

A β -PHENYLETHYLAMINE-DERIVED POSSIBLE BIOSYNTHETIC PRECURSOR TO THE AMATHAMIDES, ALKALOIDS FROM THE BRYOZOAN *AMATHIA WILSONI*

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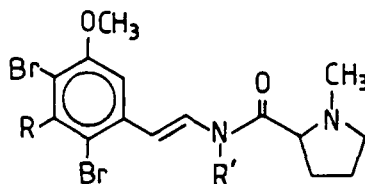
ABSTRACT.—The bryozoan *Amathia wilsoni* has yielded 2-(2,4-dibromo-5-methoxyphenyl)-ethanamine as well as the previously described amathamide alkaloids. Structural similarities suggest that the former may well be a biosynthetic precursor to the latter.

Bryozoans are colonial invertebrates, usually of marine origin. *Amathia wilsoni* Kirkpatrick, a reasonably common foliose bryozoan from Tasmanian coastal waters, has previously been shown to contain a series of brominated alkaloids 1–6, amathamides A–F (1,2). Intra-specific variability of these metabolites was measured; there was no significant variation in the alkaloid content of different colonies of the bryozoan at the same location, but differences did occur between samples of the bryozoan that had been obtained from different collection sites. It was suggested that the amathamides were biosynthesized from proline and phenylalanine.

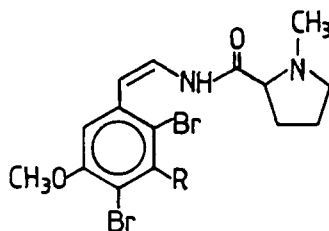
Amathamide F [5] had been earlier reported to exhibit anomalous nmr spectroscopic behavior (2). A larger scale re-collection of *A. wilsoni* from the site known to contain bryozoans enriched with amathamide F has confirmed that the alkaloid content has remained essentially unchanged. The sample of amathamide F obtained on this occasion showed none of the anomalous nmr signals which, despite claims to the contrary, must therefore have been due to an impurity (amathamide B).

A basic compound that was more polar than any of the amathamides was also isolated in low yield. Ms showed that the molecular formula was $C_9H_{11}Br_2NO$. The usually strong peak at m/z 84, which was present in the

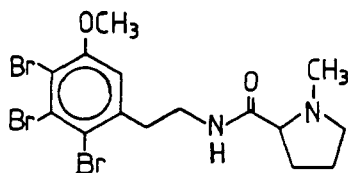
amathamides and is characteristic of *N*-methylpyrrolidines, was absent. The downfield regions of both the ¹H- and ¹³C-nmr spectra were very similar to those of the amathamides, especially amathamides A [1] and B [4]; a dibromomethoxyphenyl moiety having two protons para to each other was therefore present. The remaining nmr signals were due to two adjacent methylene groups, one of which was attached to the



- 1 R=H, R'=H
- 2 R=Br, R'=Me
- 3 R=Br, R'=H



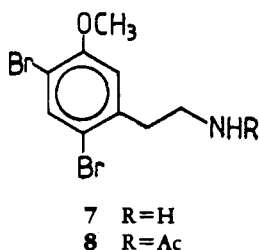
- 4 R=H
- 5 R=Br



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aromatic moiety and the other to an amino group.

Because the ^1H -nmr chemical shifts of the methylene groups were very similar to each other, the amine was acetylated before any correlation spectroscopy was attempted. An ^1H - ^1H COSY spectrum of the acetyl derivative **8** established the connectivity between the two portions of the molecule showing that the amine was the previously undescribed compound 2-(2,4-dibromo-5-methoxyphenyl)ethanamine [7]. The



strong cross peaks that were observed in the 2D spectrum are shown in Figure 1. The amine **7** is unlikely to be an artifact because it was subsequently detected in the initial CH_2Cl_2 extract of the bryozoan by both tlc and gc. This would appear to be the first report of a naturally occurring brominated β -phenylethylamine (3).

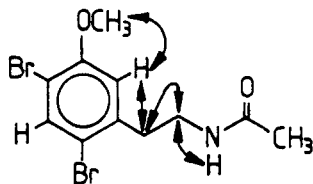


FIGURE 1. Connectivity for compound **8** established by ^1H - ^1H COSY cross peaks.

