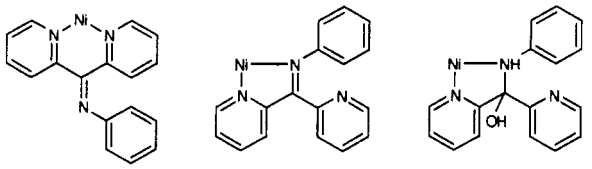


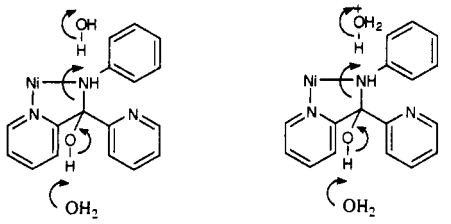
2 3 4

k_A measured in the presence of Ni(II) ion supports addition of water molecule to the Ni(II) complex of 1 to form 4.

The resistance of the carbinolamine to breakdown in the presence of Ni(II) ion indicates the kinetic stability of the Ni(II) complex of the carbinolamine. The spontaneous hydrolysis of 1 involves C–N bond cleavage in HT, the N-protonated form of the carbinolamine, as mentioned above. The rate constant for the breakdown of HT is not smaller than the observed value of k_{lim} (0.29 s^{-1}). Comparison of this value with the rate constant for the breakdown of NiT (3.5×10^{-6} s^{-1}) indicates that breakdown of NiT is slower than that of HT by more than 10^4 times.

If the amine moiety is expelled from the neutral form, instead of the protonated form, of the carbinolamine intermediate, amide anion becomes the leaving group and the activation energy is raised greatly. Even when the leaving amide anion is bound by a metal ion, it would be expelled with a great difficulty. When the amine nitrogen of the carbinolamine intermediate is bound to a metal ion, protonation of the amine would be inhibited. This would lead to the very slow breakdown of 4. In addition, expulsion of the amine moiety from 4 might be accompanied by an increase in the strain of the chelate ring in the transition state and this might be partly responsible for the slow rate.

If the carbinolamine intermediate is converted into the product through the breakdown of 4 in the presence of Ni(II) ion, expulsion of the amine moiety requires assistance from general acids such as water as indicated by 5 or hydronium ion as indicated by 6. The pH dependence of curve c in Figure 1 indicates that the expulsion of amine from the Ni(II)-bound intermediate is partially assisted by hydronium ion at low pHs.



5 6

In conclusion, Ni(II) ion exerts two opposite effects on the stability of 1. The metal ion bound to the imine nitrogen atom polarizes the imine bond facilitating the nucleophilic attack by water molecule at the imine carbon atom. On the other hand, blockade by the metal ion of the protonation of the leaving nitrogen atom greatly retards the breakdown of the carbinolamine, leading to overall inhibition of the hydrolysis of the Schiff base.

Some macrocycle complexes retain imine bonds even in water,[8] although the carbinolamine form is quite stable in the case of the Ni(II) complex of 1. The stability of a chelate ring containing an imine bond relative to that with a carbinolamine linkage or in comparison with the hydrolysis products would be governed by many structural elements. The present study suggests that the blockade of the protonation of the leaving amines in the carbinolamine intermediates by metal ions is one of the factors contributing to the extraordinary stability of imine bonds included in macrocyclic metal complexes.

(8) Gellman, S. H.; Petter, R.; Breslow, R. *J. Am. Chem. Soc.* **1986**, *108*, 2388.

Experimental Section

Compound 1 was prepared by refluxing the solution of 2,2′-dipyridyl ketone (3 g) and concd HCl (0.3 ml) in 10 mL of aniline for 30 min and was purified by separation on a silica gel column by eluting with 2:3 ethyl acetate–hexane and recrystallization from ethyl acetate; mp 147–149 °C. Anal. Calcd for $C_{17}H_{13}N_3$: C, 78.74; H, 5.05; N, 16.20. Found: C, 78.92; H, 5.02; N, 16.38. Water was distilled and deionized prior to use in kinetic studies. Nickel chloride was prepared according to the general method reported previously.[9] Reaction rates were measured with a Beckman Model DU-64 UV–vis spectrophotometer. Temperature was controlled at 25 ± 0.1 °C with a Haake E52 circulator. Ionic strength was adjusted to 1.0 M with NaCl. Buffers (0.01 M) used were chloroacetate (pH 2–3.5) and acetate (pH 3.6–5.2). The reaction mixture for kinetic runs contained 0.8 % (v/v) acetonitrile, which was used as the solvent for the stock solutions of 1.

