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Purpuramines A-I, New Bromotyrosine-derived Metabolites from the Marine Sponge *Psammaplysilla purpurea*[1]

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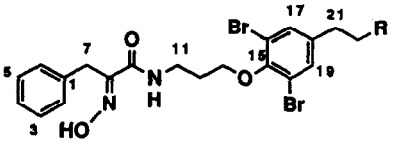
ABSTRACT
Nine new bromotyrosine-derived metabolites, purpuramines A~I (**1~9**) and phenylpyruvic acid oxime (**10**) have been isolated from the marine sponge, *Psammaplysilla purpurea*. Their structures were determined by interpretation of spectral data. Compounds **1~9** exhibited antibacterial activity against *Staphylococcus aureus*.

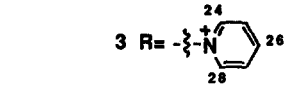
Marine sponges of the families Aplysinidae, Aplysinellidae, and Ianthellidae in the order Verongida are characterized by chemotaxonomic markers, bromotyrosine-derived metabolites which range from simple monomeric metabolites represented by aeroplysinin-1[3] to more complex bastadins;[4] complex groups are formed by combining two to four bromotyrosine-derived units through amide or ether bonds.[5] In some cases,[6, 7, 8] cysteine, homoserine, and histidine are also incorporated as their decarboxylated amines. During our studies on bioactive metabolites from Japanese marine invertebrates, we have isolated from the marine sponge *Psammaplysilla purpurea* a new class of bromotyrosine derivatives, purpuramines A-E (**1-5**), which contain a phenylalanine-derived oxime carboxylic acid portion, along with purpuramines F-I (**6-9**) containing two bromotyrosine-derived units, and phenylpyruvic acid oxime (**10**), a building block for **1-5**. We describe the isolation and structural elucidation of these metabolites.

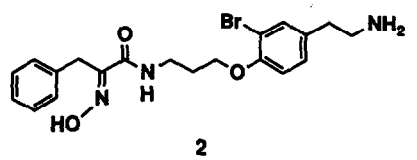
The ether-soluble portion of the EtOH extract of the sponge, collected off Hachijo-jima Island, was partitioned between MeOH/H_2O (9:1) and *n*-hexane. The aqueous MeOH phase was fractionated by ODS flash chromatography, followed by repeated HPLC on ODS to obtain purpuramines A-I (**1-9**) and **10** as TFA salts.[9] Purpuramines exhibited antibacterial activity against *Staphylococcus aureus*, but phenylpyruvic acid oxime was not active.

Purpuramine A (**1**) was positive to ninhydrin reagent and had a molecular formula of $C_{20}H_{23}Br_2N_3O_3$, which was established by high resolution FAB mass spectrum. The ^1H NMR spectrum exhibited signals assignable to a mono-substituted benzene ring (δ 7.12, 7.20, 7.25; H2-H6), a 3-aminopropanol (δ 3.60, 2.05, 4.01; H_2-11-H_2-13), a 2-aminoethyl (δ 2.88, 3.13; H_2-21, H_2-22), an isolated methylene (δ 3.91; H_2-7), and a symmetrically substituted aromatic ring (δ 7.51; H17, H19). In addition to these structural features, the ^{13}C NMR spectrum displayed singlet signals ascribed to an amide (δ 165.9; C9), aromatic carbons [δ 153.6, 137.3, 119.5 (2C); C15, C16, C18, C20], and an oxime carbon (δ 153.2; C8). Connectivities of these units were made by HMBC experiments. The two-proton singlet at δ 7.51, which was attached to carbons at δ 134.4, showed crosspeaks with C15 (δ 153.6), C17/19 (δ 134.4) which included direct and long-range correlations, and C16/20 (δ 119.5), whereas an H_2-21 triplet signal at δ 2.88 was correlated with C18 (δ 137.3) and C17/19, thereby revealing structural unit A. HMBC crosspeaks observed between H_2-11 and C9 amide carbonyl carbon, and between H_2-7 and C1, C2/C6, C8, and C9 led to structural unit B. Units A and B could be connected via an ethereal oxygen, which was indicated by chemical shifts (δ_H 4.01, H_2-13; δ_C 72.7, C13).[10] *E*-Geometry of the oxime was inferred from the chemical shift of C7, which was also true for compounds **2-10**.[11]



