Conformations of Ten-membered Ring Sesquiterpenes by *X*-Ray Crystallography

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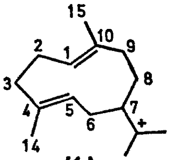
Summary The conformations of pregeijerene, shiromodiol, and elephantol have been studied by *X*-ray diffraction (in all three molecules the 14- and 15-carbon atoms are *syn*) and the stereochemistry previously assigned to shiromodiol has been revised.

THE cyclisation of *trans*-farnesyl pyrophosphate to the cation (**1**) has been postulated as the initial step in the biogenesis of the germacrane, eudesmane, and guaiane classes of sesquiterpenes.[1] Most of the eudesmane sesquiterpenes have absolute stereochemistries which can be derived from a conformation of the cation in which the 14- and 15-methyl groups are *syn*,[2] but it has not been established whether such a conformation is the energetically favoured form of the cation or merely a higher energy form which only arises during a transannular cyclisation reaction; the former hypothesis is given a measure of credence by Allen and Rogers' demonstration that germacratriene adopts the conformation (**2**) (and its mirror image) in the crystal of the 1:1 silver nitrate adduct of the hydrocarbon.[3] We now report a number of examples of conformations of ten-membered ring sesquiterpenes in which the 14- and 15-methyl groups are *syn*.



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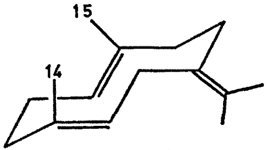

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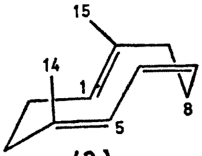

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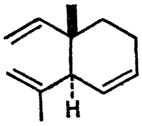

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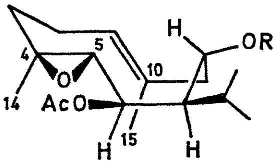

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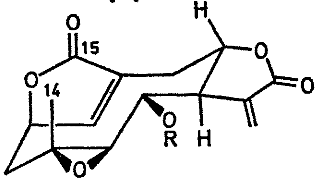

(6)

Pregeijerene,[4] the principal $C_{12}H_{18}$ hydrocarbon from *Geijera parviflora*, forms a 1:1 adduct with silver nitrate.[5] The crystals are monoclinic, of space group $P2_1/c$, with four units of $C_{12}H_{18}.AgNO_3.H_2O$ in a cell of dimensions a = 10·19, b = 9·17, c = 14·80 Å, β = 100·8°. The intensities of 1899 independent *X*-ray reflections were obtained by visual estimation of equi-inclination Weissenberg photographs taken with Cu-K_α radiation, and the atomic parameters were determined by Fourier and least-squares methods. The final value of R is 0·105. The C–C bond lengths have standard deviations of about 0·02 Å, and the valency angles have standard deviations of about 1·4°.

The *X*-ray analysis establishes that the trisubstituted double bonds have the *trans* configuration, and that the hydrocarbon exhibits the conformation (**3**) (and its mirror image) in the crystal. The silver ion is co-ordinated to the 4–5 double bond of one molecule and the 6–7 double bond of another at Ag–C distances ranging from 2·42 to 2·47 Å (average 2·45 Å). These distances are slightly shorter than the distances of 2·49 to 2·59 Å (average 2·53 Å) in the germacratriene adduct.[3]

The u.v. spectrum of pregeijerene differs substantially from that expected for a *cis-trans* conjugated cyclodecadiene, suggesting a transannular interaction between the double bonds[5] similar to that postulated in germacrol, germacrone, and costunolide.[6] The 1 · · · 5 and 10 · · · 5 intramolecular separations are distinctly short, 2·91 and 3·13 Å, and are clearly compatible with the suggested interaction. The 14 · · · 15 separation between the methyl carbon atoms is 3·49 Å.

The Cope rearrangement of pregeijerene to geijerene[4] appears to involve conformation (**3**), for an *X*-ray study of the silver nitrate adduct of geijerene showed[7] the hydrocarbon to have a *trans*-arrangement of the vinyl and isopropenyl groups, (**4**).