Acknowledgment. This work was supported by the Basic Sciences Research Program (1990) of the Ministry of Education, Republic of Korea.

Registry No. 1, 100288-61-7; 4, 135192-18-6; Ni, 7440-02-0; $PhNH_2$, 62-53-3; 2,2′-dipyridyl ketone, 19437-26-4.

(9) Suh, J.; Cheong, M.; Suh, M. P. *J. Am. Chem. Soc.* **1982**, *104*, 1654.

Crambescidins: New Antiviral and Cytotoxic Compounds from the Sponge *Crambe crambe*[1]

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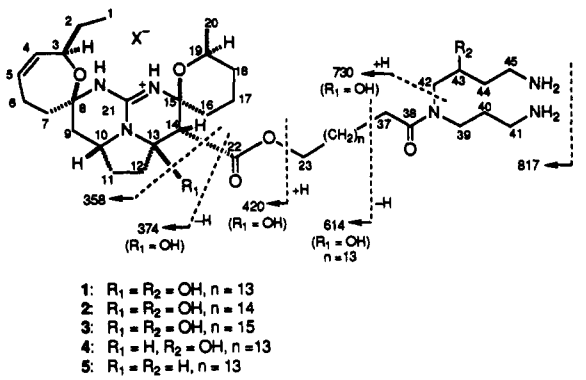
Crambescidins 816 (1), 830 (2), 844 (3), and 800 (4), a family of complex pentacyclic guanidines linked by a linear ω-hydroxy fatty acid to a hydroxyspermidine, have been obtained by bioassay-guided isolation, involving solvent partition and chromatography on Sephadex LH-20, cyano, and C-18 columns, from extracts of the red, encrusting sponge *Crambe crambe* (Order Poecilosclerida, Family Esperiopsidae). In assays on board the *R/V Garcia del Cid* during a 1988 Pharma Mar, S.A., expedition to the Western Mediterranean, extracts of *C. crambe* were regularly active vs *Herpes simplex* virus, type 1 (HSV-1), and cytotoxic to L1210 murine leukemia cells. Compounds 1, 3, and 4 inhibit HSV-1 completely, with diffuse cytotoxicity, at 1.25 μg/well and are 98% effective against L1210 cell growth at 0.1 μg/mL. The crambescidins' pentacyclic guanidine moiety has been isolated only once before,[2] and a hydroxyspermidine unit from a marine source is unprecedented.[3]

(1) Presented in part at the U.S.-Japan Joint Seminar on Bioorganic Marine Chemistry, Honolulu, HI, Dec 3, 1990.
(2) Kashman, Y.; Hirsh, S.; McConnell, O. J.; Ohtani, I.; Kusumi, T.; Kakisawa, H. *J. Am. Chem. Soc.* **1989**, *111*, 8925–8926.

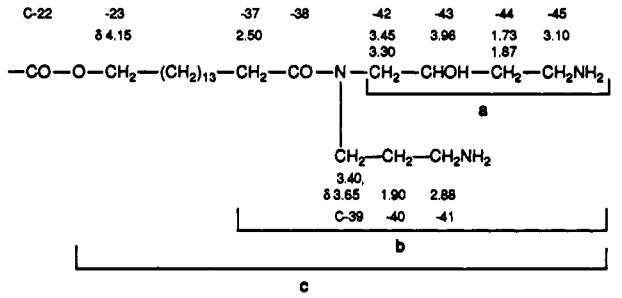
0022-3263/91/1956-5712$02.50/0

Scheme I



1: $R_1 = R_2 = OH$, n = 13
2: $R_1 = R_2 = OH$, n = 14
3: $R_1 = R_2 = OH$, n = 15
4: $R_1 = H$, $R_2 = OH$, n = 13
5: $R_1 = R_2 = H$, n = 13

