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NEOCLOVENE A NOVEL REARRANGEMENT PRODUCT OF CARYOPHYLLENE

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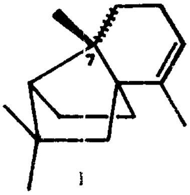
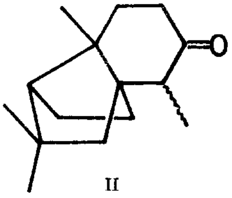
The well-known sulphuric acid-catalysed rearrangement of caryophyllene to β-caryophyllene alcohol and clovene has been fully rationalised by the structural formulations of Barton (1). In order to obtain a pure specimen of clovene for comparison with our synthetic ($\pm$)-clovene (2), we repeated the rearrangement and subjected the hydrocarbon product to preparative gas-liquid chromatography. This procedure revealed the presence of six hydrocarbons, the two main constituents being clovene and a hitherto uncharacterised isomeric hydrocarbon (3), which we designate neoclovene. We now describe the findings which point to structure (I) for neoclovene.

Neoclovene, $C_{15}H_{24}$, $[\alpha]_D^{22}$ - 72° (c, 1.78 in $CHCl_3$) contains one double bond and is, therefore, tricyclic. The N.M.R. spectrum showed three quaternary methyls [singlets at 8.80τ (3H) and 8.99τ (6H)], one allylic methyl (8.41τ) and one olefinic proton (4.91τ). Hydroboration-oxidation (4) gave two epimeric ketones (II), whose carbonyl absorptions at 1714 $cm.^{-1}$ were consistent with their assignment as cyclohexanones. Osmium tetroxide-periodate cleavage of neoclovene produced a C_{15} keto-aldehyde (III) ($\nu_{max.}$ 2708, 1729, 1702 $cm.^{-1}$.) with three quaternary methyls (singlets at 8.75, 8.84 and 8.96τ) and a methyl ketone (7.98τ); the aldehydic proton showed a clean triplet at 0.2τ (J = 2.5 cps.), thus revealing the presence of a vicinal methylene group. Sequential treatment of (III) with chromium trioxide, diazomethane and trifluoroperacetic acid produced the acetoxy-ester (IV); that this was a tertiary acetate was shown by the lack of resonance in the 5-6τ region. The corresponding free hydroxy-acid gave on sublimation a δ-lactone ($\nu_{C=O}$ 1740 $cm.^{-1}$), thus confirming that the double bond of neoclovene must be situated in a six-membered ring.



I



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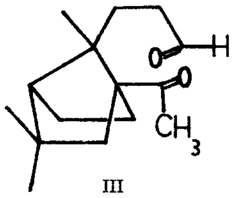

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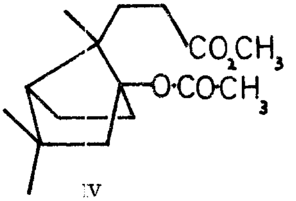

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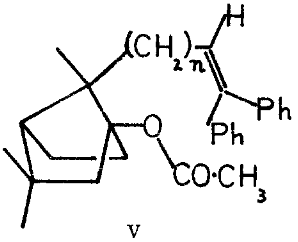
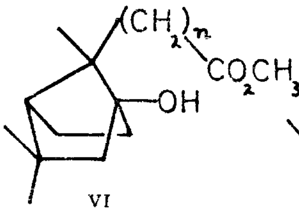
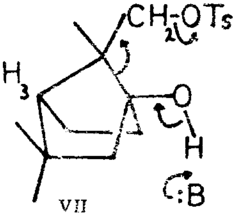


