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A STEREOSELECTIVE SYNTHESIS OF METHYL 1α-METHYL-4-KETO-*cis*-1,2,3,4,4aα,9,10,10aα-OCTAHYDROPHENANTHRENE-1β-CARBOXYLATE AND ITS CONVERSION TO (±) DESISOPROPYL-*cis*-DEHYDROABIETIC ACID AND (±) DESOXYPODOCARPIC ACID.

S. K. Dasgupta and P. C. Antony

Department of Organic Chemistry, Indian Association
for the Cultivation of Science, Calcutta-32, INDIA.

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Methyl 1-methyl-4-keto-1,2,3,4,4a,9,10,10a-octahydrophenanthrene-1-carboxylate (Ia) represents one of the four possible racemic modifications and it was envisaged as a key intermediate in syntheses of tricarbocyclic resin acids and related diterpenoids. We now report the stereoselective synthesis of Ia and the results of its direct methylation.

Dimethyl α methyl-α(3,4-dihydro-2-naphthyl)-glutarate (IVa), prepared[1] by a novel Michael reaction of methyl α(3,4-dihydro-2-naphthyl)-propionate (III) with methyl acrylate, gave on partial hydrolysis the acid-ester IVb, m.p. 72°, λ_{max}^{EtOH} 265 mμ (log ε 4.14). This was subjected to conditions of acid catalysed ring-closure*. Polyphosphoric acid cyclisation[2,3] was accompanied with dehydrogenation

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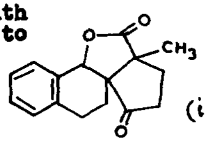
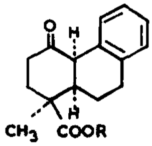
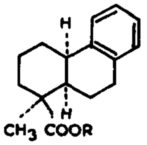
* Corresponding acid chloride on treatment with anhydrous stannic chloride in the cold led to the formation of an abnormal product (i). The details will be reported later.



(i)



I a, R = Me
b, R = H



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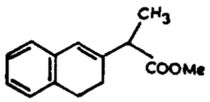

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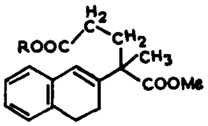

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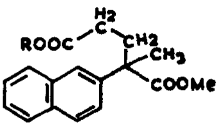

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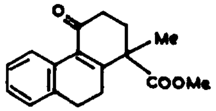
b, R = H



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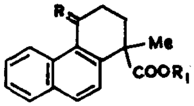
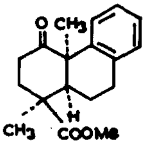
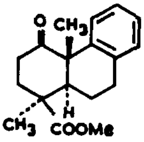


VII

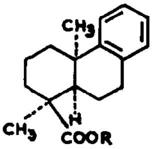
a, R = O, R_1 = Me
b, R = O, R_1 = H
c, R = CH_2, R_1 = Me



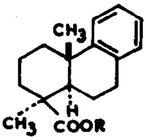
VIII



IX



X a, R = H
b, R = CH_3



XI a, R = H
b, R = CH_3

leading to the formation of the tetrahydrophenanthrene derivative VIIa ((82% yield), b.p. 175-185°/0.4 mm. (bath-temp.), λ^{EtOH}_{max} 250 mμ (log ε 4.4), 303 mμ (log ε 3.8), 317 mμ (log ε 3.89); $\nu^{CHCl_3}_{max}$ 1724 cm^{-1} and 1674 cm^{-1}; red 2,4-dinitrophenylhydrazone m.p. 241-242° (vac.); the corresponding keto-acid VIIb, m.p. 127°. The same keto-ester, characterised through the mixture melting points of the above derivatives, was prepared by the cyclisation of the acid-ester Vb, m.p. 76°, and this in turn was obtained by the partial hydrolysis of the corresponding ester[1] Va. Fused zinc chloride-acetic anhydride-acetic acid[4] at 120-125° effected a normal ring-closure giving the unsaturated keto-ester VI, b.p. 162-165°/0.1 mm., (75% yield), $\gamma^{CHCl_3}_{max}$ 1728 cm^{-1} and 1670 cm^{-1}; red 2,4-dinitrophenylhydrazone m.p. 150°. Both the keto-ester VI and VIIa on reduction with sodium borohydride followed by dehydrogenation with Pd/C (10%) at 240-270° gave in excellent yield 1-methylphenanthrene characterised through the mixture melting points (120-121°) with an authentic sample.

