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CRYSTAL AND MOLECULAR STRUCTURE OF EPIFRIEDELINOL

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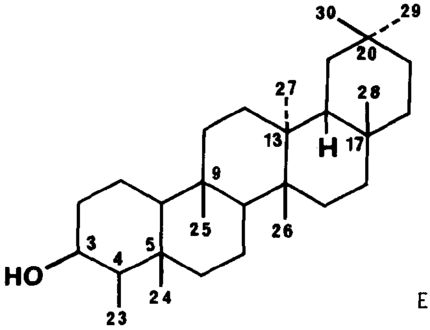
Friedelin was isolated from cork wax and its structure elucidated by chemical methods.[1] The assignment of the conformation of the cis-fused D and E rings as two chairs was based on a two-dimensional x-ray analysis of friedelan-3α-ol chloroacetate.[2] Epifriedelinol, the 3β-epimer, is naturally occurring in many plants[3] and has been isolated in high yield from the wood and bark of the local tree *Bridelia micrantha*.[4] Inspection of a Dreiding model of epifriedelinol suggested that rings D and E could not both be chairs because this conformation would force the α-methyl group at C(20) impossibly close to the axial methyl group at C(13). A structural analysis was undertaken to determine the true conformation of rings D and E.



Epifriedelinol

Suitable crystals, obtained from hexane/chloroform, were supplied by Dr. K.H. Pegel and Mr. C.B. Rogers. The crystals were monoclinic, space group C2, $\underline{a}$=13.43(2), $\underline{b}$=6.35(1), $\underline{c}$=29.59(3) Å, β=92.5(2)°, U=2521 Å^3, D_m=1.14(2)g cm^{-3}, Z=4, M=428, $C_{30}H_{52}O$, no required molecular symmetry. Integrated intensity data were collected by the multiple-film equi-inclination Weissenberg method with Ni-filtered Cu-Kα radiation for layers *h0l* to *h5l* and *0kl* to *2kl*. Intensities were measured with a densitometer; weak data were estimated visually. Attempts to solve the structure by the Patterson method failed, and the solution was finally obtained by Direct Methods with the aid of the MULTAN74 system.[5] The correct solution had ABSFOM=1.05, PSIZERO=8019, RKARLE=25.6, NQEST=-0.70. The 31-atom structure has been refined isotropically by block-diagonal least squares to R=0.17 for 2651 data. All bond lengths and angles are normal and the molecular geometry is shown in Figures 1a and b.

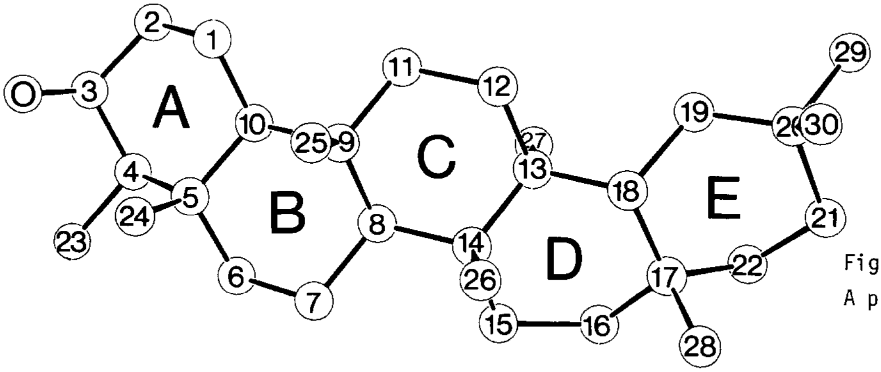


Figure 1a.
A projection down *b*.

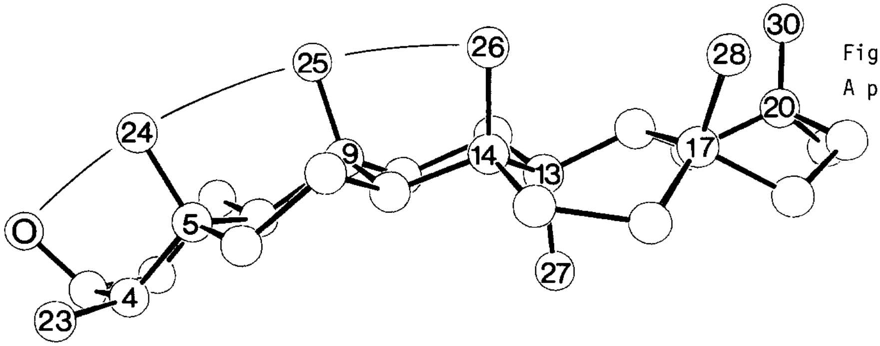


Figure 1b.
A projection down *a*.

As expected, rings A, B and C are well-defined chairs, the OH group at C(3) is axial and the methyl group, C(23), at C(4) is equatorial. The repulsions between the axial methyl groups on C(5), C(9) and C(14) cause a marked bowing of the rings A, B and C as is clearly seen in Figure 1b. This effect is well known in steroids.[6]

The *cis*-fused rings D and E are both boats and **not** chairs as was originally proposed[2] and apparently confirmed by nmr measurements.[7] The *gem* methyl groups are at C(20) and not at C(19) as indicated by Lewis and Wenkert.[8] (This latter assignment appears to be in error because it is a direct contradiction of a previous assignment[7] based on the same nmr data). The torsion angles are shown in Figure 2, and indicate that ring E is a near-ideal boat while

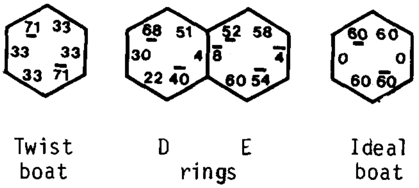


Figure 2. Torsion angles.

ring D is distorted part way towards the twist boat conformation.[9] Two other compounds have a similar conformation for rings D and E: 3-O-acetyl-16β-O-p-bromobenzoylpachysandiol B[10] and the dibromide of a C(25)-C(26) ether-bridged derivative of friedelane.[11] In these cases one might argue that either the β-substituent at C(16) or the C(25)-C(26) bridge could be causing the boat-boat conformation. The results found for epifriedelinol show that this is not so, and that the boat-boat conformation which occurs in the friedelane skeleton is the favoured conformation of lowest energy. The torsion angles therefore represent the compromise which simultaneously maximises the separations C(26)···C(28)···C(30) and C(27)···C(29) thus reducing to a minimum the non-bonded repulsions between the methyl groups on rings D and E.

Cis fusion at the D/E ring junction does not necessarily cause rings D and E to be boats, e.g. in methylmicromerol bromoacetate,[12] methyl oleanolate iodoacetate[13] and campanulin[14] rings D and E are chairs.

It is the combination of the *gem* pair of methyls at C(20), an axial α-methyl at C(13) and the *cis* fusion of rings D and E which forces the boat-boat conformation on the molecule. We conclude, therefore, that in all compounds with the friedelane skeleton the *cis*-fused D and E rings will be in the boat-boat conformation (or stretched S form[10]) and that the chair-chair conformation (or folded F form) does not exist.

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