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SEDUM ALKALOIDS. III: A REVISED STRUCTURE FOR SEDININE.

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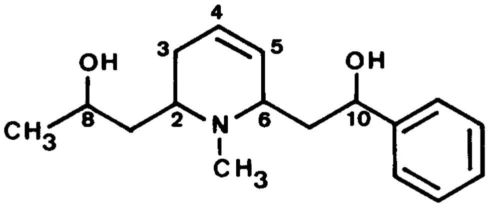
Summary: Sedinine is assigned the revised structure 2 -which also represents the absolute configuration- on the basis of single-crystal X-ray crystallography.

The piperidine alkaloid (-)-sedinine was first isolated from Sedum acre[2] and has been assigned structure 1 (trans-8-methyl-10-phenyl-4,5-dehydrolobelidiol) on the basis of spectroscopic data and chemical degradation[3,4]. More recently, this alkaloid was also shown to occur in a number of Sedum species[5]



1

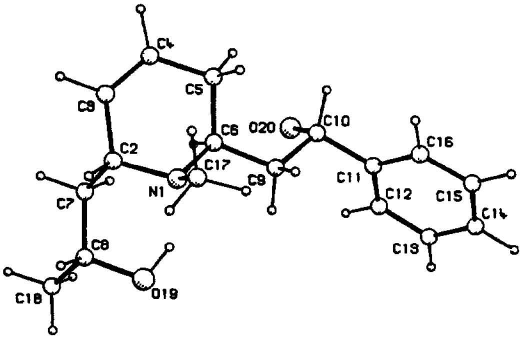
In our laboratory, some closely related alkaloids were isolated from Sedum acre and correlated with sedinine[6]. In order to establish the stereochemistry of this group of bases, an X-ray crystallographic analysis was performed on a pure sample of sedinine (ms, ir[2], nmr[4], gc, m.p. 120-121° from petroleum ether, $[\alpha]_D^{20}$ -98°(methanol, c = 1.9) and on its hydrochloride (m.p. 170-171° from 2-butanone, $[\alpha]_D^{20}$ -145° (methanol, c = 0.4).

The crystal data are as follows: $C_{17}H_{25}NO_2$, M_r = 275.39, orthorhombic, space group $P2_12_12_1$ with a = 24.446(23), b = 11.265(12), c = 5.829(4)Å, V = 1605(3)Å^3, four molecules per unit cell (Z = 4) give D_x = 1.29 Mg m^{-3} for sedinine; $C_{17}H_{25}NO_2.HCl$, M_r = 311.85, monoclinic, space group $P2_1$ with a = 6.458(2), b = 16.986(5), c = 8.045(3)Å, β = 101.37(3)°, V = 865(0.5)Å^3, two molecules per unit cell (Z = 2) give D_x = 1.20 Mg m^{-3} for sedinine hydrochloride.

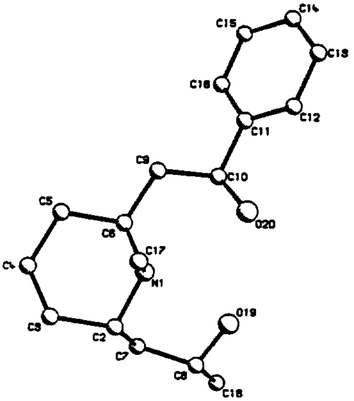
The intensity data of the two compounds were recorded on a Syntex $P2_1$ diffractometer using graphite monochromatized MoKα radiation (λ = 0.7107 Å).

For sedinine, 1041 reflections were measured of which 759, with $I > 2.5\sigma(I)$, were used in the structure determination (by MULTAN 78[7]) and refinement (SHELX 76[8]). Hydrogen atom positions were calculated except H(19) which was located from a difference Fourier Synthesis. The final R value is 0.046[9]. For sedinine hydrochloride, 1209 reflections were collected and 1195 considered as observed. The structure was solved using the YZARC 78[10] computer programme and the refinement carried out by the SHELX 76 programme. The final conventional R index is 0.079[9].

The Figure gives a perspective drawing (PLUTO 78[11]) of both molecules.



Sedinine

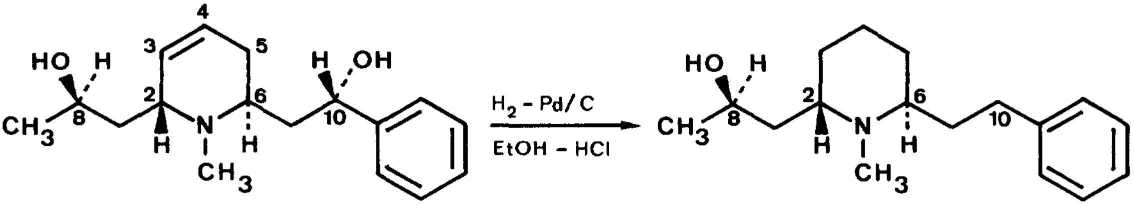


Sedinine hydrochloride

Unexpectedly, it appears from the present study that structure <u>1</u> has to be modified to <u>2</u> i.e. the double bond is between C-3 and C-4 (bond lengths 1.32(1) and 1.33(2)Å for sedinine and sedinine hydrochloride respectively) and not between C-4 and C-5 (1.51(1) and 1.50(2)Å) as was previously inferred from the results of a chemical degradation[4].

The molecular dimensions and conformation (half-chair with C_2 axis passing through the middle points of the C-3, C-4 and N-1, C-6 lines) are very similar in both heterocycles, protonated or not. The only significant difference lies in the three N-C bonds whose lengths are greater in the cation by an amount of 0.06 Å (1.53 vs 1.47 Å). Intramolecular hydrogen bonds between N-1 and O-19 exist in both crystals: N---H-O = 2.71(1)Å in sedinine; N-H---O = 2.64(2)Å in the hydrochloride.

Hydrogenolysis (Pd/C) of the benzylic hydroxyl group of 2 yielded 10-deoxydihydrosedinine 3 in 85% yield (hydrochloride: m.p. 132-134° from 2-butanone, $[\alpha]_D^{20}$ -29° (methanol, c = 1.38).



2

3

Application of Horeau's method to 3 led to the isolation of dextrorotatory 2-phenylbutanoic acid (optical yield: 4%) implying the (R) configuration at C-8[13, 14].

(-)-Sedinine is therefore (2R, 6S, 8R, 10S)-8-methyl-10-phenyl-3,4-dehydrolobelidiol.

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14. A substantially higher optical yield (24%) is obtained when the hydrochloride of 3 is used.

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