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CHEMISTRY OF SPONGES, 17.[1] A NOVEL BROMINATED BENZOCYLOOCTANE DERIVATIVE FROM *HAMIGERA TARAGENSIS*

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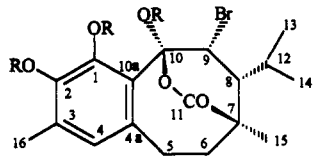
ABSTRACT.—A novel bromo benzocyclooctane [**1**] has been isolated from the sponge *Hamigera taragensis* and its structure determined by spectroscopic examination of its triethyl ether [**3**].

Hamigera taragensis Bergquist & Fromont is a sponge belonging to the family Phorbasidae (order Poecilosclerida) which was collected from the Hen and Chicken Islands, which lie to the east of Whangarei in New Zealand. Bioassay of fractions from a MeOH extract of the freeze-dried sponge showed activity against the microorganisms *Staphylococcus aureus, Candida albicans,* and *Bacillus subtilis*. Purification of the MeOH extract by reversed-phase hplc yielded, among other compounds, a bromine-containing phenolic compound, **1**. The molecular ion (*m/z* 398) corresponded with a formula of $C_{18}H_{23}BrO_5$ in the lreims. Persistent impurities, a low yield (0.002%), and the oily nature of the compound made final purification difficult.

In order to obtain a derivative more amenable for spectroscopic examination, **1** was treated with MeI and with ethyl iodide to yield a trimethyl ether, **2**, $C_{21}H_{29}BrO_5$, and a triethyl ether, **3**, $C_{24}H_{35}BrO_5$, respectively, both of which were also oils. Because compound **3** was available in the greatest quantity and purity, it was utilized for subsequent elucidation of the parent skeleton.



1 R=H
2 R=CH_3
3 R=CH_2CH_3

The ir spectrum of **3** showed absorptions for a δ-lactone group, an aryl ring, an alkyl aryl ether, a dialkyl ether, and a lone aromatic proton. The ^{13}C- and ^1H-nmr spectra of **3** (Table 1) confirmed the presence of three ethoxy groups, a pentasubstituted aromatic ring, and a lactone group (δ 175.4), and showed the presence of an aryl methyl group, an isopropyl group, and a tertiary alkyl group. Both of the methylene groups of the ethyl ethers showed diastereotropy with each proton signal appearing as a doublet of quartets. Inasmuch as the methylene protons of one of the ethoxy groups resonated at δ 3.59 and 3.79 (in contrast to those of the other two, which were observed at lower field, viz., δ 4.02, 4.03, and 4.37, 4.39), it was judged to be an alkyl ethoxy group. Furthermore, the larger chemical shift difference of the two methylene protons (Δ 0.22 ppm) for this functionality was consistent with the presence of a bromine atom vicinal to the group. A double-quantum phase-sensitive COSY (COSYPHDQ) nmr spectrum showed two spin-systems, namely, a four spin-system (δ 1.58, 2.71, 1.78, 2.06) corresponding to two contiguous methylene groups, and a nine spin-system (δ 3.11, 2.12, 1.29, 0.74, 0.83), corresponding to the fragment CH-CH-CH$(CH_3)_2$.

[1]For part 16, see Lal *et al.* (1); For part 15, see Bowden *et al.* (2).

TABLE 1. ^{1}H- and ^{13}C-Nmr Data for Compounds **1–3**.

Position	Compound							
	1[a]		**1**[b]		**2**[b]		**3**[b]	
	δ_C	δ_H	δ_C	δ_H	δ_C	δ_H	δ_C	δ_H
1	175.9		175.9		167.6		167.2	
2	156.9		155.1		154.0		153.0	
3	142.0		140.8		140.0		139.5	
4	122.9, d	6.59, s	121.7	6.57, s	126.9	6.77	126.7	6.76
4a.....	111.9		111.1		117.6		117.7	
5	35.0, t	2.67, dt	32.7	2.55, dt	33.3	2.68	34.0	2.71
		1.75, m		1.75, dt		1.60		1.58
6	29.5, t	1.75, m	28.6	1.75	29.6	1.77	29.8	1.78
		2.12, m		2.1		2.08		2.06
7	59.1, s		56.7		56.3		56.2	
8	52.5, d	2.20, m	50.6	2.2, m	51.9	2.15	51.7	2.12
9	51.8, d	4.25, d	52.0	3.88, br d	54.3	3.11	54.5	3.11
10	141.8		140.6		137.8		137.8	
10a.....	121.3		119.9		129.1		129.9	
11	181.6		180.8		175.7		175.4	
12	31.1, d	1.2, m	29.6	1.2, m	29.6	1.28	29.3	1.29
13	22.2, q	0.60, d	21.7	0.60	21.5	0.73	21.8	0.74
14	22.3, q	0.83, d	21.9	0.84	22.3	0.84	22.2	0.83
15	28.7, q	1.50, s	28.3	1.47	27.4	1.39	28.0	1.40
16	23.9, q	2.34, s	24.1	2.39	23.8	2.40	23.7	2.39
OCH_2R-1[c] .					62.0	3.81, s	70.4	4.02, dq
								4.03, dq
OCH_2R-2[c] .					51.3	3.90, s	61.1	4.37, dq
								4.39, dq
OCH_2R-10[c]					51.3	3.27, s	60.1	3.59, dq
								3.79, dq
OEt-1							15.3	1.37, t
OEt-2							14.2	1.39, t
OEt-10 ...							13.6	0.88, t

[a]In MeOH-d_4.
[b]In $CDCl_3$.
[c]R=H or CH_3.

