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Article

Auyuittuqamides A–D, Cyclic Decapeptides from *Sesquicillium microsporum* RKAG 186 Isolated from Frobisher Bay Sediment

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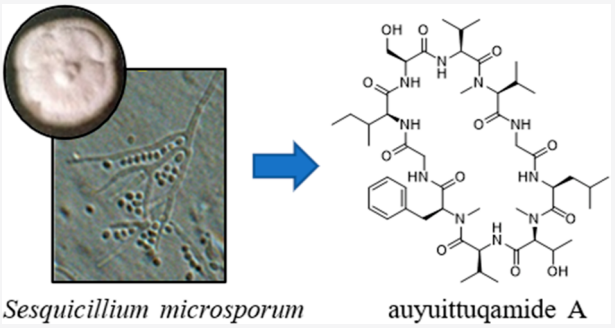
ABSTRACT: Four new cyclic decapeptides, auyuittuqamides A–D (**1**–**4**), were obtained from *Sesquicillium microsporum* RKAG 186 obtained from marine sediment collected from the intertidal zone of Frobisher Bay, Nunavut, Canada. The structures of the compounds were elucidated by NMR spectroscopy and tandem mass spectrometry. The absolute configurations of the amino acids were determined using Marfey's method.



Cyclic peptides constitute a large portion of non-ribosomally synthesized peptides. Due to their increased structural integrity over linear peptides, cyclic peptides have attracted much attention in recent years.[1] With the ability to cyclize in numerous positions along the peptide backbone, cyclic peptides present immense structural diversity, leading to a plethora of biological activities being observed.[2]

Fungi are well known for the production of natural products and have been isolated from a wide range of habitats, although there are very few reports of fungi isolated from polar marine environments.[3] Fungi from polar intertidal environments face many unique challenges and must be able to withstand extreme cold, high ultraviolet radiation, freeze–thaw cycles, and low water and nutrient availability. Despite these environmental challenges, polar marine fungi have proven to be an increasingly fruitful sources of new natural products.[4−6]

Due to its inaccessibility, Canada's arctic has remained a largely untapped resource for microbial natural product discovery. Within the Kerr lab, ongoing bioprospecting efforts from Frobisher Bay, Nunavut, have led to the isolation of several new natural products including the tetramic acid-containing natural products iqalisetins A and B[7] from the fungal isolate *Tolypocladium* sp. RKAG 373, the cyclic heptapetide mortiamides A–D[8] from the fungal isolate *Mortierella* sp. RKAG 110, and the amphiphilic siderophore imaqobactin[9] from the bacterial isolate *Variovorax* sp. RKJM 285. As part of this continued arctic bioprospecting effort, a strain of *Sesquicillium microsporum* (RKAG 186) was isolated from sediment collected from Frobisher Bay and found to produce four new cyclic decapeptides (**1**–**4**). The isolation, structure elucidation, and biological activities of these compounds are reported within.

RESULTS AND DISCUSSION

S. microsporum RKAG186 was isolated from a sediment sample collected in Frobisher Bay, Nunavut, on yeast malt medium supplemented with cottonseed oil. The isolate was identified based on analysis of the ITS nucleotide sequence and morphological observations. Isolate RKAG 186 had 98.4% ITS nucleotide sequence identity to *S. microsporum* NRRL 54217 (GenBank accession no. GU219471.1) and was identified as such.

A 1.5 L solid agar fermentation of *S. microsporum* RKAG 186 was performed. The fermentation was extracted with EtOAc, dried, and partitioned between 80% CH_3CN and hexane. The CH_3CN-soluble portion was subjected to flash chromatography and RP HPLC, yielding four new cyclic decapeptides, auyuittuqamides A (**1**) (4 mg), B (**2**) (1.5 mg), C (**3**) (3 mg), and D (**4**) (2 mg). The compounds were named after the Inuktitut word "auyuittuq", meaning "the land that never melts".

Auyuittuqamide A (**1**) (Figure 1, Table 1) was obtained as a white powder, and HRESIMS supported a molecular formula of $C_{50}H_{82}N_{10}O_{12}$, requiring 15 degrees of unsaturation. The peptidic nature of the compound was determined by analysis of the ^{1}H NMR spectrum, which revealed the presence of seven amide protons and three *N*-methyl amide substituents (δ_H 2.78, 3.16, 3.24), while the ^{13}C NMR spectrum revealed

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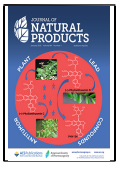

