Tetrahedron Letters No. 36, pp 3183 - 3186, 1977. Pergamon Press. Printed in Great Britain.

A NOVEL HEXACHLORO-METABOLITE FROM THE SPONGE DYSIDEA HERBACEA

R.Kazlauskas, R.O.Lidgard and R.J.Wells
Roche Research Institute of Marine Pharmacology, P.O.Box 255,
Dee Why, N.S.W. Australia 2099

W.Vetter
Department F/ZFE, F.Hoffmann-La Roche, Basel, Switzerland

(Received in UK 28 June 1977; accepted for publication 14 July 1977)

The sponge *Dysidea herbacea* has been the subject of previous studies[1,2]. A collection of *D. herbacea* from the Caroline Islands in the Pacific Ocean yielded a series of polybrominated biphenyl ethers exemplified by (1)[1] whereas material collected on the Australian Great Barrier Reef east of Townsville gave the novel tetramic acid derivative (2)[2], the first example of a naturally occurring compound containing a trichloromethyl group.

A small sample of *D. herbacea* collected north-east of Cooktown on the Great Barrier Reef yielded two major fractions. A mixture of penta- and hexabromo-biphenyl ethers, related to the compound (1) previously reported by Sharma, Vig and Burkholder[1], was accompanied by the hexachloro-metabolite (3), for which we propose the name dysidenin. This was the major metabolite isolated from the dichloromethane extract of the freeze-dried organism.

Dysidenin (3) crystallised from hexane as fine colourless needles mp 98-99° $[\alpha]_D^{21}$ -98° (c=0.5, $CHCl_3$). The molecular weight and the formula $C_{17}H_{23}Cl_6N_3O_2S$ were established by elemental analysis and by chemical ionization and high resolution mass spectrometry. Reduction of (3) with zinc-acetic acid gave the dechlorinated compound (4), $C_{17}H_{29}N_3O_2S$ (by high resolution m.s.), in good yield.

The ^{13}C n.m.r. of (3) showed resonances at 171.9, 171.2 and 168.2 p.p.m. (s, C=O or C = N) and two resonances at 142.3 (d,d;J=185.5, 5.9 Hz) and 118.9 p.p.m. (d,d;J=189.4, 15.6 Hz). Two singlets at 105.5 and 105.1 p.p.m. could be assigned to two trichloromethyl groups. High field resonances occurred at 54.0 (d), 51.9 (d), 51.4 (d), 47.3 (d), 37.4 (t), 31.0 (t), 30.8 (q), 21.8 (q), 17.3 (q) and 16.2 (q) which accounted for all 17 carbon atoms of the molecule.

Valuable information was obtained from the 100 MHz ^1H n.m.r. spectra of (3) and (4) which allowed the definition of several structural units of the molecules. Table 1 shows the resonances, coupling constants and assignments obtained in three solvent systems for (3) and in CCl_4 for (4). Extensive decoupling studies and chemical shift values suggested the partial structural units (5), (6) and (7).

The presence of a 2-substituted thiazole ring system in (3) was supported by the u.v. spectrum (λ_{max}(MeOH)240 nm, log ε 3.6), the positions and coupling constants of the low

field doublets in the $CDCl_3$ and $CDCl_3$ + CF_3COOD ^1H n.m.r. spectra (Table 1) and the positions of the ^{13}C n.m.r. low field resonances at 168.2 (s), 142.3 (d) and 118.9 (d) p.p.m. These ^{13}C resonances were very similar to those obtained for 2-acetoxymethylthiazole and 2-hydroxymethylthiazole which also showed the same ^1H n.m.r. coupling constants[3].

Reduction of (3) by zinc-acetic acid gave (4) which retained the same u.v. and low field ^1H n.m.r. characteristics (Table 1) of the parent compound (3). The molecular formula of (4) and its ^1H and ^{13}C n.m.r. spectra could be rationalised as the reduction of the two trichloromethyl groups in (3) to two methyl groups in (4), which otherwise retained all other structural features intact.

The structure of (3), assigned by combination of evidence from ^{13}C and ^1H n.m.r., u.v. and i.r. spectra (γ_{max} (KBr) 3270, 1680, 1620, 1540), was substantiated by high resolution mass spectra of (3), (4) and (8), (prepared by reduction of (3) with zinc - CH_3COOD). Fragment ions (Table 2) of all three compounds were fully consistent with those expected for N-acylated α-amino acids with an amino-alkyl-thiazole residue attached at the carboxyl group and established the structure of (3).

ACKNOWLEDGEMENTS

We thank Professor P. Bergquist for sponge identification and Drs. P. Schüdel and K. von Berlepsch for gifts of 2-acetoxymethylthiazole and 2-hydroxymethylthiazole.

REFERENCES

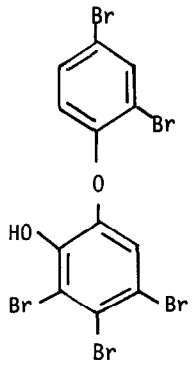
1 (a). G.M. Sharma, B. Vig and P.R. Burkholder. *Food-drugs from the sea, Proc.,* Marine Technol. Soc., 307 (1969).