1 R=NH_2





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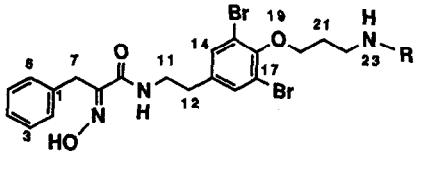
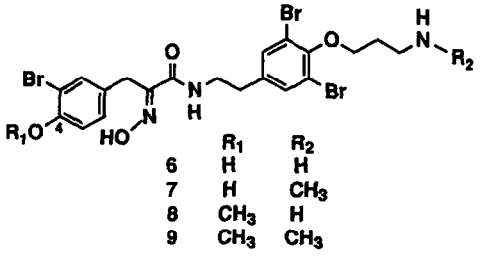
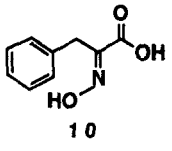


4 R=H

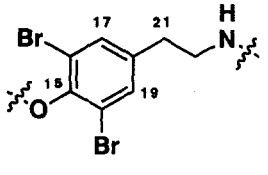
5 R=CH_3



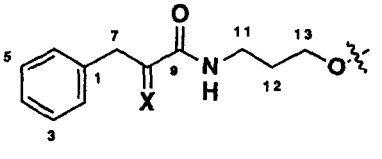
	R_1	R_2
6	H	H
7	H	CH_3
8	CH_3	H
9	CH_3	CH_3



10



A



B

Purpuramine B (2) had a molecular formula of $C_{20}H_{24}BrN_3O_3$ as determined by high resolution FAB mass spectrum. The NMR spectrum was superimposable on that of 1, except for the aromatic region. In addition to a mono-substituted benzene ring, the ^1H NMR spectrum contained three mutually coupled aromatic protons at δ 7.47, 7.18, and 6.95. Thus, purpuramine B possesses a monobromophenyl ether unit instead of a dibromophenyl ether as in 1.

The UV spectrum of purpuramine C (3) exhibited strong absorption at λmax 250 nm (ε 5600) in clear contrast with the other compounds. The ^1H and ^{13}C NMR spectral data for the C1-C21 portion were consistent with those of 1. An *N*-substituted pyridine (δ_H 8.08, 8.59, 8.88; δ_C 129.5, 146.2, 147.2) was readily assigned, and the C22 methylene signals were shifted downfield (δ_H 4.83, δ_C 63.3), indicative of connectivity between C22 and the pyridine nitrogen.[12]

Table 1. ^{13}C and ^{1}H NMR Data and HMBC Correlations for Compound **1** in CD_3OD

Atom	δ_C	δ_H	HMBC correlations
1	138.2		
2	130.1	7.25 (d, 7.5)	C4, C6, C7
3	129.3	7.20 (dd, 7.3, 7.5)	C1, C5
4	127.2	7.12 (t, 7.3)	C2, C6
5	129.3	7.20 (dd, 7.3, 7.5)	C1, C3
6	130.1	7.25 (d, 7.5)	C2, C4, C7
7	29.9	3.91 (s)	C1, C2, C6, C8, C9
8	153.2		
9	166.0		
11	37.7	3.60 (t, 6.7)	C9, C12, C13
12	30.7	2.05 (tt, 6.2, 6.7)	C11, C13
13	72.2	4.01 (t, 6.2)	C11, C12
15	153.6		
16	119.5		
17	134.4	7.51 (s)	C15, C16, C19, C21
18	137.3		
19	134.4	7.51 (s)	C15, C17, C20, C21
20	119.5		
21	33.3	2.88 (t, 7.5)	C17, C18, C19, C22
22	41.5	3.13 (t, 7.5)	C18, C21

Purpuramine D (**4**) had a molecular formula of $C_{20}H_{23}Br_2N_3O_3$ identical with **1**. The ^{1}H and ^{13}C NMR data indicated that both compounds shared common structural units, but the amide bond was formed by alternate amino group.[13] Correlation between H-10 and H-11 was confirmed by a COSY spectrum measured in DMSO-d_6.

