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ISOLATION AND ABSOLUTE CONFIGURATION OF THE AEROPLYSININ I ENANTIOMORPHIC PAIR FROM IANTHELLA ARDIS

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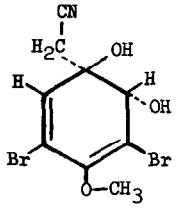
The total structure 1 has been determined for aeroplysinin I[1] an antibacterial dibromo compound isolated from a Caribbean sponge (Ianthella ardis).[2] The crystalline compound isolated was the (-)-isomer, mp 112-116°, $[\alpha]_D$-198° (c 0.5 in acetone). The structure was established from spectral and chemical data. The (+)-isomer, $[\alpha]_D$+182° (c 0.5 in acetone) was isolated from another Ianthella sample[2] and also from a Verongia[2] species. The occurrence of each enantiomorph in different genera of the same class of invertebrates is most unusual. Both isomers are equally potent in vitro antibacterials which is also uncommon.

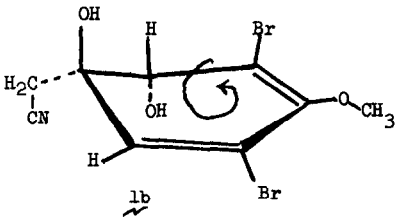
Spectroscopic examination of the (-)-isomer yielded: ms, (M^+), 336.896 ($C_9H_9NO_3Br_2$) ir (KBr) OH, (2.95μ); (C-CN), (4.42μ); nmr (see 1a) ($CDCl_3$/DMSO-d_6) δ6.34 (1H, C=C<u>H</u>, d, J=1.3 Hz); 4.27 (1H, C<u>H</u>OH, m; after exchange, d, J=1.3 Hz; 3.74 (3H,OC<u>H</u>$_3$); 2.80 (2H, C<u>H</u>$_2$) and a broad absorption at 5.5δ (2H, O<u>H</u>).

Treatment of the (-)- isomer in dilute aqueous alkali or 2N HCl provided complex mixtures; but in acetone with trifluoroacetic acid followed by tlc afforded a pure product whose physical characteristics (ir, uv, ms) were identical to those of 2 previously isolated and identified.[3] Examination of the preceding data established 1a as the structure. The inability of 1 to dehydrate easily to the aromatic system with alkali or acid indicated that the hydroxy groups were probably trans. Inspection of a Dreiding model with the hydroxyl groups in the

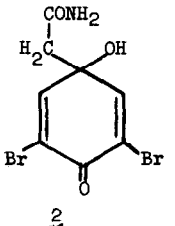
trans, quasi di-axial orientation showed the "W" relationship[4] for the olefinic proton and the methine proton which fits the small spin-coupling noted in the nmr data. Determination of the CD curve, [CD(MeOH), $\Delta\varepsilon_{282}$-15; uv (MeOH), λ 284 $_{nm}$, ε 5000] provided the absolute configuration shown in 1b. The chirality of this type of chromophore is well documented[5] and the strong negative Cotton effect indicated substantial left-handed helicity for the (-)-isomer; the angle of skew was in fact found to be 11.7°.[6]



1a



1b



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Both the (+) and the (-)-isomers of 1 have potency (MIC 20-100 γ/ml by agar dilution assay) for inhibiting Gram-negative and Gram-positive bacteria.[7] Neither isomer administered subcutaneously @ 128 mg/kg protected mice having any of four standard bacterial infections nor did either exhibit any in vitro antifungal activity.[7]

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References

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