V

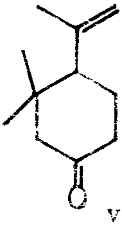
Treatment of the hydroxy-ester corresponding to (IV) with excess phenylmagnesiumbromide, followed by acetic anhydride dehydration gave (V; n= 1), whose vinyl proton resonance (1H) at 3.89τ appeared as a triplet (J= 8 cps), showing the presence of a vicinal methylene group. Ruthenium dioxide-periodate fission (5) of (V; n= 1), hydrolysis and diazomethane esterification produced the hydroxy-ester (VI; n= 1). Repetition of this Barbier-Wieland sequence on (VI; n= 1) gave the lower homologue (V; n= O), in which the vinylic proton appeared as a sharp singlet at 3.62τ, demonstrating its juxtaposition to a quaternary centre; the shift downfield of one of the methyl singlets in this compound to 8.65τ strongly indicated it to be one of the substituents at this quaternary centre. Conversion of this product to the hydroxy-ester (VI; n= O) was achieved as for the higher homologue. Lithium aluminium hydride reduction of (VI; n= O) led to the expected primary tertiary 1,3-diol, which was readily transformed to the primary mono-tosylate (VII). Base induced fragmentation of (VII), as shown, took place readily with dimsyl sodium in dimethyl sulphoxide (6) to give a ketone, $C_{11}H_{18}O$, whose spectroscopic properties showed it to be an isopropenyl-dimethyl-cyclohexanone (VIII). The determination of the precise orientation of the substituents was carried out on the saturated dihydro-compound (IX), $[\alpha]_D^{20}$ + 29.3° (*c*, 2.0 in CHCl$_3$), $\nu_{max.}$ 1718, 1429 and 1418 cm.$^{-1}$. The N.M.R. spectrum showed an unresolved multiplet at 7.65-8.05τ (4H), the geminal methyls at 8.94 and 9.14τ, and the isopropyl methyls at 8.99τ (J = 7 cps.) and 9.16τ (J = 7 cps.).



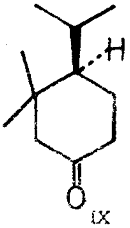
VI



VII



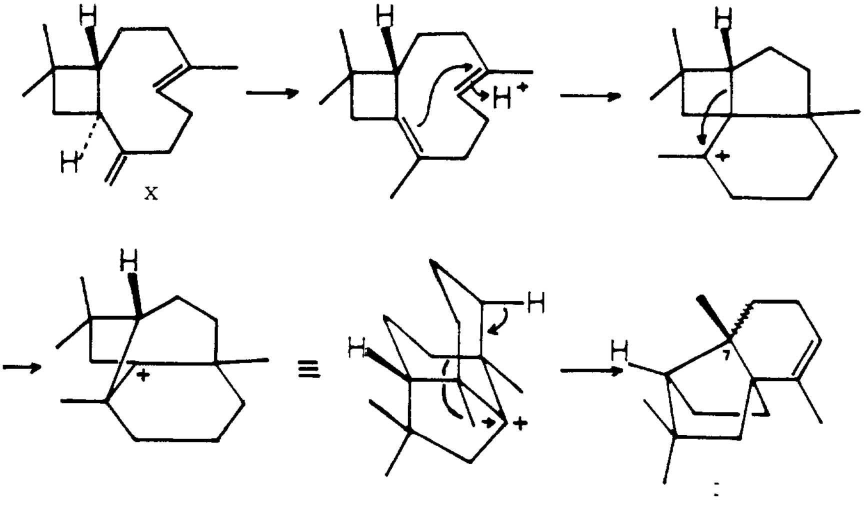
VIII



IX

Mass spectrometric examination of the corresponding ethylene ketal showed two base peaks at m/e 99 and 127, a result compatible (7) only with a ketone of structure (IX), if all α-positions are to be unsubstituted. This assignment was confirmed by synthesis of the racemic structure (IX) by 1,4-addition of methylmagnesium iodide to 4-isopropyl-3-methylcyclohex-2-en-1-one and spectroscopic identity of this substance with the degradatively derived ketone.

A rationalisation of this rearrangement of caryophyllene (X) to the neoclovene structure (I) may be envisaged by the sequence of carbonium ion shifts shown (use of classical representations implies simplicity of delineation, not partisanship !). On the basis of the known absolute configuration (X) for caryophyllene (8), this hypothesis predicts the stereochemistry as shown in (I) for neoclovene and thence the stereochemistry (IX) for the degradation ketone.



This configuration for (IX) is fully borne out by the strong positive Cotton effect* exhibited by this substance (9). Final confirmation of the predicted stereochemistry at C - 7 is now under way.

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