Purpuramine E (**5**) was the CH_2 homolog of **4**. ^{1}H and ^{13}C NMR spectra also were similar to those of purpuramine D, except for an *N*-methyl (δ_H 2.76; δ_C 27.1) and a shift in CH_2-22 (δ_H 3.32; δ_C 48.2), thereby leading to structure **5**.

Purpuramine F (**6**) exhibited UV absorption at 282 nm (ε 2600), reminiscent of a phenol.[14] A ratio of 1:3:3:1 for the molecular ion species at *m/z* 626, 624, 622, and 620 in the FAB mass spectrum revealed the presence of three bromine atoms. In fact, a molecular formula of $C_{20}H_{22}Br_3N_3O_4$ was established by accurate mass measurement for an $(M+H)^+$ ion peak at *m/z* 609.9254. The NMR spectra were quite similar to those of **4**; the C7-C22 portion was identical. The presence of three mutually coupled protons at δ_H 6.75, 7.04, and 7.35, together with the ^{13}C NMR signals at δ_C 153.7, 134.4, 130.6, 130.3, 117.1, and 110.5, were consistent with 2-bromo-4-alkyl-phenol, which replaced the mono-substituted benzene ring in **1**.

Purpuramine G (**7**), possessing a molecular formula of $C_{21}H_{24}Br_3N_3O_4$, was an *N*-methyl derivative of **6**, which was apparent from the ^{1}H and ^{13}C NMR data. An *N*-methyl group resonated at δ_H 2.76, δ_C 27.7, and considerable down-field shifts were observed for C21 and C22.

Purpuramine H (**8**)[15] had the same molecular formula as **7**. Instead of the *N*-methyl group in **7**, an *O*-methyl group (δ_H 3.82; δ_C 56.7) was present in **8**. A NOESY crosspeak observed between the *O*-methyl protons and H3 proton placed the methoxy group on C4. Decrease in intensity of the UV absorption at 280 nm (ε 1830) was consistent with methylation of the phenolic hydroxyl group.[14]

Purpuramine I (**9**) was a CH_2 homolog of **7** or **8**, which was reflected by the presence of both *N*-methyl and *O*-methyl groups (δ_H 2.76, 3.82; δ_C 27.7, 56.7). The NMR data for the C1-C6 portion were identical with those of **8**, while the *N*-methyl-3-aminopropanol portion was identical with that of **7**. Therefore, **9** was an *N*,*O*-dimethyl derivative of **6**.

Table 2. ^{13}C and ^{1}H NMR Data and HMBC Correlations for Compound **7** in CD_3OD

Atom	δ_C	δ_H	HMBC correlations
1	130.6		
2	130.3	7.03 (dd, 1.7, 8.3)	C4, C6, C7
3	117.1	6.75 (d, 8.3)	C1, C5
4	153.7		
5	110.5		
6	134.4	7.34 (d, 1.7)	C2, C4, C5
7	28.7	3.75 (s)	C2, C6, C8, C9
8	153.1		
9	165.8		
11	41.3	3.42 (t, 7.0)	C9, C12, C13
12	35.2	2.73 (t, 7.0)	C11, C13, C14, C18
13	140.3		
14	134.4	7.43 (s)	C12, C15, C16, C18
15	118.7		
16	152.1		
17	118.7		
18	134.4	7.43 (s)	C12, C14, C16, C17
20	71.5	4.06 (t, 5.7)	C22
21	33.8	2.21 (tt, 5.7, 7.2)	C20, C22
22	48.2	3.34 (t, 7.2)	C20, C21, N-CH_3
N-CH_3	27.7	2.76 (s)	C22

Phenylpyruvic acid oxime (**10**), which is a building block for **1-5**, was also isolated from the sponge. Compound **10** showed an $(M+glycerol+H)^+$ peak at *m/z* 272 in the FAB mass spectrum. The ^{1}H NMR spectrum displayed signals for a mono-substituted benzene ring and an isolated methylene (δ 3.91), while the ^{13}C NMR spectrum displayed signals for an oxime (δ 152.2) and a carboxylic acid (δ 166.9). 4-Hydroxyphenylpyruvic acid oxime was previously reported from the marine sponge *Hymeniacidon sanguinea*.[16]

The carboxylic acid oxime unit present in bromotyrosine-derived metabolites so far obtained were exclusively derived from bromotyrosines,[5] while in purpuramines A-E (**1-5**) the oxime function is part of a phenylalanine moiety, which is a new variant among verongid metabolites.