Correlation was also observed between the aromatic proton (δ 6.75) and the protons of the aryl methyl group. By the use of 2D nmr experiments at high field, including COSY, XHCORRD, and COLOC, unambiguous associations of carbons and attached protons were made, and the complete assignment of all carbon and proton signals enabled the skeleton of **3** to be determined as in Figure 1.

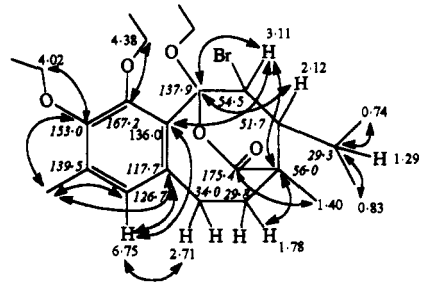


FIGURE 1. Selected ^{13}C- and ^{1}H-nmr connectivities for **3**.

The relative stereochemistry of the alicyclic ring was provisionally determined by NOESYPH nmr experiments (Figure 2) which require the lactonol bridge to possess a β-configuration. H-4 exhibited nOes to the aromatic methyl group (δ 2.39), and to the H-5 and H-6 signals at δ 2.71 and 1.78, respectively, and which were therefore assigned α-

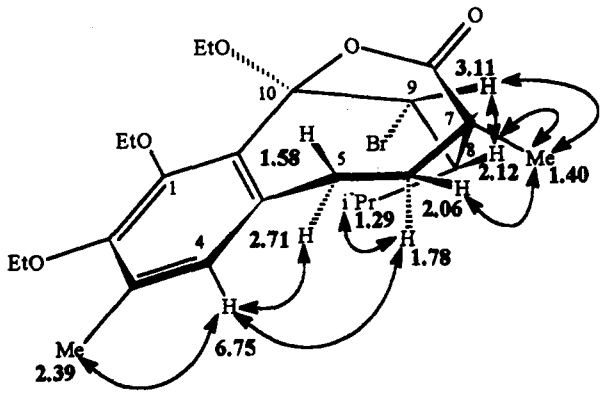


FIGURE 2. NOESYPH correlations and stereochemistry for **3**.

orientations. H-6β (δ 2.06) was correlated to the Me-7 group which in turn correlated to H-8 (δ 2.12) and H-9 (δ 3.11). The latter proton was therefore designated as H-9β. The 8-isopropyl methine proton was correlated to H-6α indicating that it had an α-orientation. Moreover, the high-field chemical shifts of the isopropyl methyl groups (δ 0.74, 0.83) suggested that these groups lay in the shielding cone of the aromatic ring, a situation consistent with the proposed structure.

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—As described previously (2).

ANIMAL MATERIAL.—The sponge was collected at a depth of 30 m by scuba diving and a reference specimen (P.O.R. 103) is held in the Museum of New Zealand, Wellington. Taxonomic identification was provided by one of us (P.R.B.).

EXTRACTION AND ISOLATION.—The freeze-dried sponge (31.6 g) was extracted with MeOH at room temperature and the extract was concentrated to small volume under reduced pressure. The solution was chromatographed (hplc) on a reversed-phase column using gradient elution (0–100% MeOH/H_2O). Isocratic elution with 60% MeOH/H_2O gave a single fraction which was active against several microorganisms. Further, hplc gave **1** as an oil (10 mg) which was contaminated by by a persistent impurity. ^{1}H- and ^{13}C-nmr data, see Table 1; eims *m/z* 398.0726 ($C_{18}H_{23}BrO$, requires 398.0729).

Trimethoxy derivative **2**.—Crude **1** (20 mg) was dissolved in dry Me_2CO (40 ml) and heated under reflux overnight with methyl iodide (1 ml) and anhydrous K_2CO_3 (0.5 g). Workup and purification by hplc (Porasil, 50% EtOAc/hexane) gave the trimethoxy derivative **2** as a colorless oil (13 mg, 60%). ^{1}H- and ^{13}C-nmr data, see Table 1; eims *m/z* 440.1195, 442.1172 ($C_{21}H_{29}BrO_5$ requires 440.1198, 442.1177).

Triethoxy derivative **3**.—Crude **1** (49 mg) was treated with ethyl iodide overnight and the mixture worked up to give an oil. Purification by hplc (Porasil, 50% EtOAc/hexane) or by cc on Si gel with EtOAc as eluent gave the triethoxy derivative **3** as a colorless oil (39 mg, 66%); $[\alpha]^{25}D$ +30.5° (c=2.8, $CHCl_3$); ir ν max 1732 (δ lactone), 1591, 1552 (aryl ring), 1264 (alkyl aryl ether), 1094 (dialkyl ether), 862 cm^{-1} (lone aromatic proton); ^{1}H- and ^{13}C-nmr data, see Table 1; eims *m/z* 482.1666, 484.1648 ($C_{24}H_{35}BrO_5$ requires 482.1668, 484.1647).

ACKNOWLEDGMENTS

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