Catalytic hydrogenation of VI with 10% Pd/C resulted in the formation of two products, the saturated ester Ia (30% yield), m.p. 131°, λ^{EtOH}_{max} 266 mμ (log ε 2.6) and 273 mμ (log ε 2.61); yellow 2,4-dinitrophenylhydrazone m.p. 235°; corresponding acid Ib, m.p. 183°; the major fraction was a liquid material. The yield of the normal crystalline product could be raised to 46% by using 30% palladium hydroxide-on-strontium carbonate[5] as a catalyst. The NMR spectral data of Ia were quite significant. Besides the signals at τ8.33 (singlet) due to the quaternary C-methyl and τ6.28 (singlet) due to the ester-methyl, a doublet centered at τ6.15 is characteristic of the 4a hydrogen. Small coupling constant, J = 5.4 c.p.s., confirms the *cis*-fused[6,7] structure of Ia. The configurations of the *gem*-methyl-carbomethoxy group and 10a hydrogen, however, follow from the conversion of Ia to the (±) desisopropyl-*cis*-dehydroabietic acid (vide infra).

The major liquid fraction obtained during catalytic hydrogenation consisted mostly of VIIc, obviously as a result of disproportionation[8] and hydrogenolysis; the U.V. spectra being $^{EtOH}_{max}$ 228 mμ (log ϵ 4.8), 273 mμ (log ϵ 3.57) and 280 mμ (log ϵ 3.58). The structure was confirmed by its conversion to the keto-ester VIIa through oxidation with chromic acid and comparing the melting points of the 2,4-dinitrophenylhydrazone derivatives (vide supra).

The keto-ester Ia was reduced through the thioketal, followed by desulphurisation with Raney-nickel[6]. It afforded IIa m.p.82-83° (84% yield); the corresponding acid IIb melted at 191-192°**. The melting point of IIa on admixture with authentic sample[9] was found to be undepressed. As the parent keto-ester could not be epimerised by either acid or base, it would be reasonable to assume that the steric configuration of the 4a

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** All of the possible four epimers have been synthesised[9] by Dr. U. R. Ghatak of this laboratory. The isomer, originally obtained[10] by Haworth *et al*, has recently been depicted[11] as a *trans*-fused structure related to podocarpic acid configuration.

position had been retained[12] in the desketo-ester IIa as well as in the acid IIb.

As the 4a hydrogen is expected to be highly reactive[13], direct methylation of the keto-ester Ia with methyl iodide in presence of dry potassium t-amylate in benzene led to the formation of VIII (52% yield), m.p. 63° and IX (3.6% yield), m.p. 159°. That the methylation had taken place at the desired position was confirmed by the absence in the NMR spectra of the characteristic doublet due to the 4a hydrogen of the parent ketone; other salient features being for VIII (quaternary methyl singlets at τ8.72 and τ8.61, and the ester-methyl at τ6.4), for IX (quaternary methyl singlets at τ8.69 and τ8.61, and the ester-methyl at τ6.28). Removal of the carbonyl function from VIII and IX was successfully achieved through the modified Wolff-Kishner reduction[14], thus affording desisopropyl-*cis*-dehydroabietic acid (Xa) (48% yield), m.p. 144-146° and (±) desoxypodocarpic acid (XIa) (63.9% yield) m.p. 231-232° respectively. The melting points of these acids and the corresponding methyl esters Xb and XIb were found to be undepressed on admixture with authentic samples[15,16].

As the *cis*-fused ring juncture of (VIII) could be isomerised[17] to *trans*-fused one by Pd/charcoal at higher temperature, the present work constitutes also a total synthesis of (±) desisopropyldehydroabietic acid.

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