Tetrahedron Letters,Vol.28,No.40,pp 4633-4636,1987 0040-4039/87 $3.00 + .00
Printed in Great Britain Pergamon Journals Ltd.

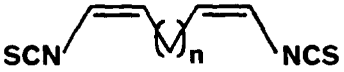
LONG-CHAIN α,ω-BISISOTHIOCYANATES FROM A MARINE SPONGE

Peter Karuso and Paul J. Scheuer*
Department of Chemistry, University of Hawaii
at Manoa, Honolulu, HI 96822

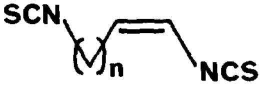
Summary. -- Eighteen long-chain aliphatic α,ω-bisisothiocyanates were isolated from a marine sponge, *Pseudaxinyssa* sp. from Fiji. Eight compounds are di-, ten are monolefinic. Three additional constituents are α-isothiocyano-ω-formyl compounds.

Isothiocyanates are well-known natural products which occur as glycosinolates in a few families of terrestrial plants, principally the Cruciferae, and are known as mustard oils.[1] At basic pH's the glycosinolates decompose into isothiocyanates. Marine-derived isothiocyanates have been isolated from sponges, where they have been found as sesqui- or diterpenes, almost always accompanied by isocyanides and formamides.[2]

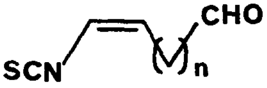
From a Fijian sponge, *Pseudaxinyssa* sp., we have isolated a series of aliphatic α,ω-bisisothiocyanates unaccompanied by isocyano or formamido analogs. Absence of isocyano analogs, which are the biosynthetic precursors of isothiocyanates in sponge sesquiterpenes[3] suggests a different biogenesis.



1 n = 14
2 n = 8
3 n = 9
4 n = 10
5 n = 11
6 n = 12
7 n = 13
8 n = 14



9 n = 16
10 n = 9
11 n = 10
12 n = 11
13 n = 12
14 n = 13
15 n = 14
16 n = 15
17 n = 17
18 n = 18



19 n = 15
20 n = 9
21 n = 16

Pseudaxinyssa sp. (603 g, frozen), which is a red encrusting sponge that was collected outside Suva harbor in June, 1983, by SCUBA at -8 m, was blended thrice with ethanol. The crude extract showed prominent isothiocyanate absorption in its IR spectrum. The combined filtrates were concentrated and subjected to solvent partition.[4] The hexane portion was separated first on silica gel (BioSil A, hexane to hexane/chloroform, 95:5), then on reversed phase HPLC (LiChrosorb 10 RP-18, MeCN). When refrigerated, the major constituent (55 mg) forms colorless needles from acetonitrile, mp ~ 15°C. Its spectral properties,[5] particularly IR absorption at 2150 cm^{-1}, UV maxima at 221 (70,000) and 265 (12,200) nm, two olefinic proton signals integrating for two protons each (δ 5.85, dt, *J* = 7.6, 1.5 Hz and δ 5.46, q, *J* = 7.6 Hz) coupled to each other and to four allylic protons at δ 2.22 (dq, *J* = 7.6, 1.5 Hz), and a composition of $C_{20}H_{32}N_2S_2$ fully described (*Z*,*Z*)-1,18-diisothiocyanooctadeca-1,17-diene (**1**). Lesser amounts of all C_{14}-C_{21} homologs, in the range of 0.5-20 mg, were separated and their structures determined by comparison of their spectral data with those of **1**. Table 1 summarizes data for the diolefinic homologs (**1**-**8**).

A series of bisisothiocyanate monolefins was eluted from silica gel following the dienes. The most abundant (21 mg) representative of this group was the C_{20} homolog (*Z*)-1,18-diisothiocyanooctadec-1-ene (**9**).[6] The diagnostic feature of its ^1H NMR spectrum is a two-proton triplet at δ 3.52 coupled to methylene protons at δ 1.7 and assigned to the methylene group vicinal to the isothiocyano function. The data for the monolefines (**9**-**18**) are shown in Table 1. The chloroform portion from the solvent partition after silica gel chromatography yielded in addition to a mixture of 5α,8α-epidioxysterols further isothiocyanates which could be separated by reversed phase HPLC (Whatman Magnum 9 ODS-3, MeCN/H_2O, 95:5). Small amounts (2.5 mg) of a C_{18} monolefinic homolog (**15**) were followed by three aliphatic aldehydes terminating in a vinylisothiocyano function. The major constituent (7 mg) was 18-isothiocyanooctadec(*Z*)-18-enal (**19**). An IR band at 1730 cm^{-1} coupled with NMR signals at δ 9.79 (1H, t, *J* = 1.9 Hz) and at δ 202.8 revealed the aldehyde function. Pertinent data are summarized in Table 1.

