NEW COMPOUNDS FROM HYPTIS. X-RAY CRYSTAL AND MOLECULAR

STRUCTURES OF ANAMARINE

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Summary. The structure (including absolute stereochemistry) of ana-
marine, a new unsaturated lactone isolated from an unclassified Hyptis
species, has been established.

In a previous communication[1] we described the isolation of two new com-
pounds - olguine and anamarine - from an unclassified Hyptis species, together
with the structure elucidation of the first of these two compounds. In the
present communication we report the structure of anamarine (1).

Combustion analysis and mass spectrometry indicated the molecular formu-
la $C_{20}H_{26}O_{10}$ for anamarine. The spectroscopic evidence suggested a close rela-
tionship between olguine and anamarine so that the same basic skeleton was
assumed for both compounds. However, a comparison of the ^{1}H-NMR spectra of the
two compounds revealed some differences. Thus, the ^{1}H-NMR spectrum of anama-
rine showed the presence of four acetoxyl groups, while no signals of oxirane
ring protons could be observed. (Olguine contained three acetoxyl groups and
two oxirane protons.) In addition, the multiplicity of the signals of the two
olefinic protons belonging to an α,β-unsaturated carbonyl function (δ6.07 and
6.90) suggested the presence of two protons at C-4. (Olguine had one acetoxyl
group at C-4 and therefore only one proton at this centre.) Irradiation of the
two H-4 protons at δ2.46 confirmed their coupling to H-2 and H-3. As in the
case of olguine, the ^{1}H-NMR spectrum of anamarine revealed the presence of a
sec-CH$_3$ group (δ1.20, J=6 Hz) and two other olefinic protons, whose signals
were centred at 5.84 ppm. The signals of the remaining protons appeared be-
tween 4.90 and 5.40 ppm, corresponding to the lactonic proton at C-5 and four

protons geminal to acetoxyl groups. The ^{13}C-NMR spectrum of anamarine showed the following bands (some of which could be assigned with certainty only after an X-ray analysis had provided the definite structure) : C-1 (δ163.1, s), C-2 (121.4, d), C-3 (144.2, d), C-4 (29.1, t), C-5 (67.3, d), C-6 (125.5, d), C-7 (132.8, d), C-8 (75.7, d), C-9 (71.9, d), C-10 (71.8, d), C-11 (70.4, d) and C-12 (15.8, q) and, in addition, those of the four acetoxyl groups.

All the spectroscopic data, including the positive Cotton effect observed in the CD curve at 260 nm, were compatible with structure (1). However, in order to confirm the location of the double bond at the side chain and to establish the stereochemistry of the four asymmetric centres at this chain, an X-ray analysis was carried out.

