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THE SYNTHESIS AND STEREOSTRUCTURE OF PUTRANJIC ACID*

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A triterpenic hydroxy acid, named putranjic acid, isolated from Putranjiva roxburghii has been synthesized from friedelane-2,3-dione, and the complete stereostructure has been determined.

Recently several friedelin derivatives have been obtained from stem-bark of Putranjiva roxburghii Wall (Euphorbiaceae).[1-11] Among them, a triterpenic hydroxy acid, named putranjic acid, has been characterized by spectral and chemical methods to be 2-hydroxy-3,4-seco-friedelan-3-oic acid (I).[1,2,6,7,9] However, the configuration of C-2 has been left undetermined. We wish to report the synthesis and complete stereostructure for putranjic acid.

Friedelane-2,3-dione (II),[12] isolated from "cork smoker wash solid",[12,13] was treated with potassium hydroxide followed by lead tetraacetate to yield norfriedelin (III),[14] which gave one spot on TLC, but was shown to contain an epimer of C-4 methyl of III by gas chromatographic examination (retention time: 31.4 and 28.8 min., respectively, column: Diasolid H-523, 250°C). On treatment with base, the mixture afforded pure norfriedelin (III), m.p. 240.5-241.5°C. The alkaline unstable component is, therefore, inferred to be 4α-methyl epimer of III.

The epimeric mixture of III was irradiated with a high pressure mercury lamp in n-hexane and converted into 5α-vinyl-10β-formylmethyl-des-A-friedelane [IV,

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* Two names "Putranjic acid" and "Putric acid" are used for the same compound. We use "Putranjic acid", which was first given by H. S. Garg and C. R. Mitra to the compound.

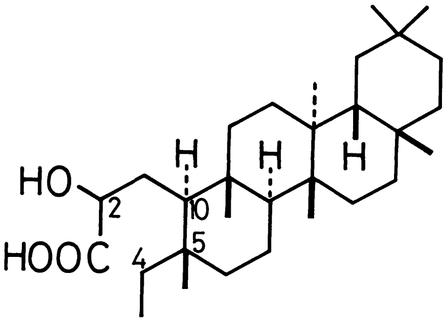
m.p. 162.5-163.5°C, M^+412].[15] The unsaturated seco-aldehyde (IV) was catalytically hydrogenated with 10% Pd-C in ethanol to give 5α-ethyl-10β-formylmethyl-des-A-friedelane [V, m.p. 181.0-181.5°C, M^+414].[9,16] The saturated seco-aldehyde (V) was dissolved in a mixture of ethanol and acetic acid, and treated with potassium cyanide at room temperature. The crude cyanohydrin (VI) in concentrated hydrochloric acid and acetic acid was heated to reflux for 1 hr. On treatment with diazomethane, the reaction products gave two hydroxy-esters (VII and VII' in a ratio of 1:1) and an acetoxy-ester (IX). The hydroxy-esters were separated by silica gel column chromatography into VII [m.p. 176.5-177.0°C, $[\alpha]_D^{25}$ -2.0° ($CHCl_3$), M^+ 474, ν_{max}(nujol) 3530, 1730, 1100 cm^{-1}, nmr(CCl_4) δ 3.78 (s, $COOC\underline{H}_3$), 3.95 (t, J= 5.5 Hz, $-\underset{|}{C}\underline{H}OH$)] and VII' [m.p. 133-134°C, $[\alpha]_D^{25}$+2.5°($CHCl_3$), M^+ 474, ν_{max}(nujol) 3520, 1708, 1065, 1025 cm^{-1}, nmr(CCl_4) δ 3.78 (s, $COOC\underline{H}_3$)].
The acetoxy-ester [IX, M^+ 516, ν_{max}(nujol) 1750, 1225, 1078, 1058 cm^{-1}, nmr(CCl_4) δ 3.76 (s, $COOC\underline{H}_3$), 2.11 (s, $OCOC\underline{H}_3$)] was hydrolyzed with potassium hydroxide and treated with diazomethane to give a mixture of VII and VII'. Oxidation of VII and VII' with Jones' reagent gave the same keto-ester [X, m.p. 153°C, ν_{max} (nujol) 1750, 1730, 1083 cm^{-1}, nmr(CCl_4) δ 3.80 (s, $COOC\underline{H}_3$), 2.65 (q, $-CO-C\underline{H}_2-$), 1.88 (t, J= 6 Hz, $C_{(10)}-\underline{H}$)]. These spectral data were identical with those of methyl oxoputranjate [m.p. 148-149°C, nmr δ 1.9 (t, J= 5.5 Hz, 1H), 2.75 (q, J= 5.5 and 4.5 Hz, 2H)][6] and methyl oxoputrate [m.p. 152-154°C, $[\alpha]_D$ +24.0°, ν_{max} (KBr) 1760 cm^{-1}, nmr(CCl_4) δ 3.82 ($COOC\underline{H}_3$), 2.67 (q, 2H, $-\underset{|}{C}H-C\underline{H}_2-CO-$), 1.9 (t, J= 5 Hz, $C_{(10)}-\underline{H}$)].[9]

