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4-EPIFRIEDELIN and 4-EPISHIONONE

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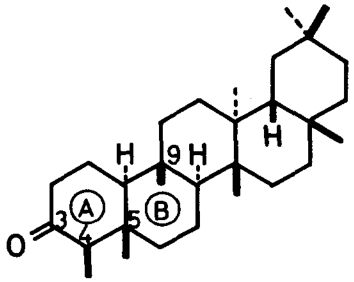
Friedelin (I) is one of the widely distributed triterpenes in the plant kingdom[1]. However, neither the preparation of its epimer, 4-epifriedelin (II)[2], nor the isolation of II from natural sources has yet been described. The observation that, while the D-homosteroid (III) is converted to its 17aα-methyl-epimer (IV) to the extent of about 30 % under equilibrating conditions[3], friedelin (I) contains none of II at equilibrium, has been explained by Ourisson et al.[4]. The deformation of ring B caused by 1,3-diaxial interaction between the 5β- and 9β-methyl groups of II produces reflex effect which brings the 4α-methyl group nearer to the 10α-hydrogen atom, resulting in destabilization of the epimer (II)(see IIa) ; this factor of destabilization does not exist in the series of D-homosteroid[4]. Thus the preparation of II would be desirable in view of verification of this effect. We have briefly mentioned the isolation of II (4-isofriedelin[5]) together with a series of compounds on photolysis of friedelin[6]. We now wish to report the characterization and structure confirmation of 4-epifriedelin (II) of particular interest. Generality in the photoepimerization of compounds of this type was shown by the formation of 4-epishionone (VI) from shionone (V).

Irradiation[7] of friedelin (I) in a boiling solution of ethanol, acetic acid-water, n-hexane or diethyl ether under a nitrogen atmosphere, using a high pressure mercury lamp, afforded a mixture which was separated by silica gel chromatography into hydrocarbon, ester, ketone, alcohol and acid fractions. Thin layer chromatography (TLC) of ketone fraction on silica gel G using benzene as developing solvent gave two spots of R_f 0.52 and 0.45 ; the product of R_f 0.52 was found to be identical with friedelin (I). The lower-moving product (R_f 0.45) was recrystallized from petroleum ether to give a single constituent as white needles, m.p. 257.5°, $\nu^{\text{nujol}}_{C=O}$ 1706 cm^{-1}, $C_{30}H_{50}O$ (mass spectrometry, M^+ 426 ; elemental analysis). The most probable structure was inferred to be a photoepimerized ketone, 4-epifriedelin (II). When ethanol, n-hexane or diethyl ether was used as solvent in irradiation, the yield of II was about 5 %, respectively.

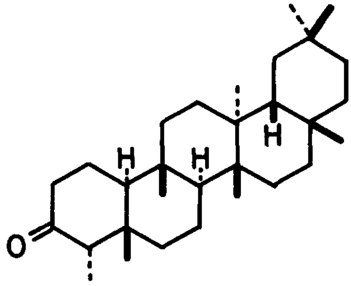
The ketone (II) and friedelin (I) are very similar in fragmentation pattern by mass spectrometry, and distinct by NMR, IR, TLC and by GLC, showing retention time (Diasolid H-523, 240°C) of 36.6 and 41.1 min respectively. The ketone (II) was adsorbed on alumina overnight and then eluted with benzene to afford an isomerized product which was found to be identical (m.p., mixed m.p., IR, TLC and GLC) with friedelin (I) ; no original ketone (II) was recovered (by TLC). When silica gel was used, no isomerization proceeded. By treatment with sodium methoxide in methanol-dioxane, ketone (II) was completely isomerized to friedelin.

These observations firmly establish the 4α(axial)-methyl configuration (IIa) for the less stable 4-epifriedelin (II), and show that the 4β-methyl-epimer (friedelin)(I) is fully favored in equilibrium, confirming Ourisson's reflex effect.

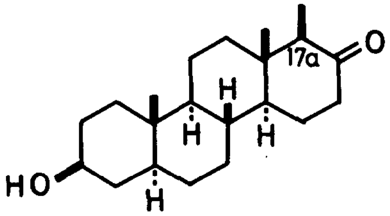
The above assignment (II) is compatible with optical rotatory dispersion curve of 4-epifriedelin (c 0.2 in dioxane : $[\Phi]_{589}$ $- 50°$, $[\Phi]^{\text{trough}}_{318}$ $- 2500°$, $[\Phi]^{\text{peak}}_{275}$ $+ 3100°$ and $[\Phi]_{214}$ $+ 1850°$) when compared with that[8] of friedelin (I). Both curves show negative Cotton effect. However, the amplitude of II (a = - 56) is smaller than that of I (a = - 130). If one assumes chair conformation for both of rings A and B, this evidence could be interpreted as that, while 4β-methyl group of I lies on octant plane, 4α-methyl group of II contributes to the positive octant (IIa'). The most probable conformation of ring A of II would be a deformed chair conformation rather than boat form which would be responsible for positive Cotton effect. Further examination coupled with NMR studies on this problem is in progress.