Crambescidin 816 (1), the most abundant component, was assigned the molecular formula $C_{45}H_{80}N_6O_7$ by HRFABMS (M + H 817.6151, Δ1.6 mmu), indicating 9 degrees of unsaturation. The hydroxyspermidine region of 1 was assigned first. HRFABMS data on fragmentation ions at m/z 730 (M + H − 87) and 614 (M + H − 203, Schemes I and II),[4] which are derived (tandem FAB, FABMS/MS, Scheme II) from the M + H ion (m/z 817), indicated losses of C_4H_9NO and $C_9H_{21}N_3O_2$, respectively. The C_4H_9NO unit was assigned, from ^1H COSY and Relay COSY data, as subunit a and extended to subunit b (giving



the $C_9H_{21}N_3O_2$ loss) by COLOC correlations between C-38 (δ 177.5) and both H-42a and H-37, as well as by COSY spectra showing connectivities between H-39a, H-39b, and H-40 and between H-40 and H-41 (^1H NMR data in Table I). ^{13}C NMR assignments (Table II) for the 3-hydroxyspermidine unit based on CSCM data were in agreement with values calculated from the chemical shifts of the spermidine residue of ptilomycalin A (**5**)[2] (supplementary material). A polymethylene chain (suggested by ^1H NMR) from C-37 to −23 was assigned by FABMS data, which provided a nearly unbroken series of homologous fragment ions from cleavages at successive methylene groups from m/z 614.4525 ($C_{36}H_{60}N_3O_5$, Δ0.8 mmu) to m/z 420.2500 ($C_{22}H_{34}N_3O_5$, Δ0.2 mmu), extending b to subunit c.

Scheme II

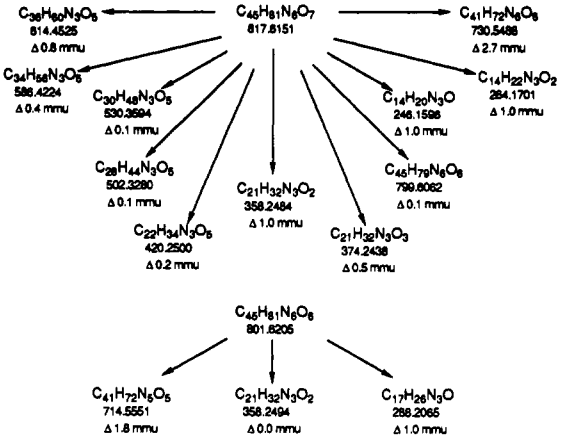


Table I. ^1H NMR Data for Crambescidin 816 (1, MeOD)

	δ, mult (J in Hz)		δ, mult (J in Hz)
H-1	0.88, t (7.0)	H-17a	1.70, m
H-2a	1.45, ddq (15.5, 10.0, 7.0)	H-17b	2.00, m
H-2b	1.65, m	H-18a	1.35, m
H-3	4.47, br d (10.0)	H-18b	1.72, m
H-4	5.50, br d (11.0)	H-19	3.96, m
H-5	5.72, br t	H-20	1.12, d (6.5)
H-6a	2.19, m	H-23	4.15, t (6.5)
H-6b	2.37, m	H-24	1.62, m
H-7a	1.95, m	H-37	2.50, m
H-7b	2.40, m	H-39a	3.40, m
H-9a	1.44, t (13.0)	H-39b	3.65, m
H-9b	2.65, dd (13.0, 4.5)	H-40	1.90, m
H-10	4.29, m	H-41	2.88, m
H-11a	1.60, m	H-42a	3.30, m
H-11b	2.41, m	H-42b	3.45, m
H-12a	2.00, m	H-43	3.96, m
H-12b	2.20, m	H-44a	1.73, m
H-14	3.46, s	H-44b	1.87, m
H-16a	1.65, m	H-45	3.10, m
H-16b	1.87, m		

