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STEREOCHEMISTRY OF SALVIN AND PICROSALVIN

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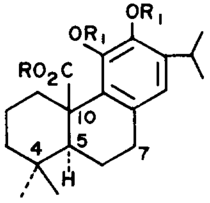
THE structure of the new diterpene (I) which we would now identify by the trivial name 'salvin', has been well-established (1), leaving its stereochemistry uncertain. We would now like to propose the A/B rings to be <u>trans</u>-fused in the compound as shown in (I). PMR spectra in pyridine solution show that one of the methyl groups at C_4 is deshielded by 19 cps in the acid (II) compared with the same signal in the ester (III). This clearly indicates that one of the C_4 methyl groups is in a 1,3-cis diaxial relationship with the carboxyl group at C_{10} (2). This can happen only if (a) the A/B rings are <u>trans</u> fused as in (II) or (b) they are <u>cis</u> and assume conformation (V) in preference to (VI). From the non-bonded interactions enumerated (which are not common to both) that destabilise each of the conformations it may be safely assumed (3)



I $R = R_1 = H$
II $R = H; R_1 = Ac$
III $R = CH_3; R_1 = Ac$
IV $R = R_1 = CH_3$

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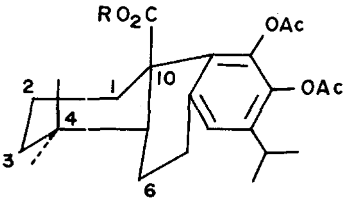
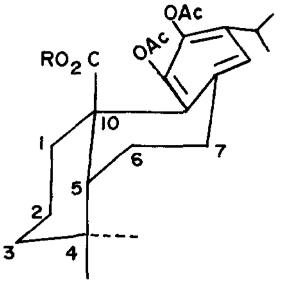
that with a cis ring fusion, (VI) would be the preferred



V



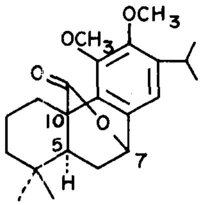
VI

Non-bonded interactions that destabilise V and VI.

V	VI
(1) C_{10}-CO_2R, $C_4\beta$-Me	(1) C_{10}-CO_2R, $C_6\beta$-H
(2) C_{10}-CO_2R, $C_2\beta$-H	(2) C_4 α-CH_3, C_7-α-H
(3) C_6-CH_2, C_1 α-H	
(4) C_6-CH_2, C_3 α-H	

conformation of the molecule. This, however, would not show any 1,3-diaxial relationship with a C_4-methyl and a C_{10}-carboxyl group. Hence the A/B rings should be trans-fused.

Picrosalvin has been shown to have structure (VII)



(VII)

and is synthesized from salvin (I) by oxidising (IV) to a C_7 ketone, reducing it with $NaBH_4$ to a C_7-hydroxyl derivative, and then lactonising (1). Hence both the diterpenes have the same stereochemistry at C_5 and C_{10}. The specific rotations of the acid (II) $[\alpha]_D$ +140°, of the lactone (VII), $[\alpha]_D$ -73.5° and that of the corresponding hydroxy acid obtained by hydrolising the lactone (VII), $[\alpha]_D$ $+31^\circ$ clearly indicate that (I) and (VII) represent the absolute stereochemistry of the two compounds (4).

Independently, E.Wenkert et al. have also recently come to the same conclusion by other methods (5), wherein they have renamed picrosalvin as carnosol.

REFERENCES

1 H. Linde, Helv. Chim. Acta, 47,1234 (1964)

2 C.R. Narayanan and N.K.Venkatasubramanian, accompanying communication.

3 R.B. Turner, J. Amer. Chem. Soc. 74, 2118 (1952); N.A.Allinger and J.I. Coke, J. Org. Chem. 26, 2096 (1961) and related papers.

4 W. Klyne, Chem. & Ind. 1198 (1954)

5 C.H. Brieskorn, A. Fuchs, J.B-son Bredenberg, C.H. McChensey and E.Wenkert, J. Org. Chem. 29, 2293 (1964).