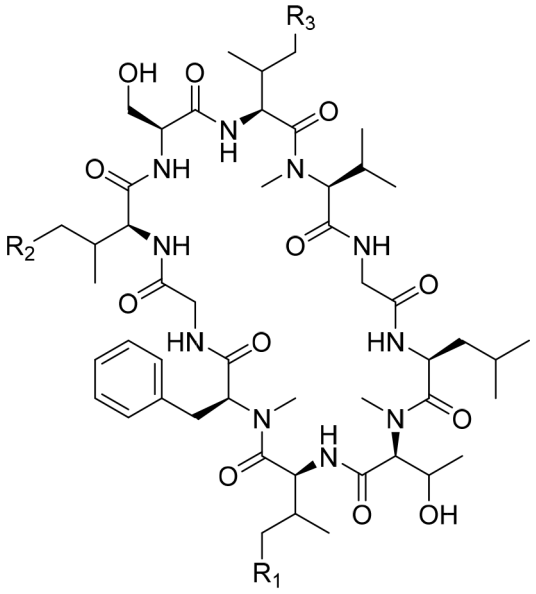

1 R_1 = H R_2 = CH_3 R_3 = H
2 R_1 = H R_2 = H R_3 = H
3 R_1 = CH_3 R_2 = CH_3 R_3 = H
4 R_1 = CH_3 R_2 = CH_3 R_3 = CH_3

the presence of 10 amide carbonyls (δ_C 167.6−173.3) and 10 α-amino acid carbon resonances (δ_C 43.0−70.2). Analysis of COSY, HMBC, HSQC, and TOCSY spectra confirmed the identity of the amino acid constituents and revealed the presence of two Val, two Gly, one Ser, one Ile, one Leu, one *N*-Me-Phe, one *N*-Me-Val, and one *N*-Me-Thr residue within the molecule. In order to account for the remaining degree of unsaturation, it was determined that this compound must be cyclic. There were three options for the mechanism of cyclization: it could either cyclize between the N- and C-terminal amino acids in a peptide bond or cyclize at the C-terminal amino acid and the hydroxy of the threonine or serine side chain in an ester linkage.[10] Due to the presence of free hydroxy groups for the Ser (δ_H 4.86) and Thr (δ_H 4.67) side chains, it was determined that this molecule cyclized in a peptide bond between the N-terminal and C-terminal amino acids.

The order of the amino acids was determined using HMBC and ROESY correlations and tandem mass spectrometry. HMBC correlations from Val-1 NH-7 (δ_H 8.70) to *N*-Me-Thr C-1 (δ_C 169.0), *N*-Me-Thr H_3-5 (δ_H 3.15) to Leu C-45 (δ_C 173.4), Leu NH-46 (δ_H 7.46) to Gly-2 C-43 (δ_C 168.3), and Gly-2 NH-44 (δ_H 7.45) to *N*-Me-Val C-37 (δ_C 169.5) established the five amino acid sequence *N*-Me-Val-Gly-Leu-*N*-Me-Thr-Val. HMBC correlations from Ile NH-24 (δ_H 7.44) to Gly-1 C-21 (δ_C 167.7) and Gly-1 NH-22 (δ_H 7.76) to *N*-Me-Phe C-11 (δ_C 169.9) established the three amino acid fragment lle-Gly-*N*-Me-Phe. A third fragment (Ser-Val) was established by HMBC correlations from Val-2 NH-33 (δ_H 8.91) to Ser C-29 (δ_C 170.2). Due to the overlapping carbonyl chemical shifts of Val-1, Val-2, and Ile (δ_C 171.6−171.7), these three fragments could not be definitively connected through HMBC correlations. ROESY correlations from *N*-Me-Val H_3-42 (δ_H 3.25) to Val-2 H-33 (δ_H 4.53), Ser NH-30 (δ_H 8.57) to Ile H-24 (δ_H 4.42), and *N*-Me-Phe H_3-20 (δ_H 2.77) to Val-1 H-7 (δ_H 4.48) connected all three fragments as a cyclic peptide whose final structure was revealed to be cyclo [-N-Me-Thr-Val-N-Me-Phe-Gly-Ile-Ser-Val-N-Me-Val-Gly-Leu-]. MS/MS analysis confirmed the sequence of the peptide (Figure S5).