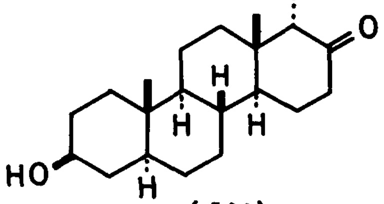
(I)



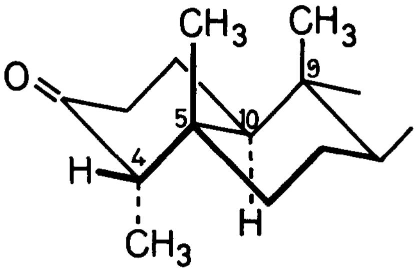
(II)



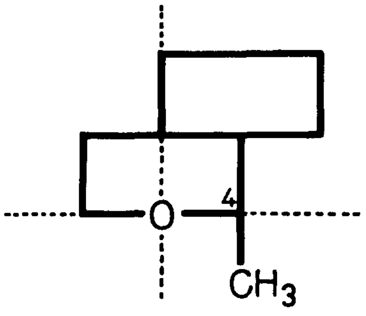
(III)



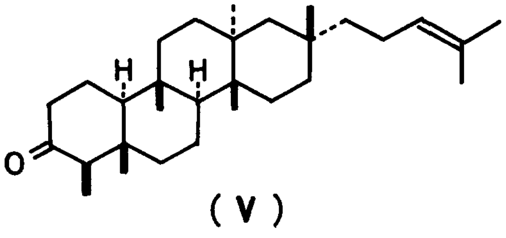
(IV)



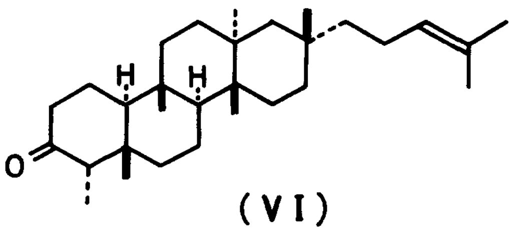
(IIa)



(IIa')



(V)



(VI)

Similarly, irradiation of shionone (V) in n-hexane afforded 4-epishionone (VI)(yield : 9 %), m.p. 153.5 - 154.5°, $\nu_{C=O}^{nujol}$ 1706 cm^{-1}, $C_{30}H_{50}O$, which was isomerized to V on treatment with sodium methoxide in methanol-dioxane. Shionone (V) and VI are distinct by NMR, IR and TLC.

The formation of 4-epifriedelin (II) and 4-epishionone (VI) could be viewed as an α-cleavage (between 3 and 4) followed by recyclization in a stereochemically different sense^{9}. A part of recovered friedelin (I) and shionone (V) should be resulted from diradical recombination to give starting ketones, respectively.

Since a facile isomerization of II to I and of VI to V was demonstrated, the presence of II and VI in nature would be expected.

REFERENCES

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2. Cf. T. Bruun, *Acta Chem. Scand.*, **8**, 76 (1954). The corresponding hydrocarbon," friedelane-II "(II, without 3-oxo group), was described. However, there seems to be lacked in spectral evidences to confirm this structure.
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4. C. Sandris and G. Ourisson, *Bull. Soc. chim. France*, 1524 (1958) ; Cf. E. L. Eliel, N, L. Allinger, S. J. Angyal and G. A. Morrison, *Conformational Analysis*, p. 345, Interscience Publishers, New York (1965).
5. We now wish to call it 4-epifriedelin.
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7. Cf. F. Kohen and R. Stevenson, *Chem. and Ind.*, 1844 (1966). The photodecarbonylation of I in diethyl ether has first been described, giving rise to 5-ethyl-10β-vinyl-des-A-friedelane and 3-norfriedelane.
8. P. Crabbé, *Optical Rotatory Dispersion and Circular Dichroism in Organic Chemistry*, p. 121, Holden-Day, San Francisco (1965).
9. Cf. e.g. : R. O. Kan, *Organic Photochemistry*, p. 81, McGraw-Hill, New York (1966), and analogous photoepimerization of steroid ketones.