The mass spectral data (Schemes I and II) demonstrate an additional loss of CO_2 with hydrogen transfer from 420.2500 to give m/z 374.2438 ($C_{21}H_{32}N_3O_3$, Δ0.5 mmu). This second carboxyl carbon at δ 168.7 and two doubly deshielded quaternary carbons (N,O-disubstituted from the chemical shifts) at δ 90.5 (C-13) and δ 84.5 are correlated (long-range C–H, COLOC) with a singlet proton at δ 3.46, establishing subunit d. Moreover, subunit d abuts subunit c, since C-22 (δ 168.7) can be correlated by HMBC with H-23 (δ 4.15).

Three isolated spin systems e–g identified from COSY and CSCM data were connected by long-range C–H correlations observed in COLOC and HMBC spectra. A terminal hydrogen (H-7b) in subunit e and H-9b in subunit f both correlated with a doubly deshielded quaternary

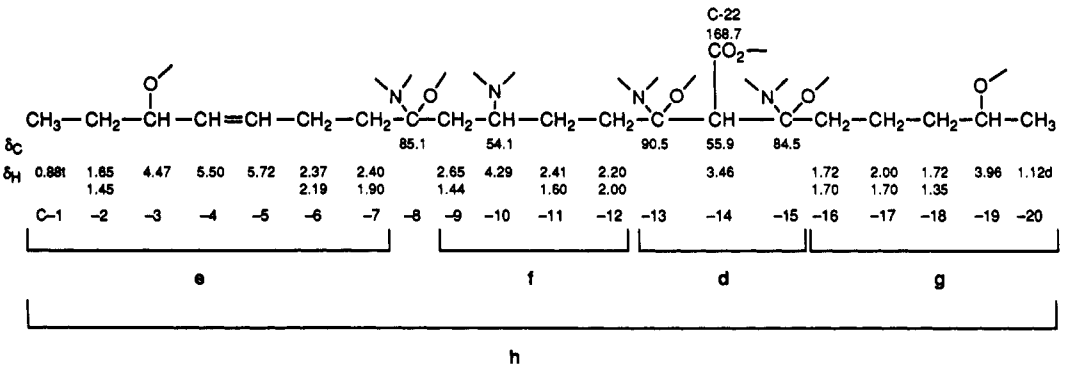


Table II. ^{13}C NMR Data for Crambescidins 816 (1), 800 (4) and 844 (3), and Ptilomycalin A (5)