Experimental Section

General Procedure

^{1}H and ^{13}C NMR spectra were recorded on either Bruker AC-300P or Bruker AM-600 NMR spectrometers. The 3.33 ppm and 49.0 ppm signals of CD_2HOD and CD_3OD were used as internal reference, respectively. The 2.49 ppm of CD_2HSOCD_3 was also used as internal reference. FABMS spectra were obtained on a JEOL JMS-SX-102 mass spectrometer by using glycerol as a matrix. UV spectra were measured on a Hitachi 330 spectrophotometer in methanol solution. IR spectra were recorded on a JASCO FT/IR-5300 spectrophotometer.

Extraction and Isolation

The sponge was collected off Hachijo-jima Island by SCUBA(-3~5 m) and kept frozen until processed. The frozen specimen (1.0 kg) was extracted three times with EtOH (3 L), and the concentrated extract was partitioned between ether (1 L x 3) and water (1 L). The ether-soluble portion was evaporated under reduced pressure to give a dark violet oil (15.03 g), which was further partitioned between *n*-hexane and 90% MeOH. The aqueous MeOH phase was fractionated by flash chromatography on ODS with 1 L each of 30% MeOH, 50% MeOH, 70% MeOH, 100% MeOH, CH_2Cl_2, and $CHCl_3$/MeOH/H_2O (7/3/0.5). The fraction eluted with 50% MeOH was rechromatographed on an ODS column (Cosmosil 20 x 250 mm) by gradient elution from 50 to 55% MeOH containing 0.1% TFA, to obtain **1** (1.31 g) and crude antibacterial materials. The latter was purified by HPLC on ODS (Cosmosil 20 x 250 mm) with 25% or 30% MeCN containing 0.1% TFA, to afford pure **2** (4.4 mg), **3** (28.4 mg), **4** (5.3 mg), **6** (9.6 mg), **7** (9.9 mg), **8** (34.8 mg), **9** (16.0 mg), **10** (13.3 mg), and impure **5**. The fraction containing **5** was finally purified by repeated HPLC on ODS with 50% MeOH containing 0.05% TFA to yield 2.7 mg of **5**.

1: IR (film) ν_{max} 1658, 1540, 1458, 1420, 1258, 1200, and 1010 cm^{-1}; UV (MeOH) λ_{max} 280 nm (ε 834); ^{1}H and ^{13}C NMR, see Table 1; HRFABMS $(M+H)^+$ at *m/z* 514.0178, calculated for $C_{20}H_{24}{}^{79}Br^{81}BrN_3O_3$ (Δ -1.4 mmu).

2: IR (film) ν_{max} 1680, 1540, 1498, 1458, 1200, 1138, 840, and 800 cm^{-1}; UV (MeOH) λ_{max} 280 nm (ε 641); ^{1}H NMR (CD_3OD) δ 2.00 (2H, tt, *J*=6.1 and 6.7 Hz, H-12), 2.88 (2H, t, *J*=7.6 Hz, H-21), 3.13 (2H, t, *J*=7.6 Hz, H-22), 3.43 (2H, t, *J*=6.7 Hz, H-11), 3.90 (2H, s, H-7), 4.02 (2H, t, *J*=6.1 Hz, H-13), 6.95 (1H, d, *J*=8.4 Hz, H-20), 7.15 (1H, t, *J*=7.3 Hz, H-4), 7.18 (1H, dd, *J*=1.8 and 8.4 Hz, H-19), 7.20 (2H, dd, *J*=7.3 and 7.5 Hz, H-3, H-5), 7.25 (2H, d, *J*=7.5 Hz, H-2, H-6), 7.47 (1H, d, *J*=1.8 Hz, H-17); ^{13}C NMR (CD_3OD) δ 166.1 (C-9), 155.9 (C-15), 153.4 (C-8), 138.1 (C-1), 134.4 (C-17), 131.6 (C-18), 130.0 (C-2, C-6, C-19), 129.3 (C-3, C-5), 127.2 (C-4), 115.0 (C-20), 113.4 (C-16), 68.3 (C-13), 41.9 (C-22), 37.7 (C-11), 33.3 (C-21), 30.2 (C-7), 30.0 (C-12); HRFABMS $(M+H)^+$ at *m/z* 434.1086, calculated for $C_{20}H_{25}{}^{79}BrN_3O_3$ (Δ +0.7 mmu).