VII and VII' were each hydrolyzed with potassium hydroxide in ethanol to give VIII [m.p. 227.0-227.5°C, $[\alpha]_D^{35}$ +19°($CHCl_3$), ν_{max}(nujol) 3520, 1720 cm^{-1}] and VIII'[m.p. 240.0-241.5°C, $[\alpha]_D^{35}$ -1.0°($CHCl_3$), ν_{max}(nujol) 3430, 1703 cm^{-1}], respectively. VIII was identical with natural product, putranjic acid, in respect of m.p. and optical rotation (putranjic acid,[2] m.p. 218-220°C, $[\alpha]_D$ +1°; putric acid,[9] m.p. 220-222°C, $[\alpha]_D$ +21.3°). Furthermore, above mentioned methyl ester (VII) showed the same spectral data as those of the methyl ester of natural product (methyl putranjate,[2] m.p. 176°C, $[\alpha]_D$ -23.5°, ν_{max} 3471, 1724, 1460, 1389, 1258 cm^{-1}, nmr δ 3.75; methyl putrate,[9] m.p. 175-176°C, $[\alpha]_D$ -8.3°, ν_{max} 1730 cm^{-1}, M^+ 474, nmr(CCl_4) δ 3.90, 4.2).

In order to decide the configuration at C-2 of putranjic acid, we have investigated the difference between optical rotation of α-hydroxy carboxylic acids bearing methylene group in β-position and that of their methyl esters (TABLE). As a rule, the differences ($[\alpha]_{acid} - [\alpha]_{Me\text{-}ester}$) are positive in S-configuration and negative in R-configuration. The configuration at C-2 of putranjic acid, therefore, must be in S-configuration and putranjic acid is shown to be (2S)-2-hydroxy-3,4-seco-friedelan-3-oic acid; that is 10β-[(2S)-2-carboxy-2-hydroxy]ethyl-5α-ethyl-des-A-friedelane (VIII).

TABLE

Acid	$[\alpha]_{acid}$(A)		$[\alpha]_{Me\text{-}ester}$(B)		Δ = A - B	
	S	R	S	R	S	R
Lactic[17]	+ 3.82°	- 2.26°	- 8.25°	+ 7.46°	+12.07°	- 9.72°
Leucic[18,19]	+19.4°	-19.4°	-12.5°	+19.2°	+31.9°	-38.6°
I	+19°(VIII)	- 1.0°(VIII')	- 2.0°(VII)	+ 2.5°(VII')	+21°	- 3.5°
Putranjic[2]	+ 1°		-23.5°		+24.5°	
Putric[9]	+21.3°		- 8.3°		+29.6°	



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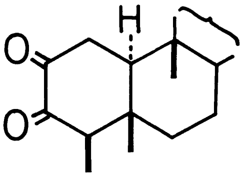

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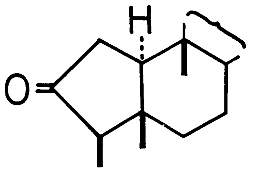

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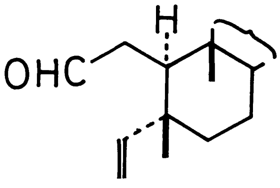

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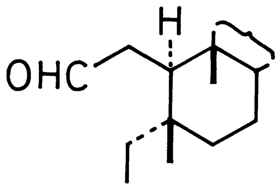

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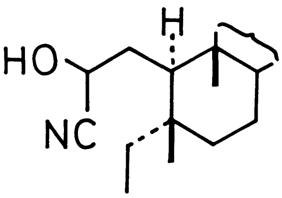

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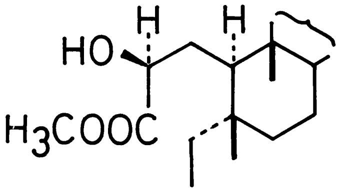
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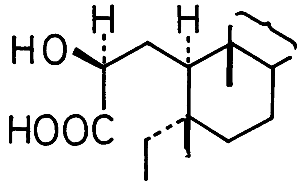
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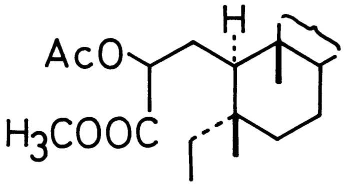
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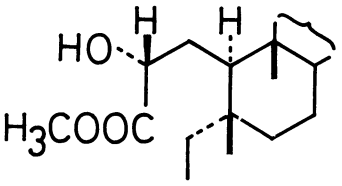
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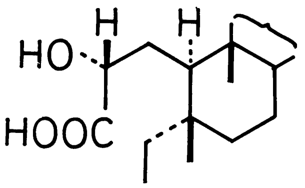
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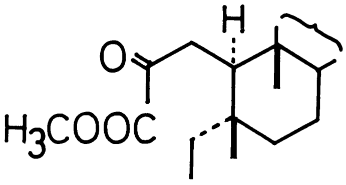
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