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SHORT COMMUNICATION

SYNTHESIS OF δ-BOSWELLIC ACID

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Abstract—The synthesis of δ-boswellic acid from α- or β-boswellic acid is reported. It is not identical with γ-boswellic acid.

Ursane and oleanane triterpenoid carboxylic acids are significant components of frankincense,[1–3] the gum of *Boswellia carteri* (Burseraceae). Among these, α- and β-boswellic acids (Ia, Ib) have been repeatedly isolated in several investigations[4–8] while a third isomer, γ-boswellic acid, has been separated only once.[9]

This situation is somewhat paralleled in the amyrin clan where the α- and β-amyrins (Ic, Id) are relatively abundant and accessible in the plant kingdom[10] while δ-amyrin (IVa) has been difficultly isolable in minor amount only from Spanish broom (*Spartium junceum* L.).[11] Since this oleanane isomer contains its ethylenic linkage in the C13(18) location and the corresponding boswellic acid (IVb) is unknown, its synthesis for comparison with γ-boswellic acid is now reported. Thus, dehydration of the methyl acetate (Ie) of α-boswellic acid affords the heteroannular diene (II) which can also be obtained by the acid isomerization of the homoannular diene derivative (III) of β-boswellic acid.[3]

Hydrogenation of II in acid-free media[12] yielded methyl δ-boswellate acetate (IVc). This levorotatory acetate and related alcohol (IVd) are clearly different from the corresponding strongly dextrorotatory γ-boswellic acid derivatives which have been plausibly represented as homoannular β-boswellic acid dienes (III) originating from dehydration of an 11-hydroxyursene. This supposition finds support in the extreme facility of dehydration of a 11β-hydroxyursene (If)[13] and in the recent confirmation of the presence of the 11-oxo congener in the triterpenoid mixture.[14]

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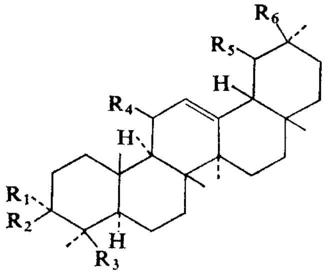
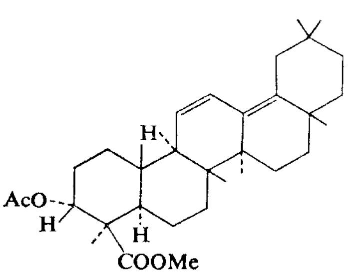
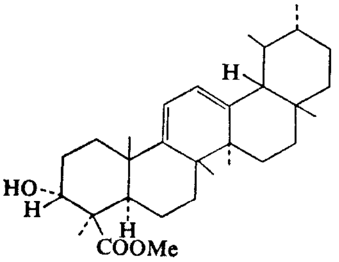


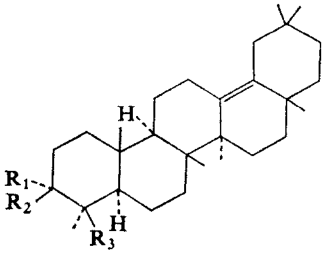
	R_1	R_2	R_3	R_4	R_5	R_6
(I) a.	OH	H	COOH	H	H	Me
b.	OH	H	COOH	H	Me	H
c.	H	OH	Me	H	Me	H
d.	H	OH	Me	H	H	Me
e.	OAc	H	COOMe	H	Me	H
f.	H	OH	Me	OH	H	Me



(II)



(III)



	R_1	R_2	R_3
(IV) a.	H	OH	Me
b.	OH	H	COOH
c.	OAc	H	COOMe
d.	OH	H	COOMe

EXPERIMENTAL

M.p.s were determined using a standardized N.P.L. thermometer. Rotations were measured in $CHCl_3$ solution in 1 dm tube at approximately 15°. U.v. absorption spectra were determined in ethanol solution.

The phrase "in the usual way" implies, in general, dilution with water, extraction with ether, washing consecutively with aqueous NaOH, water, aqueous HCl and aqueous $NaHCO_3$, followed by drying of the ethereal extract over Na_2SO_4, filtration and evaporation to dryness under reduced pressure. Hydrogenations were carried out, at room temperature, in glacial acetic acid which had been refluxed over and distilled from CrO_3. Acetylations were carried out using acetic anhydride in pyridine solution at 100° for 30 min unless otherwise specified.