Co-occurrence of mixed isothiocyano and aldehyde functions points to biogenetic similarity with the terrestrial glycosinolates, whose biosynthesis proceeds by chain elongation of methionine.[8] The biogenetic pathway of the marine isothiocyanates is not known, but presence in one animal of non-terpenoid aliphatic bisisothiocyanates and monoaldehydic isothiocyanates represents a significant departure from previously known secondary sponge metabolites. A recent report[9,10] that alkylene bisisothiocyanates selectively destroy spiracle-forming cells in *Manduca sexta* makes these compounds potential insect growth regulators.

Acknowledgment. We thank Dr. Deborah Roll for collecting the sponge, Professor P. Bergquist for identification, and Mr. Mike Burger for determining the mass spectra. We are grateful for financial support from the National Science Foundation and the University of Hawaii Sea Grant College Program under Institutional Grant NA81AA-D-0070 from NOAA, Office of Sea Grant, U.S. Department of Commerce.

Table 1.

Yields, Retention Times, Compositions of Aliphatic Isothiocyanates from *Pseudaxinyssa* sp.

Compound No.	Yield, mg	R.T., min.	MW	Composition[a]
1	55	31.6[b]	364	$C_{20}H_{32}N_2S_2$
2	20	10.8[b]	280	$C_{14}H_{20}N_2S_2$
3	16	12.6[b]	294	$C_{15}H_{22}N_2S_2$
4	5	14.8[b]	308	$C_{16}H_{24}N_2S_2$
5	1	17.4[b]	322	$C_{17}H_{26}N_2S_2$
6	6	19.2[b]	336	$C_{18}H_{28}N_2S_2$
7	7	25.8[b]	350	$C_{19}H_{30}N_2S_2$
8	0.5	38.8[b]	378	$C_{21}H_{34}N_2S_2$
9	21	37.2[c]	366	$C_{20}H_{34}N_2S_2$
10	7	17.2[c]	296	$C_{15}H_{24}N_2S_2$
11	11	19.6[c]	310	$C_{16}H_{26}N_2S_2$
12	1	22.4[c]	324	$C_{17}H_{28}N_2S_2$
13	2	26.4[c]	338	$C_{18}H_{30}N_2S_2$
14	2	27.2[c]	352	$C_{19}H_{32}N_2S_2$
15	9	17.2[c]	282	$C_{14}H_{22}N_2S_2$
16	1	41.2[c]	380	$C_{21}H_{36}N_2S_2$
17	0.5	43.2[c]	394	$C_{22}H_{38}N_2S_2$
18	0.5	14.4[c]	268	$C_{13}H_{20}N_2S_2$
19	7	24.8[d]	323	$C_{19}H_{33}NOS$
20	4	12.0[d]	239	$C_{13}H_{21}NOS$
21	1	32.9[d]	337	$C_{20}H_{35}NOS$

[a] From high resolution EIMS

[b] LiChrosorb 10 RP18, 25x0.9 cm, 100% MeCN

[c] Whatman ODS-3 Magnum, 50x0.9 cm, 100% MeCN

[d] Whatman ODS-3 Magnum, 50x0.9 cm, acetonitrile/water, 95:5

References and Notes

(1) Kjaer, A. Fortschr. Chem. Org. Naturstoffe 1960, **18**, 122-176.

(2) Burreson, B. J.; Christophersen, C.; Scheuer, P. J. Tetrahedron 1975, **31**, 2015-2018.

(3) Hagadone, M. R.; Scheuer, P. J.; Holm, A. J. Am. Chem. Soc. 1984, **106**, 2447-2448.

