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STUDIES OF SWEDISH MARINE ORGANISMS VII. A NOVEL BIOLOGICALLY ACTIVE INDOLE ALKALOID FROM THE SPONGE GEODIA BARETTI

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Abstract: From the sponge Geodia baretti a new indole alkaloid, with inhibiting activity on electrically induced contractions of an isolated Guinea-pig ileum, was isolated and assigned structure 1 based on spectral data.

The cold water sponge Geodia baretti (Bowerbank) Lamarck was collected in deep waters outside the northern Swedish west coast. Water- and petroleum ether extracts of this sponge show antibacterial and antiviral activity while the methanol extract strongly affected the isolated Guinea-pig ileum[1]. Our bioassay guided search[1,2] for pharmacologically active compounds has now led to the isolation of a new indole alkaloid, named barettin (1).

The methanol extract was chromatograhped on silica gel (flash, gradient $CHCl_3$ - MeOH) followed by preparative TLC (Silica, $CHCl_3$/MeOH 1:1) and HPLC (Lichrosorb, $CHCl_3$/MeOH/HOAc 70:30:1) which gave barettin (1) as a yellow solid (12 mg), mp 207-210°C, $[\alpha]_D$= -25° (c 3, MeOH).

High resolution MS indicated a molecular formula $C_{16}H_{14}BrN_3O_2$ and C_9H_7BrN for the fragment m/z 210/208 which suggested a bromo indole fragment. The pattern of the ^{1}H-NMR signals in aromatic region indicated that the bromine atom is attached in 5- or 6 position. By comparison with literature data of bromo indoles and particularly the recent discussion by Rinehart et al.[3] the bromine could be assigned to position 6. The UV spectrum (235, 294 and 340 nm) indicated a conjugated indole system which is emphasized by the IR data (1620 cm^{-1}, C=C) and a one proton singlet at 7.20 ppm in the ^{1}H-NMR.

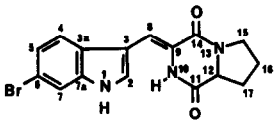
High resolution MS which gave a fragment at m/z 165 ($C_8H_9N_2O_2$) and IR data which showed NH bands at 3380 and 3190 cm^{-1} and amide carbonyl bands at 1680 and 1660 which together with the absence of amide II band suggest the presence of a diketopiperazine system connected to the bromo indole unit. The ^{13}C NMR confirms the presence of two carbonyl carbons (168.5 and 163.3 ppm). The high field part of this spectrum showed three methylene carbons (41.9, 32.5 and 25.0 ppm) and one methine carbon (56.4 ppm) along with the ^{1}NMR signals at 4.24, 3.25, 1.96 and 1.77 ppm supports the partial structure 2 and hence barettin will have structure 1. Whether 1 has E or Z configuration is unclear at present.

A compound with structure 2 has previously been isolated as a pure compound from the star-

fish Luidia clathrata[4] and diketopiperazine derivatives has been isolated from the marine sponge Tedania ignis[5].

The NMR data of the synthetic compound 3 (cyclo-L-prolyl-L-tryptophyl)[6,7] correlated nicely with barettin (1). Related compounds e.g. desoxybrevianamide E (4) have been isolated from fungi by Steyn[8].

Synthesis of barettin is underway which together with the pharmacological data will be published in a forthcoming paper.



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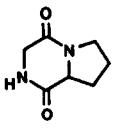

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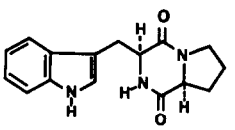

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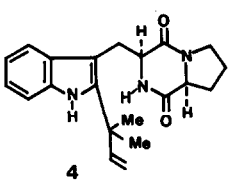

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6. P.G.Sammes and A.C.Weedon, J.C.S. Perkin I, 3048 (1979). ^{13}C NMR spectrum of the 2-methyl derivative of compound 3 was recieved from Prof. P.G.Sammes, Univ. of Leeds.
7. A sample of compound 3 was recieved from Prof. T.Hino, Chiba Univ.
8. P.S.Steyn, Tetrahedron, 29, 107 (1973).
9. Spectral data for barettin (1). UV (MeOH):λ_{max} 235 nm (ε 13000), sh 294 (5200), 340 (9700). IR (KBr):ν_{max} 3380, 3190, 1680, 1660, 1620, 1430, 1395, 1230 cm^{-1}. HREIMS m/z (rel.int.): 359.0280 (4) ($C_{16}H_{14}BrN_3O_2$=359.0270), 281(4), 211(14), 210(23), 209(17), 207.9759(22) (C_9H_6BrN=207.9763), 197(98), 194.9672(100) (C_8H_6BrN=194.9684), 165.0654(44) ($C_8H_9N_2O_2$= 165.0654), 150(22), 149(22), 129(24), 124(40), 123(27), 117(53), 116(56), 111(21), 109(21). ^{13}C NMR (CD_3OD): 168.5(C-11), 163.3(C-14), 158.6(C-9), 138.3(C-7a), 127.4(C-2), 124.5(C-5), 123.2(C-3a), 120.8(C-4), 117.6(C-6), 115.6(C-7), 111.0(C-8), 109.8(C-3), 56.4(C-12), 41.9 (C-15), 32.5(C-17), 25.0 (C-16) ppm. ^1H NMR (CD_3OD): 7.79(1H,s,H-2), 7.64(1H,d,J=1.3Hz,H-7), 7.61(1H,d,J=7.4Hz,H-4), 7.27(1H,dd,J=7.4,1.3Hz,H-5), 7.20(1H,s,H-8), 4.24(1H,m,H-12), 3.25 (2H,m,H-15), 1.96(2H,m,H-17), 1.77(2H,m,H-16) ppm. ^1H-NMR(DMSO-d6): 8.43(1H,bs,D_2O exch., N-H), 7.96(1H,s,H-2), 7.64(1H,d,J=1.7Hz,H-7), 7.61(1H,d,J=8.6Hz,H-4), 7.32(1H,bs,D_2O exch., N-H), 7.23(1H,dd,J=8.6,1.7Hz,H-5), 6.97(1H,s,H-8), 4.05(1H,m,H-12), 3.16(2H,m,H-15), 1.75 (2H,m,H-17), 1.55(2H,m,H-16) ppm (Both 90 MHz and 300 MHz instruments were used).

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