3: IR (film) ν_{max} 1670, 1200, 1130, and 800 cm^{-1}; UV (MeOH) λ_{max} 250 nm (ε 5600); ^{1}H NMR (CD_3OD) δ 2.04 (2H, tt, *J*=6.1 and 6.8 Hz, H-12), 3.27 (2H, t, *J*=7.3 Hz, H-21), 3.51 (2H, t, *J*=6.8 Hz, H-11), 3.91 (2H, s, H-7), 3.99 (2H, t, *J*=6.1 Hz, H-13), 4.83 (2H, t, *J*=7.3 Hz, H-22), 7.12 (1H, t, J=7.3 Hz, H-4), 7.20 (2H, dd, J=7.3 and 7.5 Hz, H-3, H-5), 7.25 (2H, d, J=7.5 Hz, H-2, H-6), 7.44 (2H, s, H-17, H-19), 8.08 (2H, t, *J*=5.6 and 7.1 Hz, H-25, H-27), 8.59 (1H, t, *J*=7.1 Hz, H-26), 8.88 (2H, d, *J*=5.6 Hz, H-24, H-28); ^{13}C NMR (CD_3OD) δ 166.0 (C-9), 153.9 (C-15), 153.3 (C-8), 147.2 (C-26), 146.2 (C-24, C-28), 138.1 (C-1), 136.1 (C-18), 134.4 (C-17, C-19), 130.0 (C-2, C-6), 129.5 (C-25, C-27), 129.3 (C-3, C-5), 127.2 (C-4), 119.6 (C-16, C-20), 72.3 (C-13), 63.3 (C-22), 37.7 (C-11), 36.6 (C-21), 30.7 (C-12), 29.9 (C-7); HRFABMS M^+ at *m/z* 578.0306, calculated for $C_{25}H_{26}{}^{81}Br_2N_3O_3$ (Δ +0.6 mmu).

4: IR (film) ν_{max} 1678, 1200, 1138, 840, and 800 cm^{-1}; UV (MeOH) λ_{max} 282 nm (ε 512); ^{1}H NMR (CD_3OD) δ 2.19 (2H, tt, *J*=5.7 and 7.3 Hz, H-21), 2.73 (2H, t, *J*=7.2 Hz, H-12), 3.30 (2H, t, *J*=7.3 Hz, H-22), 3.42 (2H, t, *J*=7.2 Hz, H-11), 3.88 (2H, s, H-7), 4.09 (2H, t, *J*=5.7 Hz, H-20), 7.13 (1H, m, H-4), 7.21 (4H, m, H-2, H-3, H-5, H-6), 7.45 (2H, s, H-14, H-18); ^{1}H NMR (DMSO-d_6) δ 2.06 (2H, m, H-21), 2.73 (2H, t, *J*=6.8 Hz, H-12), 3.06 (2H, m, H-22), 3.32 (2H, m, H-11), 3.78 (2H, s, H-7), 3.98 (2H, t, *J*=5.9 Hz, H-20), 7.14 (3H, m, H-3, H-4, H-5), 7.23 (2H, m, H-2, H-6), 7.48 (2H, s, H-14, H-18), 8.00 (1H, t, *J*=5.8 Hz, H-10), 11.77 (1H, s, N-OH); ^{13}C NMR (CD_3OD) δ 166.0 (C-9), 153.2 (C-8), 152.2 (C-16), 140.3 (C-13), 138.1 (C-1), 134.4 (C-14, C-18), 130.0 (C-2, C-6), 129.3 (C-3, C-5), 127.2 (C-4), 118.7 (C-15, C-17), 71.6 (C-20), 41.3 (C-11), 38.9 (C-22), 35.2 (C-12), 29.9 (C-7), 29.0 (C-21); HRFABMS $(M+H)^+$ at *m/z* 512.0141, calculated for $C_{20}H_{24}{}^{79}Br_2N_3O_3$ (Δ -4.3 mmu).

