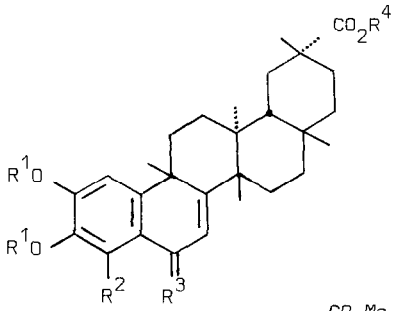
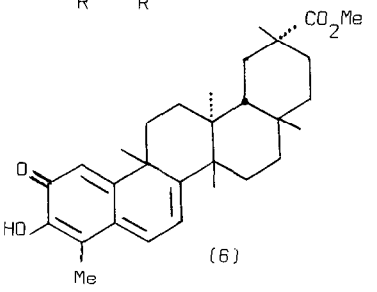
Abstract: Zeylasteral and desmethylzeylasterone, two new triterpenes from Kokoona zeylanica have been shown to be 2,3-dihydroxy-6,23-dioxo-24-nor-D:A-friedo-oleana-1,3,5(10),7-tetraen-29-oic acid methyl ester (20α) and 2,3-dihydroxy-6-oxo-24-nor-D:A-friedo-oleana-1,3,5(10),7-tetraen-23,29-dioic acid (20α), respectively, and have been related to trimethylzeylasterone. A partial synthesis of trimethylzeylasterone starting from pristimerin has been achieved.

Recently we established the structure of zeylasterone, the first of a new series of natural phenolic triterpenes as 2,3-dihydroxy-6-oxo-24-nor-D:A-friedo-oleana-1,3,5(10),7-tetraen-23,29-dioic acid-29-methyl ester (20α) (1), based on its spectral data. We now wish to report a synthesis of its trimethyl derivative (5) starting from readily available pristimerin (6) and the structure elucidation of two further triterpenes related to zeylasterone isolated from the same plant. The structures of these compounds which we have established as zeylasteral (2) and desmethylzeylasterone (3) are based on the following spectral and chemical evidence.

The light petroleum extract of the outer stem bark of K. zeylanica was separated into neutral, phenolic and acidic fractions. Neutral fraction consisted mainly of pristimerin (6), and the major compound in the acidic fraction was zeylasterone (1). The phenolic fraction on chromatography afforded zeylasteral (2)[2] (0.5%), $C_{30}H_{38}O_6$, answering Liebermann Burchard test for triterpenes and $FeCl_3$ test for phenols. UV spectrum indicated zeylasterone type chromophore (Table 1). Methylation (CH_2N_2) afforded dimethylzeylasteral (7), m.p. 201-202°, $[\alpha]_D$ - 120.3°





(6)

