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STRUCTURE (X-RAY ANALYSIS) OF MANICOLINE B, A MIXTURE OF TWO DIASTEREOISOMERS OF A NEW ALKALOID FROM DULACIA GUIANENSIS (OLACACEAE)

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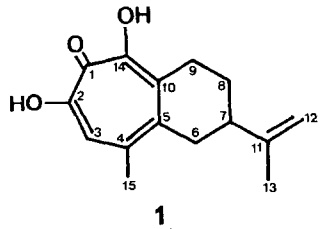
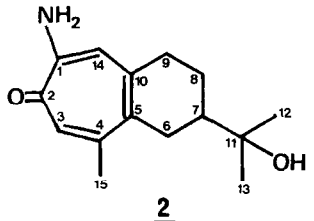
Summary : Manicoline B, isolated from the root bark of Dulacia guianensis (Olacaceae), was shown by X-ray analysis to be an equimolecular mixture of two diastereoisomers of a new alkaloid and to have structure (3).

Previous studies[1] of the root bark of Dulacia guianensis (Engl.) O. Ktze (Olacaceae) resulted in the isolation, along with the sesquiterpenoid hydroxytropolone manicol (1)[2], of two new alkaloids which have been designated manicoline A and B. The major alkaloid, manicoline A, $C_{15}H_{21}NO_2$, was shown to have structure (2) and to be the first naturally occurring α-aminotropone. We herein report the structural elucidation of the minor alkaloid, manicoline B, (3) which proved to be a mixture of two diastereoisomers.



1



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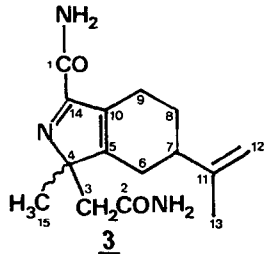
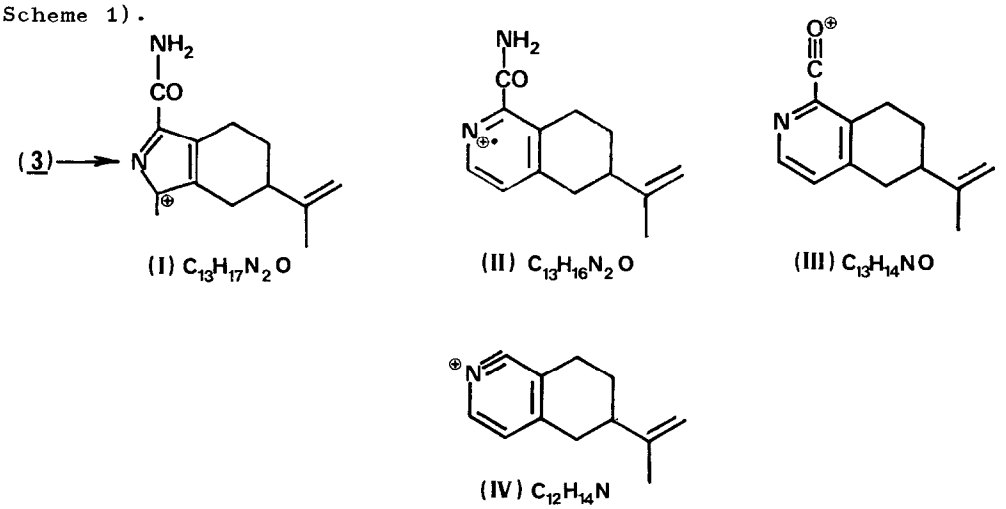


3

Manicoline B (3) crystallized from acetone as colourless crystals, m.p. 199-200°, $[\alpha]_D^{22}=+36°$ (c=0.23 ; $CHCl_3$) ; it displays a single spot on TLC in several solvent systems. The high resolution mass spectrum established the molecular formula of (3) as $C_{15}H_{21}N_3O_2$ ($M^{+\cdot}$ at m/z 275.1631) ; the CI mass spectrum showed the MH^+ ion at m/z 276 and the dimeric ion $(2\,x\,M)H^+$ at m/z 551. The u.v. spectrum (EtOH) of (3) displayed end absorption around 220 nm and maxima at 228 (ε 2112) and 272 nm (1713). The 400 MHz ^1H n.m.r. spectrum showed signals due to the isopropylidene group : a methyl resonance at δ 1.78 and two one proton signals at δ 4.81 (s) and 4.75 (d,

J=5 Hz). It also revealed the presence of a tertiary methyl group (two singlets of same intensity at δ 1.340 and 1.348 corresponding together to 3 H) in addition to two multiplets (2 H each) centered at δ 5.58 and 7.04 exchangeable with MeOD (NH_2 groups). Manicoline B (3) was negative to ninhydrin reagent and therefore the exchangeable protons should be assigned to primary amide groups.

The presence of CH_2CONH_2 and $CONH_2$ groups was supported by the EI mass spectrum of (3) showing peaks at m/z 217.3380 ($C_{13}H_{17}N_2O$; 100%), 216.1262 ($C_{13}H_{16}N_2O$; 29%), 200.1084 ($C_{13}H_{14}NO$; 67.8%) and 172.1119 ($C_{12}H_{14}N$; 16,5%) which can be attributed to ions (I) to (IV) respectively (Scheme 1).