	δ (ppm) m[a] crambescidin 816 (1)		δ (ppm), m[a,b] crambescidin 800 (4)	δ (ppm), m[a] ptilomycalin A (5)	δ (ppm), m[a,c] crambescidin 844 (3)
	MeOD	$CDCl_3$	MeOD	$CDCl_3$	MeOD
C-1	10.9, q	10.1, q	9.4, q	10.21	10.9, q
C-2	26.4, t	29.0, t	26.2, t	29.19	26.5, t
C-3	72.5, d	71.2, d	72.2, d	70.89	72.5, d
C-4	134.3, d	133.6, d	133.0, d	133.69	134.3, d
C-5	131.3, d	129.7, d	129.3, d	129.96	131.3, d
C-6	24.4, t	25.8, t	23.0, t	23.74	24.4, t
C-7	38.2, t	36.8, t	36.5, t	36.22	38.2, t
C-8	85.1, s	83.5, s	83.6, s	86.86	85.1, s
C-9	37.5, t	36.8, t	37.1, t	36.89	37.5, t
C-10	54.1, d	52.4, d	54.1, d	54.06	54.1, d
C-11	30.0, t	29.7, t	30.2, t	30.65	30.8, t
C-12	37.7, t	36.8, t	28.2, t	26.81	37.7, t
C-13	90.5, s	88.6, s	52.5, d	52.13	90.5, s
C-14	55.9, d	54.4, d	49.4, d	50.10	55.9, d
C-15	85.4, s	83.0, s	80.6, s	80.82	84.5, s
C-16	32.8, t	41.5, t	32.8, t*	31.68	32.5, t
C-17	19.1, t	18.0, t	18.1, t	18.01	19.1, t
C-18	32.4, t	32.0, t	32.1, t*	32.06	32.9, t
C-19	70.0, d	68.7, d	70.9, d	67.12	70.0, d
C-20	21.7, q	21.4, q	20.4, q	21.56	21.7, q
C-21	149.5, s	148.0, s	151.3, s	149.09	149.6, s
C-22	168.7, s	167.1, s	168.6, s	168.58	168.8, s
C-23	67.1, t	65.9, t	65.1, t	65.53	67.0, t
C-24	29.6, t	28.3, t	29.3, t	28.54	30.3, t
C-36	27.0, t	25.7, t	25.6, t	25.74	26.7, t
C-37	34.2, t	32.0, t	32.8, t*	33.21	39.2, t
C-38	177.5, s	175.4, s	176.0, s	174.87	177.5, s
C-39	43.9, t	44.1, t	42.5, t	42.13	43.9, t
C-40	26.6, t	25.8, t	25.3, t	27.03	26.6, t
C-41	38.3, t	36.9, t	36.5, t	36.13	38.2, t
C-42	54.8, t	54.4, t	53.4, t	47.59	54.8, t
C-43	68.5, d	65.9, d	67.0, d	26.07	68.5, d
C-44	32.9, t	31.9, t	32.3, t	26.43	33.0, t
C-45	38.5, t	37.1, t	37.1, t	39.25	38.5, t

[a] Multiplicities were determined by DEPT spectra: q, methyl; t, methylene; d, methine; s, quaternary carbons. [b] Signals marked * may be interchanged. [c] See ref 4 regarding numbering.

carbon (C-8, N,O-disubstituted) at δ 85.1, and another terminal hydrogen (H-12b) in subunit f correlated with the quaternary carbon (C-13) at δ 90.5. The remaining quaternary carbon (C-15) at δ 84.5 correlated to the protons on C-16 (HMBC). Thus, these units could be combined as subunit h, where the oxygens other than the carboxyl must be present in two cyclic ethers and a hydroxyl group. The latter is located on C-13 as shown by the difference in chemical shift of C-13 in 4, which lacks the hydroxyl. Therefore, the cyclic ethers join C-3, -8, -15, and -19.

A signal at δ 147.9 (149.5 in CD_3OD) in the ^{13}C NMR spectrum of 1 with no companion olefinic carbon indicates a tetrasubstituted guanidine group (in salt form), providing the nitrogens on C-8, -10, -13, and -15. Moreover, in the ^1H NMR ($CDCl_3$) spectrum the D_2O-exchangeable signal appearing at δ 10.01 on irradiation shows NOE of H-3 and the D_2O-exchangeable signal at δ 10.03 shows NOE of H-19 (Scheme III), arguing that (i) the guanidine nitrogens on C-8 and -15 (ether bearing) are monosubstituted (and the N-10 (≡N-13) nitrogen disubstituted) and (ii) O-3 is attached to C-8 and O-19 to C-15, or vice versa. The guanidine would then for geometric reasons exist in a rigid 6-5-6 ring system with C-3 to C-8 and C-15 to C-19 in 7- and 6-membered cyclic ether bridges, respectively (the reverse C-3 to C-15 and C-8 to C-19 in 14- and 13-membered ether bridges being essentially impossible on geometric grounds). The nature of the counterion was not determined but, because several isolation steps involved contact with NaCl, this was presumably Cl^-.

Comparisons of the ^1H and ^{13}C NMR data reported for ptilomycalin (5)[2] with those for 1 (Tables I and II) argue the presence of the same ring system and, probably, the same relative stereochemistry.