(1) R^1= H; R^2=CO_2H; R^3=O; R^4=Me

(2) R^1= H; R^2=CHO: R^3=O; R^4=Me

(3) R^1= R^4=H; R^2=CO_2H; R^3=O

(4) R^1= R^4=Me; R^2=CO_2H; R^3=O

(5) R^1= R^4=Me; R^2=CO_2Me; R^3=O

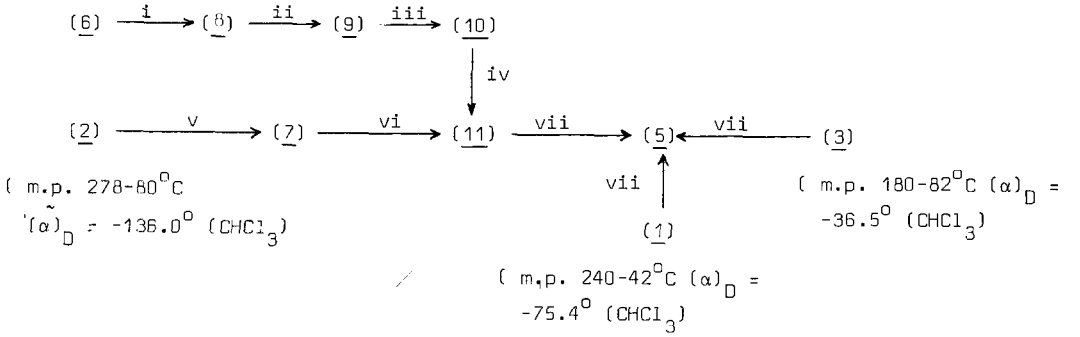
(7) R^1= R^4=Me; R^2=CHO; R^3=O

(8) R^1= H; R^2=R^4=Me; R^3=H_2

(9) R^1= R^2=R^4=Me; R^3=H_2

(10) R^1= R^2=R^4=Me; R^3=O

(11) R^1= R^4=Me; R^2=CO_2H; R^3=O



SCHEME. i) $NaBH_4$, methanol, 27°, 1hr; ii) $(CH_3)_2SO_4$, anh. K_2CO_3, anh. acetone, reflux, 4 hrs; iii) NBS, dioxan-H_2O, $CaCO_3$, hν(60W tungsten filament), 27°C, 1 hr; iv) NBS, dioxan-H_2O, $CaCO_3$, dibenzoyl peroxide, hν(IR) (5hrs); v) $(CH_3)_2SO_4$, anh. K_2CO_3, anh. acetone, reflux, 4 hrs; vi) CrO_3, H_2SO_4, acetone0°C, 15 min; vii) CH_2N_2 in ether, 15 min.

($CHCl_3$). The IR (KBr) spectrum of zeylasteral showed the presence of OH (3500-3140 cm^{-1}), saturated ester CO(1727), aromatic aldehyde CO(1650) and αβ-unsaturated Ketone CO(1642). ^1H NMR of zeylasteral and its dimethyl derivative (7) closely resembled that of trimethyl zeylasterone (5) (see Table 2). Jones Oxidation of zeylasteral (2) followed by methylation (CH_2N_2) gave trimethylzeylasterone (5)[1] (see Scheme) (m.p., mixed m.p., Co-TLC, Co-IR). The acidic fraction of the benzene extract on chromatography gave the minor component, desmethylzeylasterone (3)[2] (0.14%), $C_{29}H_{36}O_7$, methylation (CH_2N_2) of which afforded trimethylzeylasterone (5) (see Scheme).

The structures of all natural products were based on spectroscopic evidence (see above and Tables 1 and 2) and have been related to trimethylzeylasterone (5). Thus, an unequivocal synthesis of (5) starting from readily available pristimerin (6) has been attempted and achieved by the sequence (see Scheme); (i) $NaBH_4$ reduction of pristimerin (6)[3] yielding pristimerol (8, 66%); (ii) Me_2SO_4 methylation of (8) giving dimethylpristimerol (9, 99%); (iii) oxidation of (9) with NBS-hν[4] affording 6-oxodimethyl pristimerol (10, 40%); (iv) further oxidation of (10) with NBS-dibenzoyl peroxide and IR irradiation giving dimethylzeylasterone (11, 35%) which on methylation with diazomethane afforded trimethylzeylasterone (5, 98%).

Natural occurrence of (2) and (3) is of significance as they may lie in the pathway leading to the biosynthesis of zeylasterone (1). starting from pristimerin (6).

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Table 1. UV spectral data of zeylasteral (2), desmethylzeylasterone (3) and trimethylzeylasterone (5) in EtOH

Compound	λ_{max} (log ε) nm				
(2)	211(4.16)	225(4.09)	253(4.08)	291(3.71)	336(3.67)
(3)	210(4.15)	220(4.00)	250(3.99)	302(3.67)	340(3.64)
(5)	207(4.00)	225(3.88)	245(3.99)	287(3.72)	312(3.72)

Table 2. ^{1}H NMR chemical shifts (δ) of zeylasteral (2), dimethylzeylasteral (7), desmethylzeylasterone (3) and trimethylzeylasterone (5) (60 MHz in $CDCl_3$)

Compound	C-1 H	C-7 H	C-9 Me	C-13 Me	C-14 Me	C-17 Me	C-20β Me	C-4 CHO	C-4 CO_2Me	C-20α CO_2Me	2,3-di-OMe
(2)	6.36	7.30	1.56	1.10	1.33	1.18	0.56	11.00	-	3.53	-
(7)	6.36	7.03	1.61	1.13	1.33	1.18	0.63	10.30	-	3.58	3.86,4.00
(3)[a]	6.10	7.00	1.50	1.10	1.26	1.13	0.66	-	-	-	-
(5)	6.22	6.95	1.60	1.11	1.32	1.17	0.60	-	3.93	3.54	3.82,3.93

[a] ^{1}H NMR determined in DMSO-d_6

References and footnotes

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2. For physical data, see Scheme; The composition of all new compounds was confirmed by elemental analysis and/or high resolution mass spectrometry; Structural assignments are based on UV, IR, and ^{1}H NMR spectroscopic evidence.
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