

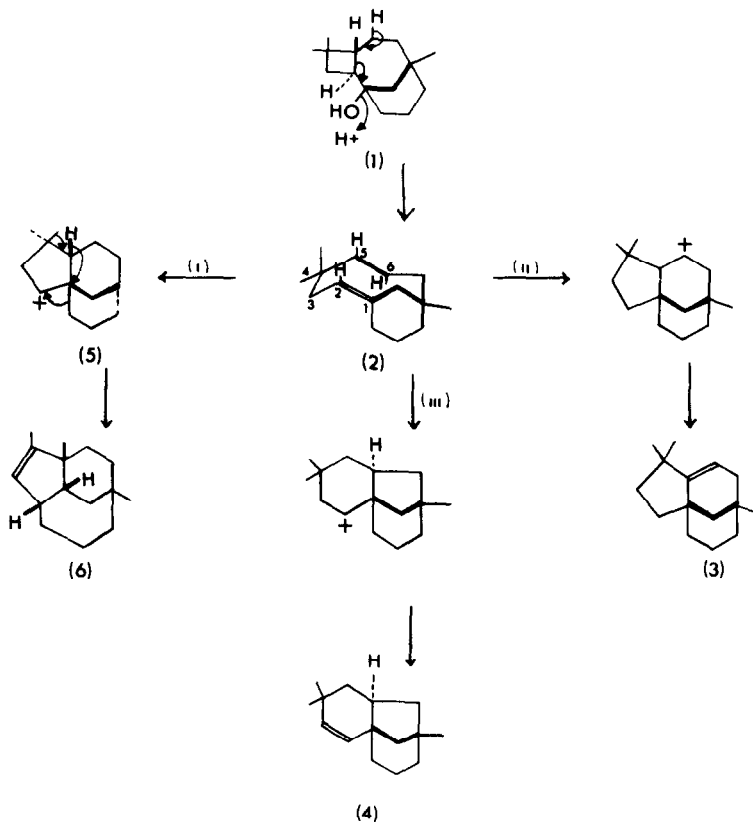
EPI-CLOVENE - AN ACID CATALYSED REARRANGEMENT PRODUCT OF CARYOLAN-1-OL

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Recently, we presented evidence for the structures of pseudoclovene-A(3)<sup>1</sup> and -B(4)<sup>2</sup> which are formed together with isoclovene (6) by treatment of caryolan-1-ol (1) with polyphosphoric acid (PPA). The suggested mechanism for these rearrangements involves the bridged cyclononadiene (2) and its subsequent cyclisations as shown below.



(i) Protonation at C(6), 1:5 Closure    (ii) Protonation at C(2), 1:5 Closure

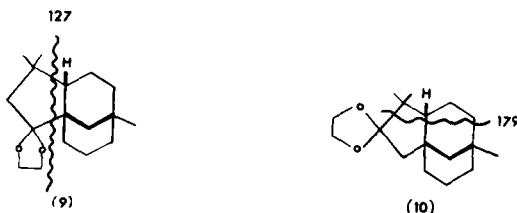
iii) Protonation at C(5), 1:6 Closure

An alternate fate for the cyclopentyl cation (5) could involve simple proton loss to produce (7) which is stereoisomeric with clovene<sup>3a,b</sup> (8), one of the major rearrangement products of caryophyllene, and hence is trivially named epi-clovene. We have now isolated and characterised another of the acid-catalysed<sup>4</sup> rearrangement products of (1) and the chemical evidence to date is compatible with the structure (7), or its enantiomer.



epi-Clovene,  $C_{15}H_{24}$ ,  $[\alpha]_D^{24} +22.2^\circ$  in  $CHCl_3$  ( $c = 0.88$ ),  $\nu_{max}$  (liquid film) 3079, 1380-1365 and  $750\text{ cm}^{-1}$ ; exhibited signals at  $\tau = 4.46$  (2H, singlet) and 8.98 (3H, singlet), 9.01 (3H, singlet) and 9.12 (3H, singlet) and catalytic hydrogenation gave epi-clovane,  $C_{15}H_{26}$ ,  $[\alpha]_D^{24} -14.40^\circ$  in  $CHCl_3$  ( $c = 2.51$ ). Bromination<sup>5</sup> of epi-clovene gave an inseparable mixture of liquid dibromides;  $\tau = 5.54$  (1H, doublet,  $J = 4\text{ Hz}$ ), 5.75 (1H, doublet,  $J = 4\text{ Hz}$ ), 8.85 (3H, singlet), 8.90 (3H, singlet), and 9.08 (3H, singlet) from which the alkene was regenerated by treatment with Zn/EtOH.