Scheme 1

The 100.6 MHz ^{13}C n.m.r. spectrum of manicoline B (3) revealed two signals of equal intensity, having close chemical shifts, for most of the carbon resonances. This fact as well as the observed splitting of the ^1H n.m.r. signal due to the tertiary methyl group suggest that manicoline B (3) was an equimolecular mixture of two isomers.

The complete structure of (3) was provided by single crystal X-ray analysis which showed unambigously that manicoline B was indeed a mixture of two diastereoisomers, epimeric at C-4. Attempts to separate the mixture failed and paucity of material prevented further investigation.

X-ray analysis : The crystals grown from acetone displayed large mosaicity. A small plate of (3), size 0.2 x 0.2 x 0.05 mm, was mounted on an automatic four-circle diffractometer using graphite-monochromatized CuKα radiation (λ=1.5418 Å). The system is triclinic, space group P_1 with two molecules in the unit cell. The parameters are : a = 11.579 (4), b = 8.859 (3), c = 8.779 (3) Å, α = 119.72 (8), β = 83.22 (7) and γ = 101.80 (7)° with a total volume of 765.4 $Å^3$. The reflections were recorded up to θ= 60° in the θ/2θ scanning mode. After Lorentz and polarisation correc-

tions 2105 structural factors were considered as observed ($I \geq 2\sigma(I)$). The analysis of the normalised structural factors clearly shows a centrosymmetric distribution suggesting that the $P\bar{1}$ space group may be a possible alternative. However, this possibility is ruled out since manicoline B (3) is optically active. The structure was solved by direct methods[3] in the P_1 space group and refined with anisotropic thermal factors for heavy atoms to a final R = 9.7%. Hydrogen atoms were introduced at their theoretical places with an isotropic thermal factor equal to that of the bonded atom. The large discrepancies between the observed bond values for the amide groups suggest a rotation around C(2) - C(3) and C(1) - C(14) bonds. Different configurations were computed without bringing any clear distinction between the N and O atoms. The crystal structure is shown in the Figure[4]. The two molecules of the unit cell are in fact diastereoisomers which crystallize together and differ only by the configuration at C-4. Both diastereoisomers are linked together by hydrogen bonds, d[O(2)... N(2')] = 2.91 Å and d[O(2')... N(2)] =2.87 Å, especially around the pseudo centre of symmetry responsible for the near centrosymmetric distribution of the E factors observed in the initial steps of the resolution.

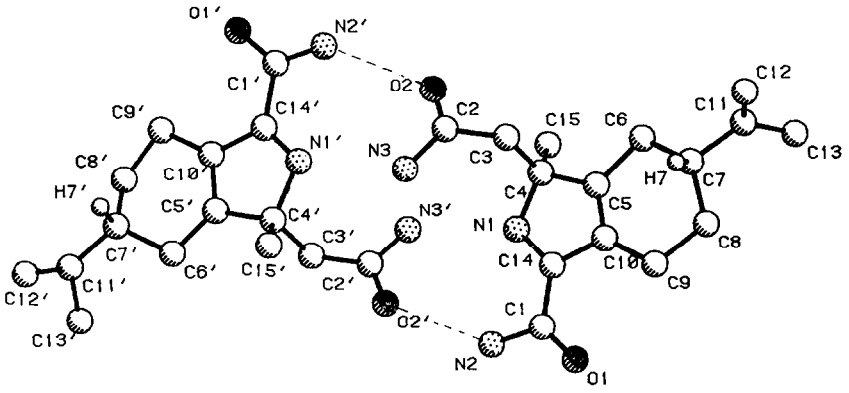


FIGURE. Crystal structure of manicoline B (3) ; the hydrogen atoms except H-7 are omitted. The numbering is that of manicoline A (2).

The biogenetic precursor of manicol (1) and manicoline A (2) was supposed to be an eudesmane type sesquiterpenoid[1,2]. It seems reasonable to assume that manicoline B (3) is formed from manicol in the manner shown in Scheme 2.

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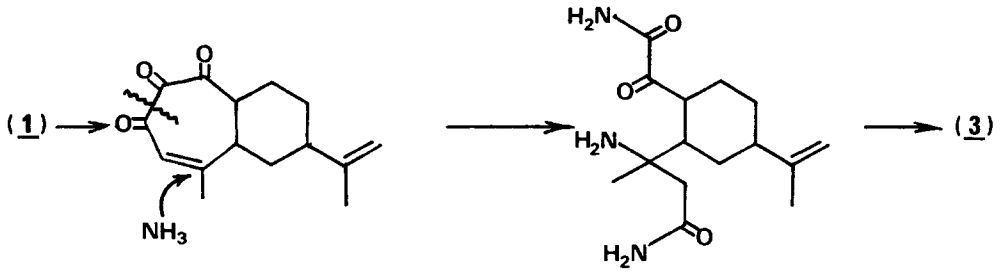

Scheme 2

REFERENCES AND NOTES

1. J. Polonsky, J. Varenne, T. Prangé, C. Pascard, H. Jacquemin, and A. Fournet, J.C.S. Chem. Comm., 1981, 731.

2. J. Polonsky, J.C. Beloeil, T. Prangé, C. Pascard, H. Jacquemin, D.M.X. Donnelly, P.T.M. Kenny, Tetrahedron, 1983, 39, 2655.

3. G. Germain, P. Main, and M. Woolfson, Acta Crystallogr., Sect. A, 1971, 27, 368.

4. The atomic co-ordinates for this work are available from the Director of the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW. Any request should be accompanied by the full literature citation for this communication.

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