It is well established that *trans*-double bonds in medium-ring olefins are subject to appreciable steric strain.[8] The 2–1–10–9 torsion angle in pregeijerene is 165°, notably different from the ideal unstrained value of 180°. The torsion angle of 1·5° associated with the *cis*-double bond 6–7, on the other hand, is not significantly different from the ideal value of 0°, and this suggests that co-ordination to a silver cation may not materially distort a double bond.[9] The 3–4–5–6 torsion angle of the complexed *trans* double bond is 150°, and this may be compared with the still greater strain inherent in the torsion angle of 138° appropriate to the complexed double bond in the silver nitrate adduct of *trans*-cyclodecene.[10]

Shiromodiol[11] acetate *p*-bromobenzoate crystallises in the orthorhombic space group $P2_12_12_1$, with four molecules of $C_{24}H_{31}O_5Br$ in a unit cell of dimensions $a = 17{\cdot}18$, $b = 13{\cdot}95$, $c = 10{\cdot}05$ Å. The *X*-ray data were collected on a Hilger and Watts' four-circle diffractometer controlled by a PDP-8 computer; Mo-K_α radiation was employed, and the equivalent reflections $h\ k\ l$ and $h\ \bar{k}\ \bar{l}$ were averaged to yield 1511 independent intensities significantly above background level. The atomic parameters were determined by Fourier and full-matrix least-squares calculations, and the value of *R* at the present stage of refinement is 0·105. The absolute configuration was established by Bijvoet's anomalous-dispersion method,[12] and is incorporated in the conformation shown in (**5**). The 14 · · · 15, 1 · · · 5, and 10 · · · 5 intramolecular separations are 3·88, 3·05, and 3·51 Å, and the 2–1–10–9 torsion angle is 167°. The stereochemistry differs from that reported previously.[11]

Elephantol *p*-bromobenzoate[13] has the absolute stereochemistry and conformation defined in (**6**). The 14 · · · 15, 1 · · · 5, and 10 · · · 5 transannular separations are 3·32, 2·98, and 3·36 Å, and the 2–1–10–9 torsion angle is 163°. Elephantol and shiromodiol have the same absolute configuration at position 7, but otherwise could be considered to be related to antipodal germacratriene conformers. The α-orientation of the 14- and 15-methyl groups in shiromodiol is locked in by the 4,5-epoxide, for conformational inversion of the 10–1–2–3–4–5–6 segment of the molecule by rotation around the 6–7 and 9–10 bonds to give a folded ring of the type shown in (**2**) or (**6**) would cause the epoxide oxygen to be inside the ring and subject to absolutely prohibitive transannular crowding.

Hikino *et al*[14] have recently reported measurements of the intramolecular nuclear Overhauser effects in furanodienone and concluded that this germacrane sesquiterpene also adopts a conformation in which the 14- and 15-methyl groups are *syn*.

The displacement of atom 10 from the plane defined by atoms 1, 9, and 15 provides a measure of the departure from trigonal (sp^2) bonding at C(10) in these medium-ring olefins. The deviations from planarity in pregeijerene (0·02 Å), shiromodiol (0·01 Å), and elephantol (0·04 Å) are small (for comparison the displacements of atom 2 are *ca.* 0·3 Å) and manifestly not of major importance in the twisting of the 1–10 double bond by *ca.* 15°.†

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† Out-of-plane bending has been invoked to account for the very great distortion of the double bond in *trans*-cyclodecene (ref.10). The 4–5 double bond in pregeijerene is characterised by an angle of 29·6° between the plane defined by atoms 3, 4, and 5, and the plane defined by atoms 14, 4, and 5, and the departure from planarity at C(4) is large, the angle between the 3–4–5 and 14–4–5 planes being 19·5°. In this case the total distortion of the double bond involves contributions of about 20° from out-of-plane bending of bonds and about 10° from pure twisting, to give the observed apparent twist of 29·6°. Extrapolation to other cyclic olefins, however, involves the assumption that the distortions from planarity are not influenced by the Ag^+ ion.

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