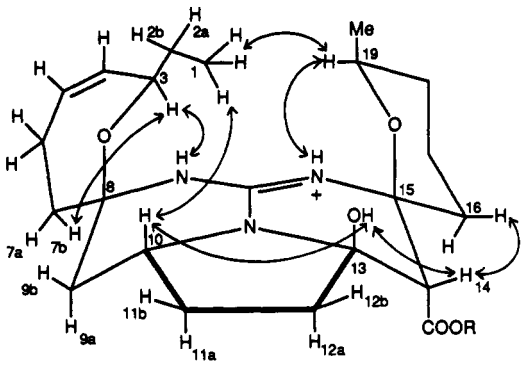
The relative stereochemistry of 1 was assigned by NOE difference spectra (CD_3OD and $CDCl_3$) and ROESY ($CDCl_3$). An NOE between O*H*-13 (δ 5.82, $CDCl_3$) and H-14 (δ 3.38, $CDCl_3$) as well as H-10 (δ 4.32, $CDCl_3$) in the ROESY and NOE difference spectra in $CDCl_3$ located them all on the same side of the molecule, and an NOE observed between H-10 and H-9b (δ 2.58, $CDCl_3$), together with the observed coupling constants between H-10 and H-9a (J = 13 Hz) and H-9b (J = 4.5 Hz), confirmed the relative stereochemistry at C-10. The NOE between H-1 and H-10 assigned the relative stereochemistry at C-8, while an NOE between H-3 (δ 4.55, $CDCl_3$) and the guanidine NH at δ10.01 (cf. above) assigned the relative stereochemistry at C-3. Similarly, NOE's between the guanidine NH at δ 10.03 and H-19 and between H-19 and H-1 assigned the relative stereochemistry at C-15 and C-19 (Scheme III).

Crambescidin 830 (2) (HRFABMS, 831.6300, M + H; Δ2.3 mmu for $C_{46}H_{83}N_6O_7$) differs from 1 by a CH_2 group.[4] FABMS/MS of m/z 831 gave fragments at m/z 744 (M + H − 87) and 628 (M + H − 203), differing from the corresponding MS/MS peaks for 1 by 14 mu, but the fragments 420, 374, and 358 were the same as in the spectrum of 1, indicating that 2 has the additional CH_2 in

(3) As far as we know there is only one report of a hydroxyspermidine moiety from a natural source (bacterial): Rosano, C. L.; Hurwitz, C.; Bunce, S. C. *J. Bacteriol.* **1978**, *135*, 805–808.

(4) The numbering of carbons follows that previously employed for ptilomycalin A (5) and is strictly valid for 1, 4, and 5. For crambescidin 830 (2) one extra carbon (a CH_2 group) is added (arbitrarily C-30a) and for crambescidin 844 (3), two extra (again, CH_2 groups, arbitrarily C-30a and C-30b).

Scheme III



the polymethylene chain. Similarly, crambescidin 844 (**3**) differs from **1** by two methylene groups in the polyethylene chain (FABMS/MS).[4]

Crambescidin 800 (**4**) (HRMS, 801.6205, M + H; Δ1.3 mmu for $C_{45}H_{81}N_6O_6$) differs from **1** by an oxygen (hydroxyl group). FABMS/MS of *m/z* 801 shows fragments corresponding to M + H − 87 and M + H − 203, identifying the hydroxyspermidine unit. At the same time, the presence of *m/z* 358 (Δ 0.0 mmu for $C_{21}H_{32}N_3O_2$) and 404 and the absence of *m/z* 374 and 420 indicate that there is a missing oxygen atom at C-13 in the pentacyclic guanidine portion, as confirmed by the doublet (J = 5.6 Hz) for H-14 replacing the singlet observed for the same proton in **1**.

Compounds **1**–**5** are probably biosynthetically related to crambines A and B, bioinactive guanidine derivatives that were recently isolated from the same sponge,[5] and to ptilocaulin and isoptilocaulin[6] as well.