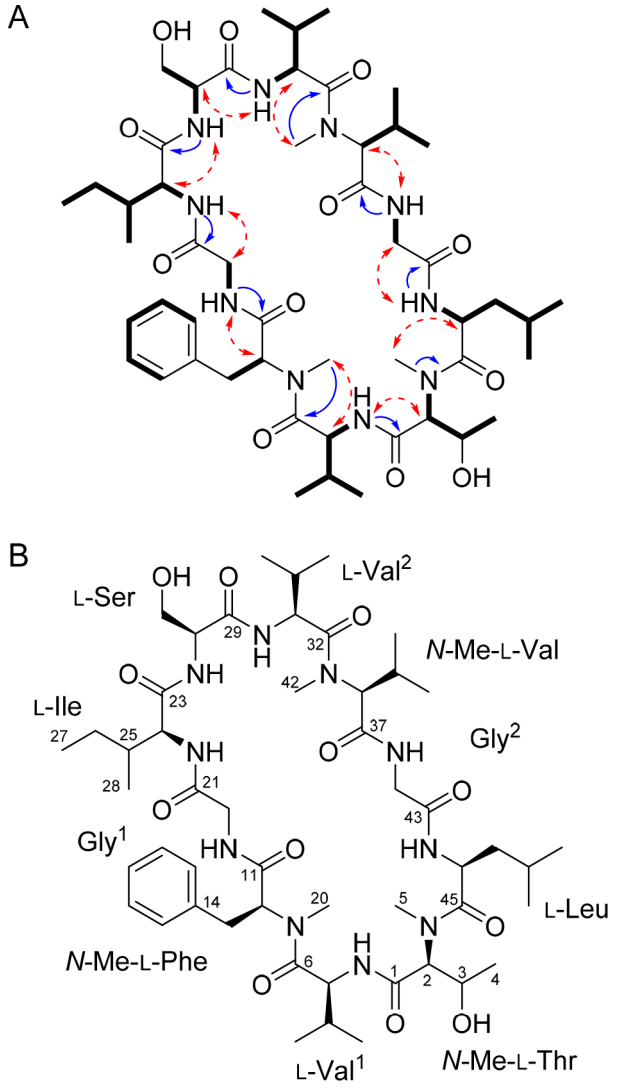

Figure 1. Two-dimensional structural characterization of **1** showing (A) key COSY (bold lines), HMBC (blue solid arrows), and ROESY (red dashed arrows) correlations. (B) Structure of **1** with absolute configuration assigned.

Auyuittuqamide B (**2**) (Table S1) was obtained as a white powder, and HRESIMS supported a molecular formula of $C_{49}H_{80}N_{10}O_{12}$, requiring 15 degrees of unsaturation. The ^{1}H NMR spectrum was very similar to that of **1** and indicated **2** was an analogue of **1** that differed by the absence of a methylene group. Analysis of the COSY and TOCSY spectra indicated the Ile residue was replaced by a Val residue. HMBC correlations from Val-3 NH-24 (δ_H 7.41) to Gly-1 C-21 (δ_C 167.8) and ROESY correlations from Ser NH-29 (δ_H 8.59) to Val-3 H-24 (δ_H 4.38) confirmed the new Val residue had replaced the Ile residue in the same location. The identity and sequence of the other amino acids were confirmed by NMR analysis and tandem mass spectrometry to be identical to **1**. Therefore **2** was assigned as cyclo [-*N*-Me-Thr-Val-*N*-Me-Phe-Gly-Val-Ser-Val-*N*-Me-Val-Gly-Leu-].

Auyuittuqamide C (**3**) (Table S2) was obtained as a white powder, and HRESIMS supported a molecular formula of $C_{51}H_{84}N_{10}O_{12}$, requiring 15 degrees of unsaturation. The ^{1}H NMR spectrum was very similar to that of **1** and indicated **3**

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Table 1. NMR Spectroscopic Data for Auyuittuqamide A in DMSO-d_6 (^{1}H 600 MHz, ^{13}C 151 MHz)