5: IR (film) ν_{max} 1678, 1204, 1140, 840, and 800 cm^{-1}; UV (MeOH) λ_{max} 282 nm (ε 600); ^{1}H NMR (CD_3OD) δ 2.22 (2H, tt, *J*=5.7 and 7.2 Hz, H-21), 2.74 (2H, t, *J*=7.1 Hz, H-12), 2.76 (3H, s, N-CH_3), 3.32 (2H, t, *J*=7.2 Hz, H-22), 3.42 (2H, t, *J*=7.1 Hz, H-11), 3.88 (2H, s, H-7), 4.10 (2H, t, J=5.7 Hz, H-20), 7.14 (1H, m, H-4), 7.21 (4H, m, H-2, H-3, H-5, H-6), 7.45 (2H, s, H-14, H-18); ^{13}C NMR (CD_3OD) δ 166.0 (C-9), 153.2 (C-8), 152.2 (C-16), 139.1 (C-13), 137.1 (C-1), 134.4 (C-14, C-18), 130.0 (C-2, C-6), 129.3 (C-3, C-5), 127.2 (C-4), 118.7 (C-15, C-17), 71.4 (C-20), 48.2 (C-22), 41.4 (C-11), 35.2 (C-12), 33.8 (C-21), 29.9 (C-7), 27.1 (N-CH_3); HRFABMS $(M+H)^+$ at *m/z* 526.0292, calculated for $C_{21}H_{26}{}^{79}Br_2N_3O_3$ (Δ -4.9 mmu).

6: IR (film) ν_{max} 1678, 1204, 1140, and 800 cm^{-1}; UV (MeOH) λ_{max} 282 nm (ε 2600); ^{1}H NMR (CD_3OD) δ 2.18 (2H, tt, *J*=5.7 and 7.2 Hz, H-21), 2.74 (2H, t, *J*=7.1 Hz, H-12), 3.30 (2H, t, *J*=7.2 Hz, H-22), 3.42 (2H, t, *J*=7.1 Hz, H-11), 3.76 (2H, s, H-7), 4.07 (2H, t, *J*=5.7 Hz, H-20), 6.75 (1H, d, *J*=8.3 Hz, H-3), 7.04 (1H, dd, *J*=2.0 and 8.3 Hz, H-2), 7.34 (1H, d, *J*=2.0 Hz, H-6), 7.43 (2H, s, H-14, H-18); ^{13}C NMR (CD_3OD) δ 166.2 (C-9), 153.7 (C-4), 153.2 (C-8), 152.2 (C-16), 140.3 (C-13), 134.4 (C-6, C-14, C-18), 130.6 (C-2), 130.3 (C-1), 118.7 (C-15), 117.1 (C-3), 110.5 (C-5), 71.6 (C-20), 41.4 (C-11), 39.0 (C-22), 35.2 (C-12), 29.0 (C-21), 28.7 (C-7); HRFABMS $(M+H)^+$ *m/z* 609.9254, calculated for $C_{20}H_{23}{}^{79}Br^{81}Br_2N_3O_4$ (Δ +5.6 mmu).

7: IR (film) ν_{max} 1680, 1200, 1400, and 800 cm^{-1}; UV (MeOH) λ_{max} 282 nm (ε 2800); ^{1}H and ^{13}C NMR, see Table 2; HRFABMS $(M+H)^+$ at *m/z* 619.9391, calculated for $C_{21}H_{25}{}^{79}Br_3N_3O_4$ (Δ -0.4 mmu).

