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DYSIDAMIDE, A NOVEL HEXACHLORO-METABOLITE FROM A RED SEA SPONGE DYSIDEA SP

T. Gebreyesus[a*], T Yosief[a], S Carmely[b] and Y Kashman[b*]
[a]Chemistry Department, AAU, P O Box 1176, Addis Ababa, Ethiopia
[b]Raymond and Beverly Sackler Faculty of Exact Sciences, School of Chemistry, Tel Aviv University, 69978 Tel Aviv, ISRAEL

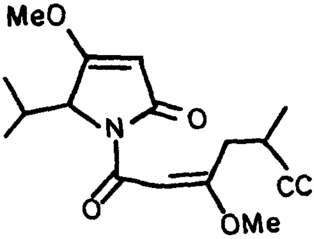
Abstract A hexachloro-metabolite, dysidamide (2) has been isolated from a Red Sea sponge Dysidea sp and its structure determined by MS, 1D and 2D NMR spectroscopy

The sponge genus Dysidea has been the source of diverse organic metabolites which have included bromophenols[1], sesquiterpenoids[2] and chlorinated compounds[3] exemplified by (1)[3a] We report the isolation of a hexachloro-metabolite (2), for which we propose the name dysidamide, from Dysidea sp

Dysidamide (2) was the major metabolite obtained from the chloroform fraction of the ethanol extract of the dried sponge collected near Massawa in the Red Sea Repeated column chromatography on silica gel (CHCl$_3$ pet.ether 1 1) afforded dysidamide (2) which crystallized as fine white needles (m p 123-124^{o}C, $[\alpha]_D^{21}$ = - 14 9^o (c = 1, CHCl$_3$) The molecular weight and the formula $C_{15}H_{21}Cl_6NO_3$ was established by chemical ionization mass spectrometry and ^{13}C-NMR

The IR spectrum (KBr) indicated the presence of hydroxl (3540, 3460cm^{-1}), carbonyl (1720cm^{-1}) and gem dimethyl (doublet at 1380cm^{-1}) groups The mass spectrum (CI-methane) showed a cluster of peaks around m/z 476 (82%, MH$^+$) with a pattern characteristic of hexachlorinated compounds[4] The major peaks at m/z 440 (100%, MH$^+$-HCl), 404 (5%, MH$^+$-2HCl), 358 (13%, MH$^+$-CCl$_3$), 316 (7%, MH$^+$-C$_4$H$_6$Cl$_3$), 288 (18%, MH$^+$-C$_5$H$_6$Cl$_3$O) 252 (13%, 288-HCl) and 128 (60%, $\underbrace{\text{CH(OH)CH=N}^+\text{HC(O)C}}\text{Me}_2$) could all be accounted for by structure (2)

The ^{13}C NMR spectrum showed two singlets at 106 97 and 105 86 ppm typical of the trichloromethyl grouping [3a] and two carbonyl signals at 179 84 and 172 39 ppm which agree



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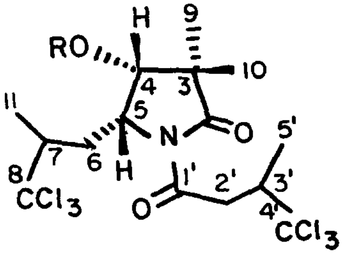
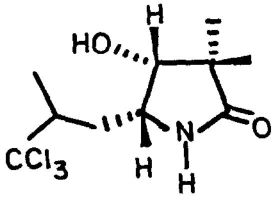


2 Dysidamide , R=H
4 R= Ac



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with an N-acylated-2pyrolidinone system[3a] The remainder of the ^{13}C NMR spectrum consisted of resonances (Table 1) which accounted for the remaining 11 carbon atoms of the molecule Valuable information was obtained from the 360 MHz ^1H NMR spectra of dysidamide (2), its acetate4[5] and the hydrolysis product 3 (Table 1) The structure was substantiated both by a C-H correlation (Table 1) and a H-H COSY experiments[6]. The later experiment enabled the assignment of all the protons in the molecule The relative stereochemistry at C-4 and C-5 was determined from NOE measurements on the acetate derivative, 4 (9% enhancement between H-4 & 5)

TABLE 1 ^1H & ^{13}C NMR Data and H-C Correlations of Compounds 2 & 3 in d_6-acetone

	2		3	
C-H#	δ_C	δ_H	δ_C	δ_H
1-H				6 80 brs (NH)
C2	179 84 s		179 69 s	
C3	46 55 s		44.20 s	
C4-H	72 50 d	4 24 dd(J=5 2,7 6 Hz) 4 90 d(J=5 2 Hz,OH)	76.29 d	3 94 brd(J=5 1Hz) 4 30 brs(OH)
C5-H	57 64 d	4 40 ddd(J=4 2,5 9,7 6 Hz)	51 54 d	3 77 ddd(J=10 2,5 1,3 6 Hz)
C6-H	33 70 t	2 30 ddd(J=4 2, 9 7, 14 1 Hz) 2 10 ddd(J=2 6,5 9, 14.1 Hz)	33.36 t	2 22 ddd(J=13 4, 10 2, 2.4 Hz) 1 60 ddd(J=13 4, 10 4, 3.6 Hz)
C7-H	54 27 d	3 07 ddq(J=2 6, 9 7, 6 4 Hz)	52 78 d	1 93 ddq(J=10 4, 2 4 6.4 Hz)
C8	106 97 s		106 43 s	
C9	19 50 q	1 14 s	17 60 q	0 96 s
C10	23 87 q	1.16 s	22 49 q	0.97 s
C11	16 65 q	1 37 d(J=6 4 Hz)	15.16 q	1.26 d(J=6 4 Hz)
C1'	172 39 s			
C2'-H	42 00 t	3 52 brd(J=16 9, 1 7 Hz) 3 20 dd(J=16 9, 9 5 Hz)		
C3'-H	51 34 d	3 23 ddq(J=1 7, 9 5, 6 3 Hz)		
C4'	105 86 s			
C5'-H	17 00 q	1 33 d(J=6 3 Hz)		

C-H Correlations C-No/H-No's 2/4, 9 & 10, 3/9, 10, 5 & OH, 4/6, 9, 10, 5/OH; 6/11, 7/5; 8/6, 11, 9/10, 4, 10/9, 11/6, 6 , 1'/2',2', 2'/5', 3'/2',5';4'/2',5',5'/2'

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5 Compound 4. δ_H ($CDCl_3$,360MHz) 5 19d(H-4,J=7 4), 4 57ddd(H-5,J=7.0,7 4,2 3), 3 61dd(H-2',J=18 1,2.3), 3 32ddq(H-3',J=2 3,9 4,6 4), 3 17dd(H'-2',J=18 1,9 4), 2 99ddq(H-7, J=2.6,9.8,6.4), 2 25ddd(H-6,J=14.5,6.1,2.3), 2.20s(AcO-4), 1.86ddd(H'-6,J=14.5,9.8,4.0) 1 39d(Me-5',J=6 4), 1.32d(Me-11,J=6.4), 1 28s(Me-10), 1.24s(Me-9).

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