(4) Kupchan, S. M.; Britton, R. W.; Ziegler, M. F.; Sigel, C. W. J. Org. Chem. 1973, **38**, 178-179.

(5) Cpd 1 -- uv: λ_{max}^{hex} 221 (70,000), 265 (12,200) nm; IR: $\nu_{max}^{CHCl_3}$ 3010, 2926, 2854, 2150, 1633, 1476, 1388, 1300, 1102, 809, 782, 772, 745 cm^{-1}; ^{1}H NMR (CDCl$_3$): δ 5.85 (2H, dt, J = 7.6, 1.5 Hz), 5.46 (2H, q, J = 7.6 Hz), 2.22 (4H, dq q, J = 7.6, 1.5 Hz), 1.4 (4H, br q), 1.3 (20H, s); ^{13}C NMR (CDCl$_3$): δ 134.0, 133.2, 115.0, 29.6, 29.5, 29.4, 29.1, 28.6, 27.3(2); MS: M$^+$ m/z 364.20308; C$_{20}$H$_{32}$N$_2$S$_2$ requires 364.20070; M$^+$-NCS m/z 306.22556; C$_{19}$H$_{32}$NS requires 306.22555; m/z 364 (M$^+$ 39%), 331(40), 306(100), 272(12), 115(11), 112(24), 98(90), 95(20), 85(22), 81(27), 69(23), 55(38).

(6) Cpd 9 -- UV: λ_{max}^{hex} 212 (69,500), 262 sh (12,300), 270 (13,400) nm; IR: $\nu_{max}^{CCl_4}$ 2928, 2855, 2087, 1470, 1388, 1345 cm^{-1}; ^{1}H NMR (CDCl$_3$): δ 5.85 (1H, dt, J = 7.6, 1.5 Hz), 5.46 (1H, q, J = 7.6 Hz), 3.52 (2H, t, J = 6.6 Hz), 2.22 (2H, dq, J = 7.6, 1.5 Hz), 1.7 (2H m), 1.4 (4H m), 1.3 (12H, br s); ^{13}C NMR (CDCl$_3$): δ 132.9, 115.3, 45.2, 30.1, 29.3(2), 29.2, 29.0, 28.8, 28.6, 27.3, 26.6, NCS not observed). MS: M$^+$ m/z 282.1213; C$_{14}$H$_{22}$N$_2$S$_2$ requires 282.1224; m/z 282 (M$^+$ 17%), 249 (39), 226 (11), 225 (33), 224 (100), 112 (47), 99 (68), 98 (72), 69 (50).

(7) Cpd 19 -- UV: λ_{max}^{hex} 211 (39,400), 263 sh (6,400), 270 (7,200) nm; IR: $\nu_{max}^{CCl_4}$ 2928, 2855, 2085, 1730, 1634, 1464, 1387 cm^{-1}; ^{1}H NMR (CDCl$_3$): δ 9.79 (1H, t, J = 1.9 Hz), 5.85 (1H, dt, J = 7.6, 1.5 Hz), 5.46 (1H, q, J = 7.6 Hz), 2.43 (2H, dt, J = 7.3, 1.5 Hz), 2.22 (2H, dq, J = 7.6, 1.5 Hz), 1.63 (2H, m), 1.4 (2H, br q), 1.3 (22H, s); ^{13}C NMR (CDCl$_3$): δ 202.8, 134.0, 133.2, 115.1, 43.9, 29.6(8), 29.4, 29.3, 29.2, 28.6, 27.3, 22.1. MS: M$^+$ m/z 323.2269; C$_{19}$H$_{33}$NOS requires 323.2283; M$^+$-SH, m/z 290.2489; C$_{19}$H$_{32}$NO requires 290.2484; m/z 323 (M$^+$ 70%), 295 (14), 290 (50), 280 (3), 262 (48), 250 (40), 222 (14), 99 (85), 83 (80), 43 (100).

(8) Dewick, P. M. Nat. Prod. Rep. 1984, **1**, 545-549.

(9) Matolcsy, G.; Ujvary, I.; Riddiford, L. M.; Hiruma, K. Z. Naturforsch. 1986, **41c**, 1069-1072.

(10) We are indebted to Professor Glenn D. Prestwich for bringing this paper to our attention prior to publication.

(Received in USA 1 July 1987)