8: IR (film) ν_{max} 1678, 1202, 1138, 842, 800, and 722 cm^{-1}; UV (MeOH) λ_{max} 280 nm (ε 2000); ^{1}H NMR (CD_3OD) δ 2.18 (2H, tt, *J*=5.7 and 7.6 Hz, H-21), 2.75 (2H, t, *J*=7.2 Hz, H-12), 3.30 (2H, t, *J*=7.6 Hz, H-22), 3.42 (2H, t, *J*=7.2 Hz, H-11), 3.79 (2H, s, H-7), 3.82 (3H, s, O-CH_3), 4.08 (2H, t, *J*=5.7 Hz, H-20), 6.90 (1H, d, *J*=8.5 Hz, H-3), 7.18 (1H, dd, *J*=1.8 and 8.5 Hz, H-2), 7.42 (1H, d, *J*=1.8 Hz, H-6), 7.44 (2H, s, H-14, H-18); ^{13}C NMR (CD_3OD) δ 165.8 (C-9), 155.9 (C-4), 153.0 (C-8), 152.2 (C-16), 140.3 (C-13), 134.7 (C-6), 134.4 (C-14), 131.8 (C-1), 130.4 (C-2), 118.7 (C-15), 113.2 (C-3), 112.2 (C-5), 71.6 (C-20), 56.7 (O-CH_3), 41.3 (C-11), 38.9 (C-22), 35.2 (C-12), 29.0 (C-21), 28.7 (C-7); HRFABMS $(M+H)^+$ at *m/z* 619.9349, calculated for $C_{21}H_{25}{}^{79}Br_3N_3O_4$ (Δ -4.6 mmu).

9: IR (film) ν_{max} 1670, 1200, 1135, 838, 798, and 721 cm^{-1}; UV (MeOH) λ_{max} 280 nm (ε 1800); ^{1}H NMR (CD_3OD) δ 2.21 (2H, tt, *J*=5.6 and 7.6 Hz, H-21), 2.74 (2H, t, *J*=7.1 Hz, H-12), 2.76 (3H, s, N-CH_3), 3.30 (2H, t, *J*=7.6 Hz, H-22), 3.42 (2H, t, *J*=7.1 Hz, H-11), 3.79 (2H, s, H-7), 3.82 (3H, s, O-CH_3), 4.05 (2H, t, *J*=5.6 Hz, H-20), 6.89 (1H, d, *J*=8.4 Hz, H-3), 7.17 (1H, dd, *J*=2.0 and 8.4 Hz, H-2), 7.42 (1H, d, *J*=2.0 Hz, H-6), 7.43 (2H, s, H-14, H-18); ^{13}C NMR (CD_3OD) δ 165.8 (C-9), 155.9 (C-4), 153.0 (C-8), 152.2 (C-16), 140.3 (C-13), 134.7 (C-6), 134.4 (C-14, C-18), 131.8 (C-1), 130.4 (C-2), 118.7 (C-

15), 113.2 (C-3), 112.2 (C-5), 71.6 (C-20), 56.7 (O-CH_3), 41.3 (C-11), 38.2 (C-22), 35.2 (C-12), 33.8 (C-21), 28.7 (C-7), 27.7 (N-CH_3); HRFABMS $(M+H)^+$ at *m/z* 639.9457, calculated for $C_{22}H_{27}{}^{81}Br_3N_3O_4$ (Δ -3.3 mmu).

10: A white powder; IR (film) ν_{max} 1694, 1650, 1600, 1480, 1452, 1430, 1282, 1200, 1132, 1120, 1072, 1020, 920, 890, 740, and 688 cm^{-1}; ^1H NMR (CD_3OD) δ 3.91 (2H, s, H-7), 7.16 (1H, m, H-4), 7.23 (4H, m, H-2, H-3, H-5, H-6); ^{13}C NMR (CD_3OD) δ 166.9 (C-9), 152.2 (C-8), 138.0 (C-1), 130.0 (C-2, C-6), 129.3 (C-3, C-5), 127.3 (C-4), 31.0 (C-7)

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