Tetrahedron Letters,Vol.23,No.12,pp 1299-1300,1982 0040-4039/82/121299-02$03.00/0
Printed in Great Britain

THE RELATIVE STEREOCHEMISTRY OF HYPERFORIN - AN ANTIBIOTIC FROM HYPERICUM PERFORATUM L.

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Summary: The relative stereochemistry of hyperforin, an antibiotic from Hypericum perforatum has been determined by X-ray diffraction measurements.

Osborn[1] demonstrated as early as 1943 that extracts of a number of species of Hypericum (other than H. perforatum) were active against Staphylococcus aureus. In 1954 Neuwald and Hagenström[2] examined the antibacterial activity of Hypericum perforatum var. vulgare Neil and found the petroleum ether and acetone extracts of the flowering herb and dry fruits to be active against S. aureus. Gaind and Ganjoo[3] confirmed their results and also obtained evidence for the presence of two compounds, designated hyperesin 1 and 2, exhibiting activity against a number of Gram-positive organisms. Extracts of H. perforatum have been used clinically in Russia to treat infections[4], and have been patented in the United States as a food preservative.[5]

Russian workers described in 1971 the isolation and characterization of one active constituent, named hyperforin, from H. perforatum.[4] More recently, 1978, the same group suggested the structure of hyperforin without, however, elaborating on its stereochemistry.[6] The present preliminary note confirms the proposed structure and describes the relative stereochemistry of hyperforin.[7]

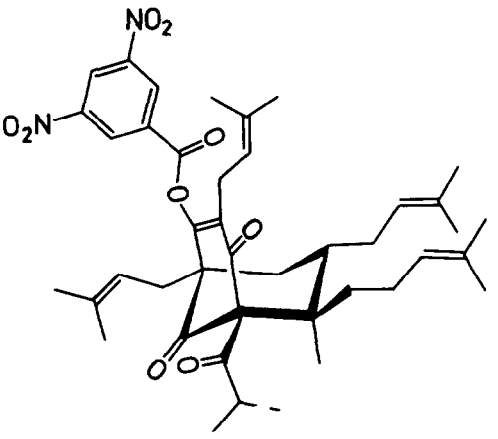

Fig. 1. Hyperforin 3,5-dinitrobenzoate ester

The structure, including relative stereochemistry, of hyperforin was established ependently on the basis of a detailed ^{1}H - and ^{13}C NMR study[8] and an X-ray diffraction lysis of the corresponding 3,5-dinitrobenzoate ester, $C_{42}H_{54}N_2O_9$, cf. Fig. 1.

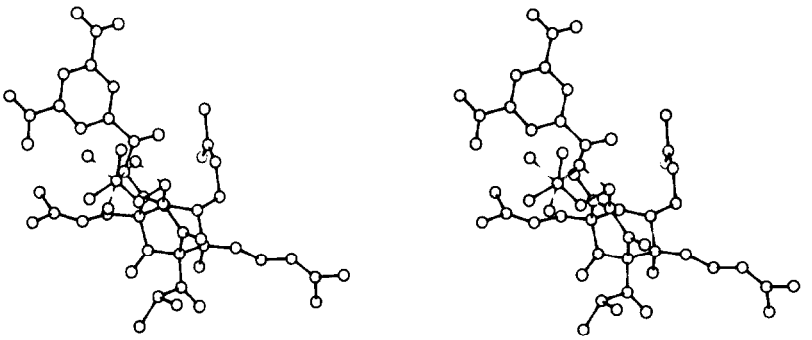

Fig. 2. Stereoscopic view of the 3,5-dinitrobenzoate ester of hyperforin.

A stereoscopic view of the 3,5-dinitrobenzoate ester of hyperforin is presented in Fig. 2. substituents attached to the bicyclic ringsystem are equatorial, except the methyl group h is axial. It may be noted that the vinylic $-CH_2-CH=C(CH_3)_2$ chain is disordered. Bond ances and angles are normal within estimated limits of error (0.01 Å and 1°).

The crystals are monoclinic with cell dimensions a = 10.450(4) Å, b = 12.613(5) Å, c = 95(6) Å, β = 118.75(3)°, space group $P2_1$, and Z = 2 (D_m = 1.18 gcm^{-3}, D_x = 1.21 gcm^{-3}). structure was solved by direct methods[9] and refined by full-matrix least squares technique n R-value of 6.3% (R_w = 4.3%) for 2043 reflections measured on an automatic four-circle ractometer at -150 °C. Detailed crystal structure information is available from Groth.

Work is in progress to elucidate the absolute configuration of hyperforin.

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he isolation of hyperforin from an acetone extract of H. perforatum and the synthesis of he corresponding 3,5-dinitrobenzoate ester will be described in detail later. The physical roperties of hyperforin and its derivative were in good agreement with those previously eported.[4,6]

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(Received in UK 26 January 1982)