The Conformation of Levopimaric Acid and Related Dienes

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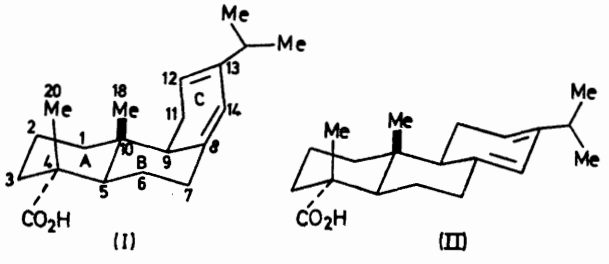
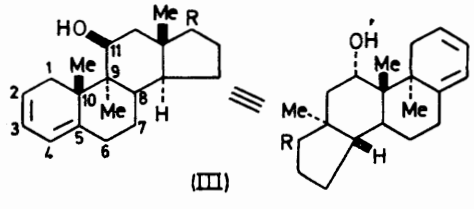
Summary *X*-Ray crystallography shows that levopimaric acid has a folded conformation in the solid state in agreement with conclusions derived earlier from its o.r.d. spectrum, and this is explained in terms of the '4,4-dimethyl effect'.

CONSIDERABLE evidence from o.r.d.[1] and n.m.r. spectra[1,2] and surface film[3] measurements, and from its photochemical reactions,[4] indicates that levopimaric acid exists in a B/C folded conformation (I), rather than in the *a priori*





expected 'extended' one (II). We now provide unequivocal evidence for this folded conformation in the solid state, from an *X*-ray crystallographic examination.

Thus, levopimaric acid crystallizes in the orthorhombic space group $P2_12_12_1$, $a = 15{\cdot}644$, $b = 19{\cdot}387$, and $c = 11{\cdot}851$ Å. The structure was solved by the symbolic addition procedure[5] and the 3317 independent reflections have been refined to R 6·0%. The asymmetric unit contains two independent molecules which exist as a dimer by the formation of two OH · · · H bonds between their carboxy-groups. The conformation of the two molecules is quite similar and is illustrated for one of the molecules in the Figure. The angle between the least-squares plane of

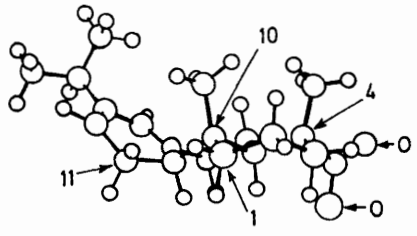


FIGURE. *Conformation of levopimaric acid.*

rings A and B and that of ring C is 40 and 36° for the two molecules. In the diene system, the torsion angle about the C(13)–C(14) bond is −9·1 and −11·8° in the same order for the two molecules. The cross-sectional area of 58·0 Å^2 derived from these data is reasonably close to the value of 52·3 Å obtained[3] from surface film measurements.

From the *X*-ray data, together with the physical information[1-4] already quoted, it may confidently be concluded that levopimaric acid has the same folded conformation (I) in solution. Our *X*-ray data thus fully confirm the conclusions

drawn earlier[1] from the o.r.d. data on the basis of the chirality rule for cisoid dienes.[1c]

Two tentative explanations for this conformational preference have been advanced[1,6] but we believe that a more complete explanation is to be found essentially in terms of the '4,4-dimethyl effect'[7] previously invoked, and now used in modified form, to rationalise certain subtle conformational effects in various 4,4-dimethyl steroids and related compounds.[8] Thus if levopimaric acid were in the planar conformation there would be a 4,4-dimethyl effect (across rings B and C) between (*a*) the C(10)-methyl group and the 11β-hydrogen atom and (*b*) between the C(1)–C(10) methylene bond (which we regard as effectively equivalent to a methyl group and the 11α-hydrogen atom. The corresponding interactions (across rings A and B) between the substituents attached to C(1) and C(9) are skew. Also, the C(10)-methyl group and the 11β-hydrogen atom would be coplanar and lean towards each other (*cf.* ref.6). In the folded conformation (I) the interaction between the C(10)-methyl group and the 11β-hydrogen-atom has been removed; there are now 4,4-dimethyl effects between the two hydrogens at C(1) and the eclipsing C(9) hydrogen atom and the C(9)–C(11) bond respectively; the substituents at C(10) and C(11) are skew. Hence the folded conformation (I) is energetically more stable by loss of (*a*) the C(10)-methyl group–11β-hydrogen atom interaction (*cf.* ref. 6) and (*b*) substitution of a 4,4-dimethyl effect between one methyl group and three hydrogen atoms, for one between two methyl groups and two hydrogen atoms. This explanation for the folded conformation of levopimaric acid was originally advanced by one of us (W.B.W.).

The steroidal diene (III) is in many respects analogous to levopimaric acid but has a positive Cotton curve,[6] in contrast to the acid (I). This difference may be rationalised in similar terms as follows. In the planar conformation of the diene (III), there is the same interaction between the coplanar α-methyl group at C(9) and the 1α-hydrogen atom, as in levopimaric acid. In addition, 4,4-dimethyl effects operate between the α-methyl group at C(9), the C(9)–C(11) bond, and the two eclipsing hydrogen atoms at C(1); the substituents at C(10) and C(11) are skew. In the folded conformation of the diene (III), corresponding to (II), 4,4-dimethyl effects would exist between the two substituents (α-hydrogen atom and β-hydroxy-group) at C(11) and the C(10) methyl group and the C(1)–C(10) methylene bond, respectively, as well as a small increase in the C(10) methyl group–1β-hydrogen interaction (*cf.* ref. 6). The substituents at C(1) and C(9) are skew. It is thus understandable that the diene (III) should remain in an extended conformation, although the diminution of the $\Delta\epsilon$ value of compound (III) reflects a small decrease in the chirality of the diene system consequent upon accommodation of the relevant interactions by an incipient movement towards a folded conformation.

The conformations of the other dienes reported by Burgstahler *et* al.[6] may be similarly rationalised. Full details will be published elsewhere.

Added in proof: We are informed by Dr. Elliot Charney that the observed o.r.d. curve of levopimaric acid is almost coincidental with the o.r.d. curve calculated (E. Charney, *Tetrahedron*, 1965, **21**, 3127) using the mean value of 10·5° for the torsion angle about C(13)–C(14)

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[8] Unpublished work by W. B. Whalley and associates.