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A NOVEL SYNTHESIS OF A TRICYCLO $(7.5.0^{1,5}.0^{1,9})$ TETRADECANE RING SYSTEM RELATED TO GASCARDIC ACID.

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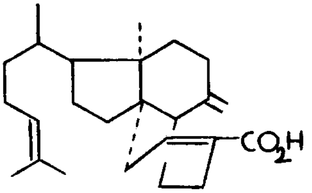
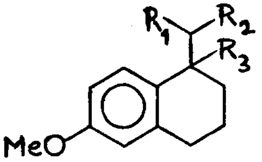
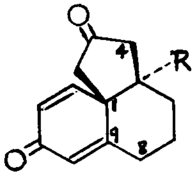
Gascardic acid (1)[1], the first well documented member of the sesterterpene family, is characterised by a unique tricarbocyclic ring system. In view of the recent publications[2] on tricarbocyclic sesterterpenes, we report the preliminary results leading to the synthesis of (10) related to gascardic acid and also the synthesis of (5b) embodying suitable functionalities which may ultimately serve the purpose of realising the synthesis of the complete carbon skeleton of gascardic acid.



(1)

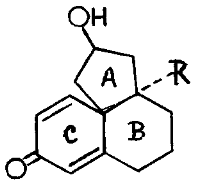


(2a) $R_1 = CN, R_2 = CO_2Et, R_3 = H$
(2b) $R_1 = CN, R_2 = CO_2Et, R_3 = CH_3$
(3a) $R_1 = CO_2H, R_2 = R_3 = H$
(3b) $R_1 = CO_2H, R_2 = H, R_3 = CH_3$
(4a) $R_1 = COCHN_2, R_2 = R_3 = H$
(4b) $R_1 = COCHN_2, R_2 = H, R_3 = CH_3$

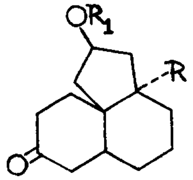


(5a) R = H
(5b) $R = CH_3$

Ethyl 6-methoxy-1,2,3,4-tetrahydronaphthylidene-1-cyanoacetate was subjected to catalytic reduction (Pd/C 10%, EtOH) and also to 1 : 4 addition with ethereal methylmagnesium iodide in presence of anhydrous cuprous iodide to afford (2a) and (2b) respectively; (2a); ν_{max} ($CHCl_3$) 2260, 1730, 1600 cm^{-1}; δ(CCl_4) 6.90 (1H, d, J = 8 Hz), 6.67 - 6.43 (2H, m), 4.20 (2H, q, J = 6.5 Hz), 3.67 (3H, s), 1.35 (3H, t, J = 6.5 Hz); (2b); ν_{max} ($CHCl_3$) 2260, 1730, 1600 cm^{-1}; δ (CCl_4) 7.03 (1 H, d, J = 8 Hz), 6.67 - 6.43 (2H, m), 4.10 (2H, q, J = 6.5 Hz), 3.70 (3H, s), 1.47 (3H, s), 1.23 (3H, t, J = 6.5 Hz). Hydrolysis and decarboxylation of (2a) and (2b) afforded the acids (3a) and (3b) in 80% yield; (3a)[3]; δ (CCl_4) 11.35 (1 H, s); (3b); δ(CCl_4) 11.00 (1H, s); 1.37 (3H,s). The corresponding acid chlorides were treated with ethereal diazomethane resulted in the formation of the diazomethylketones (4a) and (4b). The purified (short-packed alumina column) diazomethylketones were subjected to solvolytic cyclization[4] with trifluoroacetic acid leading to the formation of (5a) and (5b) as crystalline solids in 60-65% yield; (5a); m.p. 121°; λ_{max} (EtOH) 244 nm (ϵ = 14,600); ν_{max} ($CHCl_3$) 1735, 1655, 1620, 1610 cm^{-1}; δ ($CDCl_3$) 6.90 (1H, d, J = 10 Hz), 6.33 (1H, dd, J=10, 2 Hz), 6.20 (1H, s); m/e 202 (M^+); (5b); m.p. 137°; λ_{max} (EtOH) 245 nm (ϵ = 15,400); ν_{max} ($CHCl_3$) 1735, 1655, 1620, 1610 cm^{-1}; δ ($CDCl_3$) 6.83 (1H, d, J = 10 Hz), 6.33 (1H, dd, J = 10,2 Hz), 6.23 (1H, s); 1.03 (3H, s); m/e 216 (M^+). Both of them are homogeneous in glc. The stereochemical assignment of A/B ring is evidently *cis* which follows through the sequence of participation reaction and from considerations of the geometry of indanone systems.

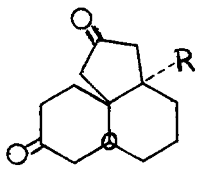


(6) R = H



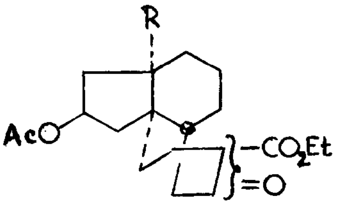
(7) R=R1=H

(9) R=H,R1=Ac



(8a) R=H, solid

(8b) R=H, liquid



(10) R = H

Studies on reduction of the dienone with a view to generate the asymmetric centre at C-9 and subsequent expansion of the ring C have been carried out with (5a). The saturated carbonyl group of (5a) was preferentially reduced with sodium borohydride to afford (6); ν_{max} ($CHCl_3$) 3460, 1650, 1620, 1610 cm^{-1}; $\sim$ 95% (glc). This was subjected to catalytic reduction (Pd/C 10%, EtOH) to afford (7); ν_{max} ($CHCl_3$) 3450, 1710 cm^{-1}; δ ($CDCl_3$) 4.47 (1H, m), 1.90 (1H, s). This on Jones oxidation afforded a solid crystalline diketone (8a); m.p. 106°; ν_{max} ($CHCl_3$) 1735, 1710 cm^{-1}. The chemical reduction (lithium, liquid ammonia) of (5a) followed by subsequent Jones oxidation of the resulting product afforded a liquid diketone (8b); ν_{max} ($CHCl_3$) 1735, 1710 cm^{-1}. Both the diketones are homogeneous in glc but differ in their relative retention time and spectral data. It is difficult at this stage to assign any definite stereochemistry arising out of these reductive processes in view of the published conflicting data[5]. X-ray analysis will determine the absolute stereochemistry.

For the formation of five-six-seven membered ring system, the alcohol (7) was converted to the corresponding acetate (9); ν_{max} ($CHCl_3$) 1715 cm^{-1}. This was subjected to ring expansion[6] reaction with ethyl diazoacetate catalysed by triethyloxonium fluoroborate to afford (10)[7] in a good yield; ν_{max} ($CHCl_3$) 1715, 1630 cm^{-1}; m/e (M^+) 336; glc- two peaks ($\sim$ 1:1); violet colouration (Fe^{3+}). It may be noted that in the case of asymmetrical ketones, homologation is not regiodirective and two possible isomeric products in almost equal quantities are formed[8].

The introduction of the methylene group at C-8 is possible through the condensation of (5) with formaldehyde. The introduction of the C_8 - side chain at C-4 may also be realised through the hydroxyl group in (7).

Acknowledgement

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References and Notes

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7. Satisfactory analytical data were obtained for all the new compounds described. Nmr spectra were carried out in a T-60A spectrometer. Glc experiments were carried out in a Hewlett-Packard gas chromatograph model 5730 A using the columns SE-52 and 3% OV-225.

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