CHEMISTRY LETTERS, pp. 803-804, 1988.

Two Bromopyrroles from a Marine Sponge *Agelas* sp.

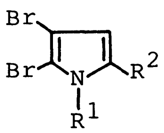
Haruhiko TADA* and Takehiko TOZYO
Shionogi Research Laboratories, Shionogi & Co., Ltd., Fukushima-ku, Osaka 553

Extremely unstable bromopyrrole metabolites were isolated from a sponge *Agelas* sp. and characterized as 2,3-dibromopyrrole and 2,3-dibromo-5-methoxymethylpyrrole.

Many bromopyrrole metabolites have been isolated from marine animals.[1)] In this report, we describe the isolation and characterization of two bromopyrroles which are extremely unstable.

The frozen sponge material from *Agelas* sp. was directly immersed in dichloromethane for simultaneous defrosting and extraction. Chromatography of the separated organic layer yielded 2,3-dibromopyrrole (1) and 2,3-dibromo-5-methoxymethylpyrrole (2a) from the non-polar fraction, and five previously known 2,3-dibromopyrroles (3a, 3b, 4a, 4b, and 5) from the polar fraction.

The first bromopyrrole 1 was obtained from a SiO_2 column eluted by hexane. In the hexane solution 1 was relatively stable, but when the solvent was removed the residue immediately turned into an intractable black mass. In order to measure the spectra of the eluate, the hexane solution was exchanged for deuteriochloroform or deuteriomethanol-d_4 solution by repeated addition and evaporation. The MS [negative SIMS; m/z 226, 224, 222 (rel. int. 1:2:1)] and the IR spectrum [$CHCl_3$; 3460 and 3230 cm^{-1} (NH)] together with the NMR spectra (Table 1) suggested the structure to be 1. The arrangement of two bromine atoms was determined based on the following considerations: 1) as the molecule is not symmetrical (the two protons are not equivalent), 2,5- and 3,4- arrangements can be eliminated 2) all the dibromopyrrole metabolites hitherto isolated were 2,3-dibromo derivatives 3) $^3J_{H,H}$ (3 Hz) is a reasonable value for $^3J_{2,3}$ (2.6 Hz) but not for $^4J_{2,4}$ (1.3 Hz) of pyrrole[2)] 4) NOE's were observed at [H-5]→H-4 (4.1%) and [H-4]→H-5 (5.8%).



	R^1	R^2
1	H	H
2a	H	CH_2OMe
2b	Me	CH_2OMe
3a	H	COOH
3b	Me	COOH
4a	H	COOMe
4b	Me	COOMe
5	H	$CONH_2$

The second new bromopyrrole 2a was obtained from SiO_2 chromatography with elution by hexane-dichloromethane (9:1). The hexane solution slowly (rapidly in the CH_2Cl_2 or $CHCl_3$ solution) turned red-violet at room temperature. Only the dilute methanol solution covered with argon gas was relatively stable and could be stored in a refrigerator. After repeated solvent exchange procedure, spectral data of 2 were obtained. The MS [negative SIMS; m/z 270, 268, 266 (rel. int. 1:2:1)] coupled with NMR spectra (Table 1) led to the formula 2a. Although six isomers are possible for a compound with

Table 1. NMR Data of Bromopyrroles and Pyrrole

	$\underline{1}$	$\underline{2a}$	$\underline{2b}$	Pyrrole[2]
(^1H-NMR)				
H-4	6.70 (t)	6.15 (d)	6.21	6.68
H-5	6.20 (t)	---	---	6.22
HN	9.35 (br)	8.86 (br)	---	ca. 8.0
NMe	---	---	3.58	
$CH_2O\underline{Me}$		3.32 (s)	3.26 (s)	
$\underline{CH_2}OMe$		4.33 (s)	4.32 (s)	
(^{13}C-NMR)				
C-2	100.1	100.3	105.6	117.9
C-3	98.4	98.2	96.7	107.9
C-4	112.5 (178 Hz)[a]	111.8 (178 Hz)[a]	112.7 (178 Hz)[a]	107.9 (171 Hz)[a]
C-5	120.8 (188 Hz)[a]	129.9	130.3	117.9 (184 Hz)[a]
NMe	---	---	33.5	
$CH_2O\underline{Me}$		57.5	57.1	
$\underline{CH_2}OMe$		66.7	66.1	

a) $^1\underline{J}_{C,H}$ value.

two bromine atoms and a methoxymethyl group on a pyrrole ring, three of the six could be eliminated because a ^{13}C-NMR chemical shift value (δ 111.8) with a $\underline{J}$-value ($^1\underline{J}_{C,H}$ 178 Hz) is assignable to C-4. Of the remaining three possible formulas, 2a was the most plausible because almost all the related metabolites, e.g. 3a to 5, had two bromine atoms at C-2 and C-3. Synthetic trials starting from methyl pyrrole-2-carboxylate to obtain 2a or 2b were unsuccessful; however, $LiAlH_4$ reduction of 4b followed by methylation (MeI/MeONa-MeOH) furnished 2b, which proved to be identical with the methylated product (CH_2N_2/MeOH) of 2a.

The isolated dibromopyrroles 1 and 2a are the first occurrence from nature, though 1 has been prepared for an electrochemical study of polypyrroles.[3)]

We thank Dr. T. Hoshino of Hiroshima University for identification of the sponge.

References

1) C. Christophersen, "Marine Alkaloids," in "The Alkaloids," ed by A. Brossi, Academic Press Inc., London (1985), Vol. 24, pp. 25-111; W. Fenical, "Marine Alkaloids and Related Compounds," in "Alkaloids: Chemical and Biological Perspectives," ed by S. W. Pelletier, John Wiley & Sons, N.Y. (1986), Vol. 4, pp. 275-330.

2) W. Brügel, "Handbook of NMR Spectral Parameters," Heyden & Son, Ltd., London (1979), Vol. 2, p. 602.

3) P. Audebert and G. Bidan, Synthetic Metals, 15, 9 (1986); Chem. Abstr., 105, 134643g (1986).

(Received February 6, 1988)