Hydroboration/oxidation of epi-clovene gave a mixture (45:55) of two ketones  $\nu_{max}$  (liquid/film)  $1740\text{ cm}^{-1}$ ;  $\tau = 7.8$  (2H, doublet,  $J = 12\text{ cps}$ ), 8.05 (2H, doublet,  $J = 3\text{ cps}$ ), 9.0 (3H, singlet), 9.05 (3H, singlet), 9.1 (6H, singlet) which was converted into a mixture of the corresponding ethylene ketals, (9) and (10). Neither the ketone nor ketal mixtures was separable other than by analytical g.l.c., but the mass spectra of the two ketones (g.c./m.s.) revealed fragmentation patterns virtually identical to those of clovan-2- and -3-one and the ketone fragmentation patterns<sup>6</sup> were identical to those of the ketals of clovan-2 and -3-one, the base peak appearing at 127 and 179 m/e respectively. The four ketones, clovan-2 and -3-one and epi-clove- and -3-one, were separable by analytical g.l.c. employing SCOT columns.



The above evidence pointed to (7) or its enantiomer for epi-clovene and hence (11) or its enantiomer for epi-clovane. Danishefsky has recently reported<sup>7</sup> a total synthesis of (+)-epi-clove- and g.c./m.s. comparison of his material with our sample showed them to be identical

The reduction of pseudoclovene-A,  $[\alpha]_D^{20} -23.3^\circ$  in  $\text{CHCl}_3$  ( $c = 1.21$ ), was then examined in an attempt to correlate epi-clovene with a compound of known absolute configuration.<sup>1</sup> Employing either  $\text{B}_2\text{H}_6/\text{CH}_3\text{CH}_2\text{CO}_2\text{H}$ <sup>8</sup> or  $\text{B}_2\text{H}_6/\text{Hg}(\text{OAc})_2/\text{NaBH}_4$ ,<sup>9</sup> chemical reduction of (3) failed completely, whereas catalytic hydrogenation at 80 p.s.i. and  $80^\circ$  over palladium in ethanol/ $\text{HClO}_4$ <sup>10</sup> gave exclusively clovene,  $[\alpha]_D^{24} -10.4^\circ$  in  $\text{CHCl}_3$ , ( $c = 1.20$ ). Catalytic reduction of clovene,  $[\alpha]_D^{25} -21.7^\circ$  in  $\text{CHCl}_3$  ( $c = 1.96$ ), obtained from rearrangement of caryophyllene gave clovene,  $[\alpha]_D^{24} +10.64^\circ$  ( $c = 0.860$ ), (12),<sup>3c</sup> hence the reduction of (3) takes place from the  $\alpha$ -face to the exclusion of the hoped-for  $\beta$ -addition.



In terms of the suggested mechanism for the formation of isoclovene, it is gratifying to report that epi-clovene is converted into isoclovene by treatment with sulphuric acid/ $\text{Et}_2\text{O}$  whereas clovene is stable to these conditions.

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 (b) Treatment of caryophyllene with conc.  $\text{H}_2\text{SO}_4/\text{Et}_2\text{O}$  or P.P.A. or  $\text{P}_2\text{O}_5/\text{DMF}$  gives a mixture of hydrocarbons but in no case is epi-clovene formed.  
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4. 0.05 moles of the alcohol was dissolved in a 0.1 M solution of  $\text{P}_2\text{O}_5$  in dimethylformamide (125 ml) and left for 24 hours at  $120^\circ\text{C}$ . epi-Clovene constituted 20% of the hydrocarbon product from these reaction conditions and was also formed in smaller yields from treatment of carolan-1-ol (11.5 g) with polyphosphoric acid (80 mls) at  $120^\circ$  for 30 minutes.

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