Thermal Isomerisation of a Hexatriene System: Synthesis and Rearrangement of 2-Methyl-3-(*cis*, *cis*-penta-1,3-dienyl)cyclohex-2-en-1-one

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Summary A stereospecific non-concerted cyclisation of a triene system leading to a synthesis of $\Delta^{1,10}$-*trans*-4,5-dimethyl-6-decalone is reported.

THE *cis*-4,5-dimethyldecalin ring system (I) is found in numerous sesqui-, di-, and tri-terpenoid natural products. Until recently[1] introduction of the two methyl groups with a *cis*-relationship represented a considerable synthetic challenge. Our approach was to make use of the predictive powers of the Woodward–Hoffmann rules[2] governing the stereochemistry of electrocyclic reactions of the hexatriene system. The first objective was a synthesis of the *cis,cis*-trienone (VII) which, on cyclisation, would give an intermediate having the correct functionality for conversion into several terpenes of the eremophilone type.

Reaction of the enol ether[3] (II) with the Grignard derivative of (III) [b.p. 85°/15 mm, ν_{max} 3300 and 2140 cm.$^{-1}$], and subsequent acid treatment, afforded the acetylenic alcohol (IV) [55%; b.p. 140°/0·02 mm; ν_{max} 3400, 2230, and 1660 cm.$^{-1}$; λ_{max} 277 nm (ϵ 16,400); τ† 8·73(d, 3H, J 6·5 Hz), 8·12 (s, 3H) 6·80 (s, 1H), and 6·06 (m, ^{1}H); semicarbazone, m.p. 162°]. Dehydration of (IV) ($POCl_3$–pyridine, followed

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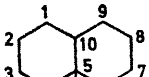
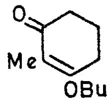
† N.m.r. spectra measured in CCl_4 solution and all new compounds have satisfactory analytical data.

by treatment with Oediger's base) gave a 60% yield of a 4 : 1 mixture of olefins (V) and (VI). The *trans*-isomer (VI) was much less stable than (V) and the percentage of (VI) in the mixture decreased rapidly on storage at 0°. The *cis*-isomer (V) [m.p. 33°; ν_{max} 2160, 1660, and 1590 cm^{-1}; λ_{max} 220 (ϵ 7800) and 310 nm (16,500); τ 8·20 (m, 6H), 4·45 (d.q., H_a, J_{ab} 10·4 Hz, $J(CH_3-H_a)$ 1·5 Hz), 4·10 (d.q., H_b, J_{ab} 10·4 Hz, $J(CH_3-H_b)$ 6·5 Hz)] and the *trans*-isomer (VI) {ν_{max} 2160, 1660, and 1590 cm.$^{-1}$; λ_{max} 220 and 310 nm; τ 8·15 (m, 6H), 4·42 [d.q., H_a, J_{ab} 15·2 Hz, $J(CH_3-H_a)$ 1·5 Hz] 3·9 (d.q., H_b, J_{ab} 15·2 Hz, $J(CH_3-H_b)$ 6·3 Hz]} were separated by g.l.c. (11 ft. × ⅜ in. 10% Carbowax on Chromosorb P at 210° with nitrogen 18 lb./in.^{2}). It was essential to determine whether the known geometry of the terminal double bond in (V) would be stable to subsequent reaction conditions, thus (V) was treated with Lindlar's catalyst and also heated to 275° and in both cases was re-isolated unchanged.



(I)



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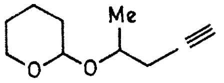
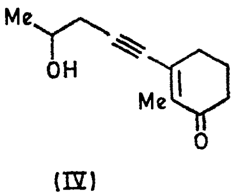
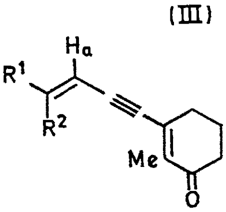


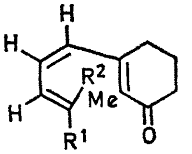
(III)



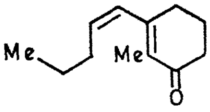
(IV)



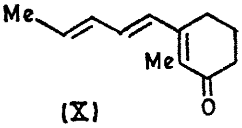
(V) $R^1 = H_b ; R^2 = Me$
(VI) $R^1 = Me ; R^2 = H_b$



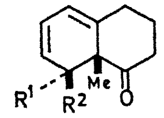
(VII) $R^1 = H ; R^2 = Me$
(VIII) $R^1 = Me ; R^2 = H$



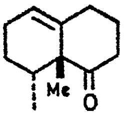
(IX)



(X)

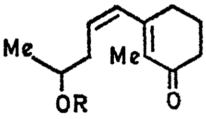


(XI) $R^1 = H ; R^2 = Me$
(XII) $R^1 = Me ; R^2 = H$

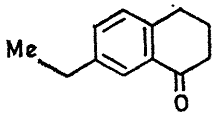


(XIII)

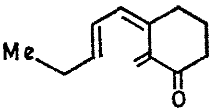
(XIV)



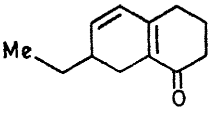
(XV) R = H
(XVI) R = CO_2Et



(XVII)



(XVIII)



(XIX)

Partial hydrogenation of the *cis*-isomer (*V*), using Lindlar's catalyst and heptane as solvent, yielded a mixture[4] containing 70% all-*cis*-trienone (VII) [ν_{max} 1660 and 1590cm^{-1}; λ_{max} 230 and 295 nm] which was not separated from 20% starting acetylene (V) and 10% over-reduction product (IX). This mixture was used in the subsequent thermal rearrangements. The all-*cis*-trienone (VII) was found to be transformed efficiently to the all-*trans*-trienone (X) [b.p. 97°/0·3 mm; ν_{max} 1660 cm^{-1}; λ_{max} 320 nm (ϵ 17,600); τ 8·30 (s, 3H), 8·21 (d, 3H, J 6 Hz), 4·05 (m, 4H)] by irradiation at 250, 310, and 350 nm.