Experimental Section

General. NMR spectra were obtained with QE-300 (300-MHz, ^{1}H; 75-MHz ^{13}C), NT-360 (360-MHz, ^{1}H), or GN-500 (500-MHz, ^{1}H; 125-MHz, ^{13}C) spectrometers; chemical shifts (δ) are reported in ppm referenced to the solvent peak. High- and low-resolution fast-atom bombardment (FAB) mass spectra were measured on a ZAB-SE spectrometer, FABMS/MS spectra on a 70 SE-4F instrument in the Mass Spectrometry Laboratory, School of Chemical Sciences. HPLC was performed on a system equipped with a Model 110A pump and a Model R-401 differential refractometer, using either a cyano column (25 cm, 0.5-cm i.d., 10-μm particle size, CH_3CN:0.01 M NaCl = 9:1) or a C-18 column (25 cm, 0.8-cm i.d., 5-μm particle size, MeOH:0.1 M NaCl = 9:1).

Extraction and Isolation. Isolation was guided by performing HSV-1 antiviral assays on all extracts and separated fractions. *C. crambe* sponges (sample 12-10-88-2-14) were collected by SCUBA (0 to 9 m) in October 1988 from Isla de Formentor (Cueva), Palma de Mallorca, Spain (39°55′05″N/3°08′05″E) and were identified by Dr. M. J. Uriz-Lespe, Pharma Mar. The material was kept frozen until extracted with MeOH–toluene (3:1). The extract was evaporated in vacuo to give 4.65 g, which was partitioned between $CHCl_3$ and 1 M NaCl (1:1, 100 mL × 3). Separation of the chloroform-soluble (bioactive) fraction on LH-20 with MeOH afforded a bioactive fraction (1.97 g), which was partitioned with hexane–EtOAc–MeOH–H_2O (4:7:4:3). The active lower phase (1.4 g) was purified by HPLC (cyano column, flow rate 1.8 mL/min), affording four fractions. Separation of the active fraction (t_R = 9.8 min) on a reversed-phase (C-18) column (flow rate, 1.8 mL/min) afforded crambescidins 800 (**2**, t_R 8.30 min, 9 mg, 0.2% dry weight), 816 (**1**, t_R 8.75 min, 50 mg, 1.1%), and 830 (**3**, t_R 10 min, 3.5 mg, 0.1%) and a fraction which was further purified by HPLC with the same C-18 column and solvent at a flow rate of 1.2 mL/min to give crambescidin 844 (**4**, t_R 15.2 min).

Crambescidin 816 (1): colorless oil; $[\alpha]^{25}$D −20.14 (*c* 0.4, MeOH); HRFABMS, see supplementary material, S-1; FABMS, see supplementary material, S-8; FABMS/MS, see supplementary material, S-2; ^{1}H NMR ($CDCl_3$, 500 MHz), see supplementary material, S-3; (CD_3OD, 500 MHz), see Table I; ^{13}C NMR, see Table II; ^{1}H COSY (MeOD, 500 MHz), see supplementary material, S-7a and b; HETCOR (MeOD), see supplementary material, S-4; HMBC (MeOD), see supplementary material, S-5; COLOC (MeOD), see supplementary material, S-6.

Acetylation of Crambescidin 816. A solution of crambescidin 816 (8 mg) in pyridine (1.4 mL) was stirred at rt overnight with excess Ac_2O. The resulting evaporation residue was purified by reversed-phase chromatography (RP-18) (MeOH–NaCl(0.1 M) (8:2)) to yield 9.1 mg of acetylated material.

43-*O*-Acetyl-41,45-*N*,*N*′-diacetylcrambescidin 816: HRFABMS 943.6497, $C_{51}H_{87}N_6O_{10}$ (Δ −1.3 mmu); ^{1}H NMR (MeOD, 300 MHz) δ 0.89 (t, J = 7 Hz, 3 H, H-1), 1.13 (d, J = 6.5 Hz, 3 H, H-20), 1.32 (br s, H-26 to H-34), 1.42 (t, J = 13 Hz, 1 H, H-9a), 1.43 (m, 1 H, H-2a), 1.92 (s, 3 H, NCOCH_3), 1.94 (s, 3 H, NHCOCH_3), 2.01 (s, 3 H, OCOCH_3), 2.63 (dd, J = 4.5, 7.3 Hz, 1 H, H-9b), 3.20 (m, 4 H, H-45 and H-41), 3.40 (m, 1 H, H-42a), 3.48 (s, 1 H, H-14), 3.58 (m, 2 H, H-39 and H-42), 3.95 (m, 1 H, H-19), 4.16 (t, J = 6.5 Hz, 2 H, H-23), 4.32 (m, 1 H, H-10), 4.45 (br d, 1 H-3), 5.15 (m, 1 H, H-43), 5.51 (br d, J = 11 Hz, 1 H, H-4), 5.71 (br t, 1 H, H-5).