Methyl 3α-*Acetoxyolean*-13(18)-*en*-24-*oate* (*IVc*)

A solution of methyl 3α-acetoxyoleana-11,13(18)-dien-24-oate (550 mg, m.p. 180–182°, $[\alpha]_D -70°$) in acetic acid (200 ml) was added to a suspension of freshly reduced Pt (from 200 mg PtO_2) in acetic acid (100 ml) and the mixture shaken with H_2 for 48 hr at room temperature when absorption was complete. The catalyst was removed by filtration and the filtrate evaporated to dryness under reduced pressure to yield a residue which crystallized from $CHCl_3$–methanol to give *methyl* 3α-*acetoxyolean*-13(18)-*en*-24-*oate* (IVc) as plates (400 mg), m.p. 190–191°, $[\alpha]_D -40°$ (*c*, 5·3). (Found: C, 77·1; H, 10·1. $C_{33}H_{52}O_4$ required: C, 77·3; H, 10·2 per cent.) λ_{max} at 207 nm ($\epsilon = 8850$) (ϵ_{215} 5600; ϵ_{220} 3420).

Methyl 3α-*Hydroxyolean*-13(18)-*en*-24-*oate* (*IVd*)

A solution of methyl 3α-acetoxyolean-13(18)-en-24-oate (300 mg) in methanolic KOH (5 per cent, 250 ml) was refluxed for 1 hr. Isolation of the product in the usual way yielded *methyl* 3α-*hydroxyolean*-13(18)-*en*-24-*oate* (IVd) which crystallized from $CHCl_3$–methanol as plates (200 mg), m.p. 274–275°, $[\alpha]_D -14°$ (*c*, 1·5).

(Found: C, 79·0; H, 10·6. $C_{31}H_{50}O_3$ required: C, 79·1; H, 10·7 per cent.) λ_{max} at 206 nm ($\epsilon = 5350$) (ϵ_{210} 4200; ϵ_{220} 2300). Acetylation of IVd using pyridine–acetic anhydride gave IVc from $CHCl_3$–methanol as plates, m.p. and mixed m.p. 188–190°, $[\alpha]_D -41°$ (*c*, 2·3).

11β-*Hydroxyurs*-12-*en*-3β-*yl Acetate* (*If*)

A solution of 11-oxours-12-en-3β-yl acetate[10] (1 g) in ether (500 ml) was refluxed with $LiAlH_4$ (1 g) for 2 hr. The product, isolated avoiding the use of mineral acid, was treated with pyridine–acetic anhydride at room temperature for 20 hr. The acetylated product, isolated avoiding the use of mineral acid, was crystallized from $CHCl_3$–methanol to yield 11β-*hydroxyurs*-12-*en*-3β-*yl acetate* as plates (650 mg), m.p. 170–172°, $[\alpha]_D -14°$ (*c*, 1·5). (Found: C, 79·7; H, 10·8. $C_{32}H_{52}O_3$ required: C, 79·3; H, 10·8 per cent.) λ_{max} at 210 nm ($\epsilon = 5550$).

Dehydration of 11β-*Hydroxyurs*-12-*en*-3β-*yl Acetate*

(*a*) A mixture of 11β-hydroxyurs-12-en-3β-yl acetate (250 mg) acetic anhydride (30 ml) and anhydrous sodium acetate (250 mg) was refluxed for 2 hr. The product, isolated in the usual way, crystallized from $CHCl_3$–methanol to yield ursa-9(11):12-dien-3β-yl acetate as needles (150 mg), m.p. and mixed m.p. 165–167°, $[\alpha]_D +318°$ (*c*, 1·2).

(*b*) A solution of 11β-hydroxyurs-12-en-3β-yl acetate (250 mg) in acetic acid (250 ml) was heated on the steam-bath with concentrated HCl (5 ml) for 2 hr, allowed to stand at room temperature for 16 hr and again heated for 6 hr. The product, isolated in the usual way, crystallized from $CHCl_3$–methanol to yield ursa-9(11): 12-dien-3β-yl acetate as needles (100 mg), m.p. and mixed m.p. 165–167°, $[\alpha]_D +317°$ (*c*, 0·9).