

Mechanism of the Formation of Herbertene from *trans*-Didehydrobicycloparnesol

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Product and ^{13}C labelling studies of the rearrangement of *trans*-didehydrobicycloparnesol (+)-(1) to partly racemised herbertene [(+)-(2)] have led us to propose a mechanism for the reaction.

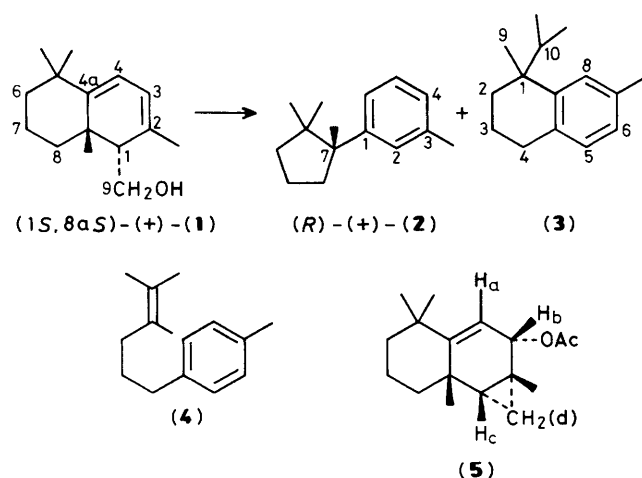
Several years ago we reported¹ the unexpected formation of herbertene² (2) from *trans*-didehydrobicycloparnesol (1).† We have now studied the mechanism of this acid-catalysed rearrangement. Six key experiments have led to a better founded mechanistic proposal than before.¹

(1) The by-product has now been identified as 1,2,3,4-tetrahydro-1-isopropyl-1,7-dimethylnaphthalene (3). The position of the CH_3 group on the aromatic ring was confirmed by double resonance and differential nuclear Overhauser

experiments, revealing the relationship of H-4 (m, δ 2.65—2.59) and H-5 (δ 6.8, d, $J_{5,6}$ ca. 8, $J_{5,4}$ ca. 0.5 Hz). Moreover compound (4)‡ has been cyclised quantitatively to (3) under the conditions of the rearrangement (HCO_2H , 0.02 M HClO_4 , 5—10 min reflux). Cyclisation of (1) in $\text{CF}_3\text{CO}_2\text{D}$ (cat. amount H_2SO_4) yielded (3) with complete deuteration at C-10; this also points to (4) as an intermediate.

† This structure can also be regarded as didehydro-*epi*-drimenol or (as numbered in the formula) a hexahydronaphthalene derivative.

‡ Compound (4) is available in four steps from 2-(4-methylphenyl)-ethanol by bromination, alkylation with *t*-butyl acetoacetate, decarboxylation, and Wittig reaction of the resulting ketone with isopropyl-triphenylphosphonium bromide.



(2) Optically pure§ [(1*S*, 8*aS*)] (+)-(1) $\{[\alpha]_D^{20} + 517^\circ$ (CHCl_3 , c 1.4), $+505^\circ$ (EtOH , c 1.2); $\Delta\epsilon$ (271 nm, n -hexane) $+18.8\}$ was prepared by hydrolysis of its recrystallized camphanoate (m.p. 107°C). Its rearrangement furnished (+)-(2) $\{[\alpha]_D^{20} + 50.2^\circ$ (CHCl_3 , c 1.5) $\}$ and *rac*-(3) $\{[\alpha]_D^{20} 0^\circ$ (CHCl_3 , c 0.4) $\}$. The optical rotation value found for (+)-(2) implies partial racemisation, since natural herbertene $\{(S) - (-)(2), [\alpha]_D - 48.3^\circ$ (CHCl_3 , c 1.3) $\}$ after ozonolysis gave rise to (*S*)-(-)-camphanic acid with $[\alpha]_D - 13.2^\circ$;² cf. (*R*)-(+)-camphanic acid with $[\alpha]_D + 20^\circ$ derived from (*R*)-(+)-cuparene.⁴

(3) $[9\text{-}^2\text{H}_2] - (1)$ was prepared by reduction of the corresponding ethyl ester⁵ with LiAlD_4 . Rearrangement of this material furnished $[4\text{-}^2\text{H}] - (2)$ with *ca.* 80% deuterium [mass spectroscopic evidence and n.m.r. (δ 7.1–6.98 CH-4)].

(4) $[1,9\text{-}^{13}\text{C}_2] - (1)$ (7% ^{13}C) was synthesised from β -ionone and doubly-labelled Horner reagent (prepared from $[1,2\text{-}^{13}\text{C}_2]$ bromoacetic acid), by thermal cyclisation of the corresponding ester,^{5,6} and reduction of the resulting ester. The doubly labelled (1) showed $J(^{13}\text{C}, ^{13}\text{C})$ 35 Hz [δ 61.5 (C-9, t) and 53.8 (C-1, d)]. Rearrangement of this material yielded (2) with ^{13}C -labels on C-2 (d, δ 127.8) and C-4 (d, δ 126.1), *i.e.* the vicinal ^{13}C labels were separated during the rearrangement. In (3) the labels have been randomised on C-5, C-6, and C-8 and -8a [C-8a, s, δ 145.1; C-8, d, δ 127.2; $J(^{13}\text{C}\text{-}8\text{a}, ^{13}\text{C}\text{-}8)$ 58.4 Hz; C-5, d, δ 128.7; C-6, d, δ 125.7; $J(^{13}\text{C}\text{-}5, ^{13}\text{C}\text{-}6)$ 57.2 Hz].