The isolation of this substituted β -phenylethylamine suggests that the amathamides are biosynthesized from phenylalanine by a series of aromatic substitution reactions and a decarboxylation giving the amine, which is then reacted with a proline derivative to form

saturated amathamides such as **6**, which are then dehydrogenated to give the unsaturated amathamides **1-5**.

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—Spectrometers, procedures, and material used were as described previously (2). A voucher specimen of *A. wilsoni* has been lodged in the marine specimen collection of the Chemistry Department, University of Tasmania.

EXTRACTION AND PURIFICATION.—Freeze-dried *A. wilsoni* (446 g), collected at Clyde Island ($43^\circ 0.4' \text{ S}$, $147^\circ 58.1' \text{ E}$) in January 1988, was extracted in the usual way (2) to give five previously known alkaloids, amathamide A [**1**] (6 mg, 0.001%), amathamide B [**4**] (43 mg, 0.010%), amathamide D [**6**] (58 mg, 0.013%), amathamide E [**3**] (54 mg, 0.012%), and amathamide F [**5**] (172 mg, 0.039%), and 2-(2,4-dibromo-5-methoxyphenyl)ethanamine [7] (30 mg, 0.007%) as a colorless oil: R_f 0.08 [silica, CH_2Cl_2 -MeOH (9:1)].

2-(2,4-DIBROMO-5-METHOXYPHENYL)ETHANAMINE [7].—Found (NH_3 cims) $[\text{M} + \text{H}]^+$ 307.9290, $\text{C}_9\text{H}_{12}^{79}\text{Br}_2\text{NO}$ requires 307.9284; ^1H nmr δ 1.8 variable (bd s, 2, NH_2), 2.87 (t, 2, $J = 6.09$ Hz, H-2), 2.98 (br s, 2, H-1), 3.88 (s, 3, OMe), 6.79 (s, 1, H-6'), 7.70 (s, 1, H-3'); ^{13}C nmr 2 (C_6D_6) δ 41.1 (CH_2 , C-2), 42.7 (CH_2 , C-1), 56.3 (Me, OMe), 111.2 (C, C-4'), 114.9 (CH, C-6'), 115.8 (CH, C-2'), 137.1 (CH, C-3'), 140.6 (C, C-1'), 156.3 (Me, C-5'); ir ν max 3365 (w), 3273 (w), 3007 (w), 2932 (m), 2849 (m), 1583 (m), 1562 (w), 1474 (s), 1441 (m), 1371 (s), 1304 (w), 1252 (s), 1170 (w), 1055 (s), 877 (w) cm^{-1} ; eims m/z (%) 278 $^{79}\text{Br}_2$ (16), 277 $^{79}\text{Br}_2$ (7), 263 $^{79}\text{Br}_2$ (6), 247 $^{79}\text{Br}_2$ (4), 229 ^{79}Br (20), 228 ^{79}Br (100).

ACETYLATION.—2-(2,4-Dibromo-5-methoxyphenyl)ethanamine (2.98 mg) was reacted with Ac_2O and pyridine at room temperature in the usual manner (4) and the product purified by SiO_2 chromatography to yield *N*-acetyl-2-(2,4-dibromo-5-methoxyphenyl)ethanamine [**8**] (1.91 mg): found 348.933, $\text{C}_{11}\text{H}_{13}^{79}\text{Br}_2\text{NO}_2$ requires 348.931; ^1H nmr δ 1.97 (s, 3, MeCO), 2.94 (t, 2, $J = 6.90$ Hz, C-2), 3.51 (q, 2, $J = 6.90$ Hz, H-1), 3.87 (s, 3, MeO), 5.55 (br s, 1, NH), 6.78 (s, 1, H-6'), 7.70 (s, 1, H-3'); ir ν max 3284 (m), 3086 (w), 2932 (m), 2850 (m), 1653 (s), 1584 (w), 1560 (m), 1474 (s), 1445 (m), 1371 (s), 1294 (m), 1250 (s), 1169 (w), 1062 (m), 1047 (m), 874 (w); eims m/z (%) $[\text{M}]^+$ 349, $^{79}\text{Br}_2$ (3), 290 $^{79}\text{Br}_2$ (24), 273 ^{79}Br (8), 270 ^{79}Br (20).

²Locant numbers for the atoms in the aromatic ring are designated by a '.

ACKNOWLEDGMENTS

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