(b). G.M. Sharma and B. Vig. *Tetrahedron Letters,* 1715 (1972).

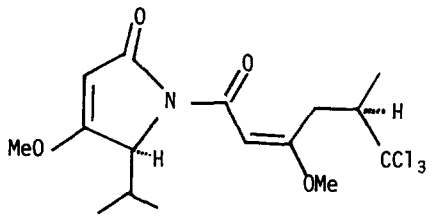
2. W. Hofheinz and W.E. Oberhänsli, *Helv.Chim.Acta,* 60, 660 (1976).

3. 2-Acetoxymethylthiazole:- ^1H n.m.r. ($CDCl_3$) δ7.70 (d,J=3Hz), 7.30 (d,J=3 Hz). ^{13}C n.m.r. 142.8 p.p.m. (d,d;J=187.5, 6.8 Hz), 120.2 p.p.m. (d,d;J=188.9, 14.6 Hz).
2-Hydroxymethylthiazole:- ^1H n.m.r. ($CDCl_3$) 7.62 (d,J=3.5 Hz), 7.22 (d,J=3.5 Hz). ^{13}C n.m.r. 142.8 p.p.m. (d,d;J=186.5, 5.9 Hz), 119.1 p.p.m. (d,d;J=189.9, 15.6 Hz).

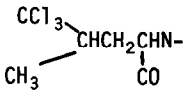
4. Ratio of $CDCl_3$/TFA-d_1 = 9/1.



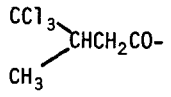
(1)



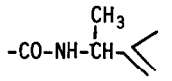
(2)



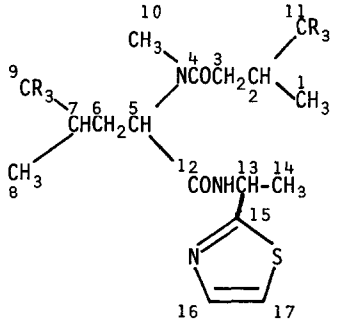
(5)



(6)



(7)



(3) R = Cl

(4) R = H

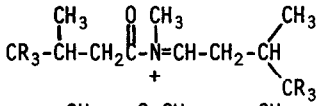
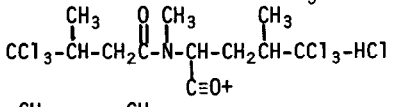
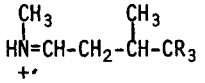
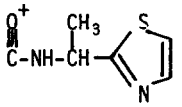
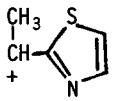
(8) R = D

TABLE 1

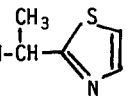
C-H	(3)-$CDCl_3$	(3)-C_6D_6	(3)$CDCl_3$/TFA-d_1	(4)-CCl_4	Multiplicity
C1-H	1.36*	1.24	1.28 or 1.32	0.92	3H, d, J = 7Hz
C2-H	3.3	3.40	3.2		1H, m
C3-H_a	2.5	2.2	2.5-3.0	2.10	1H, m
C3-H_b		2.4			1H, m
C5-H	5.27	5.42	5.24	5.08	1H, d,d,J = 4,11Hz
C6-H_a	3.10	3.01	2.70	1.50	1H, m
C6-H_b	1.94	2.2	1.94		1H, m
C7-H	2.20	2.0	2.2		1H, m
C8-H	1.33*	1.24	1.28 or 1.32	0.92	3H, d, J = 7Hz
C10-H	3.04	2.61	3.12	2.88	3H, s
C13-H	5.2	5.32	5.60	5.0	1H, d of q, J= 7,8Hz
C14-H	1.56	1.40	1.74	1.44	3H, d, J = 7Hz
C16-H	7.60	7.35	8.04	7.50	1H, d, J = 3.5Hz
C17-H	7.26	6.54	7.78	7.02	1H, d, 3.5Hz
-NH	6.86	7.21	-	7.12	1H, bd, J = 8Hz

* Tentative assignments.

TABLE 2

(3) R = Cl	(4) R = H	(8) R = D		
543 (0.2)	339*(2)	345	$C_{17}H_{23}N_3O_2SR_6$	M^+
508*(8)	-	-	$C_{17}H_{23}N_3O_2SCl_5$	$M^+ - Cl$
-	283*(3)	286	$C_{13}H_{18}N_3O_2SR_3$	$M^+ - CR_3-\overset{CH_3}{\overset{\vert}{C}}=CH_2$
388*(19)	184*(46)	190	$C_{11}H_{16}NOR_6$	
380*(7)+		-	$C_{12}H_{15}NO_2R_5$	
202*(100)	100*(100)	103	$C_6H_{11}NR_3$	
155*(12)	155*(4)	155	$C_6H_7N_2OS$	
112*(56)	112*(53)	112	C_5H_6NS	

*Mass matched by high resolution m.s.

+212 (MH^+ - ) is the major fragment ion in the CI(CH_4) mass spectrum of (4).