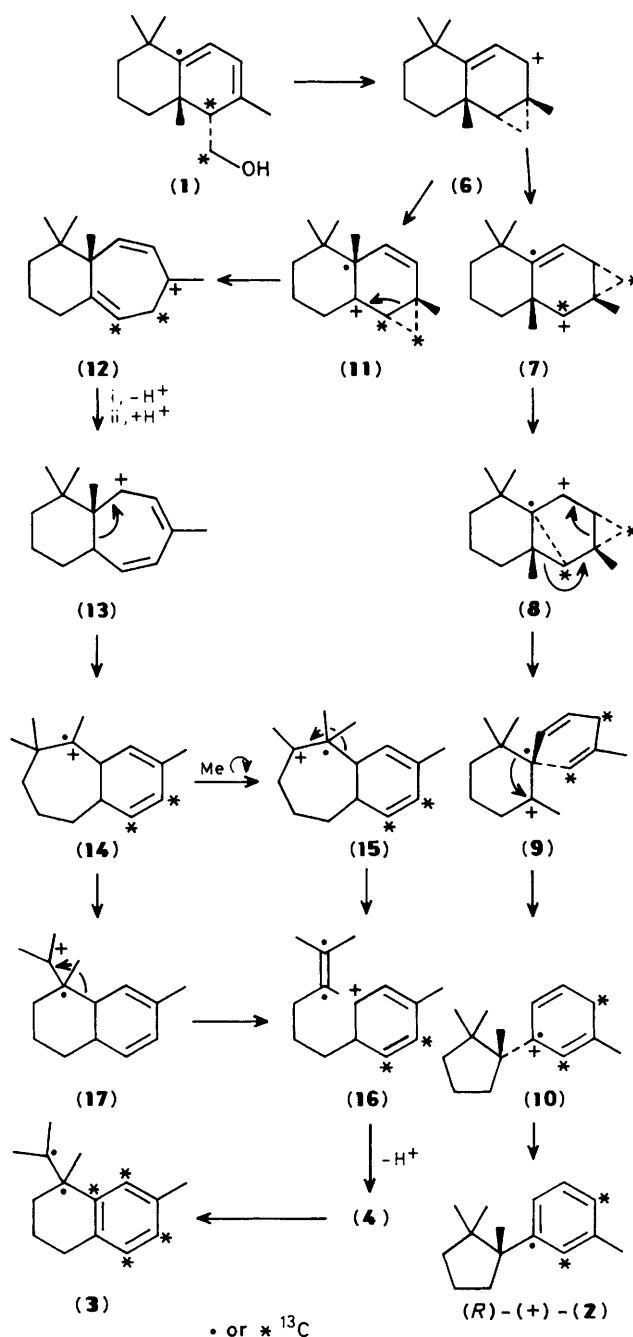
(5) $[4\text{-}^{13}\text{C}] - (1)$ (4% ^{13}C) was prepared in ten steps from 6-methylhept-5-en-2-one and $[2\text{-}^{13}\text{C}]$ bromoacetic acid by well known synthetic procedures. Herbertene (2) derived from $[4\text{-}^{13}\text{C}] - (1)$ carried the label on C-1, whereas in (3) the label was randomised on C-1 (s, δ 39.6) and C-10 (d, δ 37.1).

(6) Finally, the very labile tosylate from (1) (m.p. $67\text{--}69^\circ\text{C}$) was solvolysed (HOAc/NaOAc , 25°C , 30 min) to give the acetate (5) (70% yield).|| Acidic treatment of (5) (HCO_2H , cat. HClO_4 , reflux, 5 min) yielded (2) and (3) in the ratio

§ Optical purity was proven by g.l.c. analysis of the derivatives of (\pm)-(1) and (+)-(1) with (*R*)-(+)-Mosher acid (baseline separation).

|| The strongly positive c.d. allows us to deduce³ the absolute configuration of (+)-(1) as 1*S*, 8*aS*.

|| The structure and stereochemistry of (5) can be deduced unequivocally from n.m.r. spectra, *i.e.* ^1H n.m.r., ^{13}C n.m.r., ^1H , ^{13}C -2D, ^{13}C -INADEQUATE, and differential nuclear Overhauser experiments: H_b δ 5.7 (br. s), H_a δ 5.14 (d, J_{ab} *ca.* 2 Hz), H_c δ 0.5 (dd, J_{ca} 5.5 Hz), H_d δ 0.72 and 0.22 (each dd, J_{gem} *ca.* 8 Hz).



Scheme 1

3.5 : 1. This suggests that the cation corresponding to (5) might be a common intermediate for both (2) and (3).

In Scheme 1 we have tried to accommodate all the foregoing findings in a mechanistic proposal. The intermediacy of (6) is made probable through the isolation of (5) [experiment (6)]. From here the reaction branches. A cyclopropylcarbinyl rearrangement (6) \rightarrow (7) is the reason for the separation of the vicinal ^{13}C labels in experiment (4). The vinylcyclopropylcarbinyl \rightarrow bicyclopentylcarbinyl rearrangement (7) \rightarrow (8) is followed by the formation of the spirobicyclic intermediate (9) or by a synchronous process (8) \rightarrow (10). In step (9) \rightarrow (10) one would expect partial or total racemisation [see experiment (2)]. Loss of a proton in (10) yields the partially racemised (*R*)-(+)-(2).

On the other hand migration of the angular CH_3 group in (6) gives (11), which through ring enlargement yields (12). The latter furnishes (13) by deprotonation-protonation, which is followed by ring enlargement/ring contraction and gives (14). Here the reaction again branches [experiment (5)]: either CH_3 migration (14) \rightarrow (15) or methylene migration (14) \rightarrow (17) takes place. Both intermediates (15) and (17) acquire stability by rearrangement to (16), which is a protonated form of (4). The symmetrical intermediate (4) cyclises to (3) with randomisation of the labels in the aromatic ring [experiment (4)].

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