Crambescidin 800 (4): colorless oil; HRFABMS, see Scheme II; FABMS and FABMS/MS, see supplementary material, S-8 and S-2; ^{13}C NMR, see Table II. Further purification was carried out after acetylation (Ac_2O/Py, rt, overnight) by HPLC (RP (C-18) column, dp = 5 μm; MeOH/0.1 M NaCl (9:1); flow rate 1.8 mL/min; detection by RI) affording 5.9 mg of a major compound (t_R = 16.35 min) and some other minor compounds that are being identified.

43-*O*-Acetyl-41,45-*N*,*N*′-diacetylcrambescidin 800: HRFABMS 927.6550, $C_{51}H_{87}N_6O_9$ (Δ −1.5 mmu); ^{1}H NMR (MeOD, 300 MHz) δ 0.82 (t, J = 7 Hz, 3 H, H-1), 1.08 (d, J = 6.5 Hz, 3 H, H-20), 1.29 (br s, H-26 to H-34), 1.40 (t, J = 12.7 Hz, 1 H, H-9a), 1.88 (s, 3 H, NHCOCH_3), 1.90 (s, 3 H, NHCOCH_3), 2.01 (s, 3 H, OCOCH_3), 2.62 (dd, J = 4.5, 12.8 Hz, 1 H, H-9b), 3.07 (d, J = 5.6 Hz, 1 H, H-14), 3.18 (m, 4 H, H-45 and 41), 3.35–3.58 (4 H, H-42 and H-39), 3.82 (m, 1 H, H-19), 4.05 (m, 1 H, H-13), 4.12 (t, J = 6.5 Hz, 2 H, H-23), 4.32 (m, 1 H, H-10), 4.38 (m, 1H, H-3), 5.12 (m, 1 H, H-43), 5.50 (br d, 1 H, H-4), 5.70 (br t, 1 H, H-5).

Crambescidin 844 (3): colorless oil; $[\alpha]_D^{25}$ −10.32° (*c* 0.19, MeOH); FABMS see supplementary material, S-8; HRFABMS 845.6471 (Δ 0.9 mmu); FABMS/MS, see supplementary material, S-2; ^{13}C NMR, see Table II; ^{1}H NMR (MeOD, 500 MHz) δ 0.89 (t, J = 7 Hz, 3 H, H-1), 1.12 (d, J = 6.5 Hz, 3 H, H-20), 1.43 (t, J = 13 Hz, 1 H, H-9a), 2.65 (dd, J = 4.5, 13 Hz, 1 H, H-9b), 2.88 (m, 2 H, H-41), 3.00 (m, 2 H, H-45), 3.42 (s, 1 H, H-14), 3.67 (m, 1 H, H-39b), 3.98 (m, 2 H, H-19 and H-43), 4.18 (t, J = 6.5 Hz, 2 H, H-23), 4.31 (m, 1 H, H-10), 4.48 (br d, 1 H, H-3), 5.51 (br d, 1 H, H-4), 5.72 (br t, 1 H, H-5).

Fraction Containing Crambescidin 830 (2): colorless oil; HRFABMS 831.6300; FABMS and FABMS/MS, see supplementary material.

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Registry No. **1**, 135257-45-3; **2**, 135257-47-5; **3**, 135283-73-7; **4**, 135257-46-4.

Supplementary Material Available: ^{1}H, ^{13}C, COLOC, COSY, CSCM, HMBC, and ROESY NMR data for **1**; FABMS AND FABMS/MS data for **1**–**4** (12 pages). Ordering information is given on any current masthead page.

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