A single crystal of 0.19x0.24x0.35 mm was used to establish the crystal structure of anamarine. The X-ray spectrum shows orthorhombic symmetry, space group $P2_12_12_1$ with $\underline{a}$=21.825(1), $\underline{b}$=11.945(1), $\underline{c}$=8.3736(2) Å, V=2183.0(1) Å[3], D_c=1.30 g cm^{-3} and Z=4. The intensity of 2071 independent Friedel pairs was measured up to Θ=65° with an automatic four-circle diffractometer. Graphite monochromated CuK$_\alpha$ radiation and an ω/2Θ scan technique were used. 1,887 Friedel pairs were considered as observed on the criterion I>2·σ(I). The absorption effect was ignored and the Lorentz and polarization factors were applied as usual. The structure was solved by using the Multan programme[2]. Most of the remaining calculations were performed with the X-RAY 70 System[3]. Atomic coordinates and anisotropic thermal parameters for non-hydrogen atoms were refined by least-squares analysis using unit weights. A difference synthesis showed all H atoms as the most prominent peaks of the map. An appropiate weighting scheme was chosen to give flat dependence of $<w(F_o-F_c)^2>$ vs. $<sin\Theta/\lambda>$ and vs. $<F_o>$ [4]. The positional parameters of the H atoms were also refined in the last steps of the weighted least-squares analysis, where both hkl and $\overline{hkl}$ reflexions were included. All 30 Friedel pairs with F_o>40 and $sin\Theta/\lambda$<0.16 showed appreciable secondary extinction effects and were rejected for the refinement. The final unweighted and weighted disagreement indices were R=0.061 and R_w=0.087. The anomalous dispersion effect of the oxygen atoms was used to establish the absolute configuration of the molecule, shown in Figure 1. Comparison of the 65 more relevant Bijvoet pairs with F_o>20·σ(F_o) $|\Delta|F_c||$>0.09 and $|\Delta|F_o||$>0.03 gave the following discrepancy indices [5]:average Bijvoet difference of 0.513 (0.563 for the reversal enantiomorph), average Bijvoet ratio of 0.067 (0.074) and $\sum|\Delta F_o^2-\Delta F_c^2|/\sum|\Delta F_o^2|$= 0.953 (1.054. These results are obviously a poor indication of the correct enantiomorph, but in any case are supported by the results obtained for the related compound olguine[1], which presents the same absolute configuration at C5.
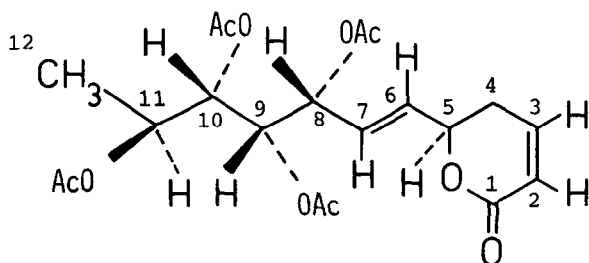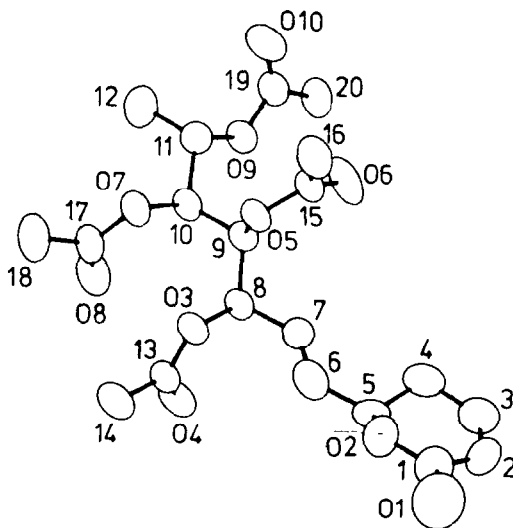
(1)

Figure 1. Structure and X-ray model of anamarine, showing its absolute configuration.

The six-membered ring presents the same conformation as that found for olguine[1]. It can be described as a somewhat distorted envelope, the C5 atom being at the flap. The best least-squares plane passing through C1-C2=C3-C4 gives the following atomic deviations (Å) for both molecules :

	C1	C2	C3	C4	C5	O1	O2
Olguine	0.009	-0.019	0.019	-0.009	-0.720	0.286	-0.231
Anamarine	0.008	-0.017	0.017	-0.008	-0.660	0.149	-0.107

The C6-C7 bond length of 1.255(5) Å is too short compared with the value of 1.34 Å normally observed for a Csp^2-Csp^2 bond. This unexpected result was obtained not only after the least-squares refinement, but also after several difference maps calculated without the contribution of these two atoms. More-over, the remote possibility of taking these atoms for sp C atoms or N atoms was discarded on the basis of the following considerations: 1) both hydrogen atoms attached to these atoms appear as very prominent peaks on the difference map; 2) a chemical analysis does not detect the presence of nitrogen; and 3)

the thermal parameters for these atoms compare well with those of other C atoms of the structure. It can therefor be concluded that for some reason this Csp^2-Csp^2 bond is considerably short. It is also interesting to note in this connection that the C5-C6 bond length is 1.547(5) Å, which is also somewhat long in comparison with the expected value of 1.50 Å for a Csp^2-Csp^3 bond. This can probably be explained in terms of an electron transfer from the C5-C6 bond to the C6-C7 bond. An interesting feature of this structure is the fact that the absolute configuration at C10 is the reverse of that in the same atom of the related compound olguine[1]. On the other hand, the trans conformation of the H atoms attached to C6 and C7 is in contrast to the cis conformation in olguine. The only probable explanation of these differences would appear to be different biogenetic origins for these two molecules.

<div align="center">REFERENCES</div>

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