Thermal cyclisation of the all-*cis*-trienone (VII) should be a disrotatory process[2] leading to (XI) since only the orbital symmetry of the π-electrons participating in the bond-forming reaction need be considered. Thus, the carbonyl function can be ignored when considering the stereochemistry of a *concerted* thermal cyclisation in (VII). Heating (VII) [70% pure, from hydrogenation of (V)] at 275° for 50 sec. afforded the unexpected cyclised product (XII) [70% (based on % (VII) present in mixture being cyclised]; b.p. 58°/0·1 mm; ν_{max} 1705 and 1590 cm^{-1}; λ_{max} 250, 260, 270, and 275 nm (ϵ 3600); τ 9·2 (d, 3H, J 7 Hz), 8·85 (s, 1H), 4·3 (m, 3H)] which was checked for homogeneity on a number of g.l.c. systems (Carbowax 5, 20%; SE30 5,20%). The same cyclisation product was obtained from (VIII). The stereochemistry of the two methyl substituents in the cyclisation product was proved by hydrogenation of (XII), using Lindlar catalyst, to the dihydro-derivative (XIII) [80%; m.p. 45°; b.p. 80°/0·5 mm; ν_{max} 1705 cm.$^{-1}$; τ 9·19 (d, 3H, J 6·65 Hz), 8·78 (s, 3H), 4·72 (m, H)] which was identical in g.l.c. behaviour and spectroscopic properties with an authentic sample of (XIII)‡ whose structure has been established.[5] Chlorotris(triphenylphosphine)rhodium(I) failed to reduce the diene system of (XII) and may offer a method of reduction of isolated double bonds, in the presence of such conjugated systems.

Explanation of the abnormal stereochemistry of the product (XII) may be derived from considerations of steric and electronic effects. In the disrotatory process (VII) → (XI), the two methyl substituents of the hexatriene system experience severe steric interactions and would be expected to raise the energy required for cyclisation. A similar effect has been noted in the thermal isomerisation of all-*cis*-octatetraene[6] (XIV). Also, cyclisation of (VII) by a non-concerted radical pathway should be rendered energetically more favourable by the presence of the adjacent carbonyl function, and would lead to the *trans*-relationship of the two methyl substituents in (XII).

Reduction of (IV) (Lindlar catalyst) quantitatively afforded the dienone (XV) [ν_{max} 3400, 1660, 1650, and 1610 cm^{-1}; λ_{max} 263 nm (ϵ 8300); τ 8·89 (d, 3H, J_{ab} 5 Hz), 8·33 (s, 3H), 6·60 (s, 1H), 6·20 (m, 1H), 4·33 (d.t., 1H, J 7·5 and 12 Hz), and 3·9 (d, 1H, J 12 Hz); semicarbazone m.p. 114°].

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‡ Kindly supplied by Professor R. M. Coates.

Irradiation of (XV) at 250 nm produced the *trans*-dienone [λ_{max} 283 nm (ϵ 13·600); τ 8·85 (d, 3H, J 6·5 Hz), 8·20 (s, 3H), 6·30 (s, 1H), 6·20 (m, 1H), 3·83 (d.t., 1H, J 15 and 7 Hz), and 3·40 (d, 1H, J 15 Hz)]. Conversion of (XV) into carbonate (XVI) followed by pyrolysis at 325° for 55 sec., resulted in elimination to give a mixture of (VII) and (VIII), which cyclised spontaneously to (XII). Prolonged pyrolysis of the carbonate (XVI) at 325° afforded a new product [λ_{max} 320 nm; ν_{max} 1660 cm^{-1}], which on attempted isolation was quantitatively transformed into 6-ethyltetralone (XVII) [ν_{max} 1680 and 1610 cm^{-1}; λ_{max} 220 (ϵ 10,500), 252 (10,050), and 300 nm (3500); τ 8·90 (t,3H, J 7 Hz), 7·95 (m, 2H), 7·50 (q, 2H, J 7 Hz, superposed on m, 2H), 7·18 (t. 2H, J 6 Hz), 3·20 (d, 1H, J 8 Hz), 2·86 (q, 1H, J 8 and 2 Hz), and 2·30 (d, 1H, J 2 Hz)]. Heating (XII) at 325° also yielded 6-ethyltetralone (XVII), the formation of which must firstly involve ring opening to the trienone (VIII) which can undergo a [1,7]sigmatropic rearrangement[2] to give (XVIII). Cyclisation of (XVIII) would then lead to the primary product (XIX) which would be expected to undergo ready oxidation to 6-ethyltetralone (XVII).

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