position	δ_C, type	δ_H (J in Hz)	position	δ_C, type	δ_H (J in Hz)
N-Me-Thr			Ser		
1	169.0, C		29	170.2, C	
2	61.7, CH	5.04, d (9.7)	30	55.2, CH	4.60, m
3	62.9, CH	3.89, m	30-NH		8.57, d (7.2)
3-OH		4.66	31	60.7, CH_2	3.67, dd (10.0, 7.4)
4	20.5, CH_3	0.89, d (6.1)			3.48, dd (10.0, 7.8)
5	30.6, CH_3	3.15, s	31-OH		4.86, s
Val[1]			Val[2]		
6	171.6, C		32	171.6, C	
7	52.9, CH	4.48, m	33	54.1, CH	4.53, m
7-NH		8.70, d (9.4)	33-NH		8.91, d (9.8)
8	30.7, CH	1.90, m	34	30.0, CH	2.01, m
9	19.3, CH_3	0.78, m	35	19.5, CH_3	0.84, m
10	17.6, CH_3	0.73, d (6.7)	36	18.1, CH_3	0.83, m
N-Me-Phe			*N*-Me-Val		
11	169.9, C		37	169.5, C	
12	66.6, CH	3.93, dd (10.3, 4.1)	38	70.2, CH	3.30, m
13	33.9, CH_2	3.33, m	39	27.5, CH	2.50, m
		2.97, dd (14.0, 10.3)	40	21.8, CH_3	1.04, d (6.6)
14	138.9, C		41	19.3, CH_3	0.83, m
15/19	128.3, CH	7.28, m	42	40.0, CH_3	3.25, s
16/18	129.2, CH	7.23, m			
17	126.3, CH	7.21, m	Gly[2]		
20	39.2, CH_3	2.77, s	43	168.3, C	
			44	43.0, CH_2	3.84, m
Gly[1]					3.36, m
21	167.7, C		44-NH		7.45, m
22	42.8, CH_2	3.79, dd (16.9, 4.8)			
		3.17, m	Leu		
22-NH		7.76, t (5.5)	45	173.4, C	
			46	46.3, CH	4.91, m
Ile			46-NH		7.46, m
23	171.7, C		47	40.5, CH_2	1.65, m
24	54.9, CH	4.42, m			1.17, m
24-NH		7.44, m	48	23.8, CH	1.63, m
25	37.4, CH	1.84, m	49	23.2, CH_3	0.82, m
26	23.6, CH_2	1.46, m	50	21.8, CH_3	0.84, m
		1.20, m			
27	10.5, CH_3	0.77, m			
28	15.0, CH_3	0.81, m			

was an analogue of **1** that differed by the presence of a methylene group. Analysis of the COSY and TOCSY spectra indicated that one of the Val residues was replaced by an Ile residue. HMBC correlations from Ile-1 NH-7 (δ_H 8.63) to *N*-Me-Thr C-1 (δ_C 168.8) and ROESY correlations from *N*-Me-Phe H-21 (δ_H 2.82) to Ile-1 H-7 (δ_H 4.59) confirmed the position of the new Ile residue. The identity and sequence of the other amino acids was confirmed by NMR analysis and tandem mass spectrometry to be identical to **1**. Therefore **3** was assigned as cyclo [-*N*-Me-Thr-Ile-*N*-Me-Phe-Gly-Ile-Ser-Val-*N*-Me-Val-Gly-Leu-].

Auyuittuqamide D (**4**) (Table S3) was obtained as a white powder, and HRESIMS supported a molecular formula of $C_{52}H_{86}N_{10}O_{12}$, requiring 15 degrees of unsaturation. The ^{1}H NMR spectrum was very similar to that of **3** and indicated **4** differed by the presence of a methylene group, which corresponded to the replacement of the final Val residue with an Ile residue. HMBC correlations from Ile-3 NH-34 (δ_H 8.85) to Ser C-30 (δ_C 170.0) and ROESY correlations from *N*-Me-Val H_3-44 (δ_H 3.27) to Ile-3 H-34 (δ_H 4.69) confirmed the position of the Ile. The identity and sequence of the remaining amino acids were confirmed by NMR analysis and tandem mass spectrometry to be identical to **3**. Therefore **4** was assigned as cyclo [-*N*-Me-Thr-Ile-*N*-Me-Phe-Gly-Ile-Ser-Ile-*N*-Me-Val-Gly-Leu-].

Amino acid configurations of **1**−**4** were determined by Marfey's analysis.[11] Compounds **1**−**4** were hydrolyzed with 6 M HCl and treated with 1-fluoro-2,4-dinitrophenyl-5-L-alanine amide (L-FDAA). The hydrosylate was analyzed by LC-HRMS and compared to L-DAA-derivatized amino acid standards. Due to a lack of commercially available *N*-Me-D-Thr, an analytical standard was prepared from Fmoc-*N*-Me-D-Thr-(tbu)-OH. A lack of availability of a commercial standard of *N*-Me-D-*allo*-Thr meant this stereocenter was unable to be resolved in the final structure. Additionally, due to a lack of separation of L-Ile and L-*allo*-Ile by LC-HRMS using a C18 stationary phase, the configuration at the β-carbon remains ambiguous.

Compounds **1**−**4** were tested for cytotoxic activity against the breast cancer cell lines MCF-7 and HTB-26 as well as against a human epithelial keratinocyte cell line but were inactive (IC_{50} > 10 μM, Table S4). No antimicrobial activity was observed for **1**−**4** when tested up to 128 μM.

Auyuittuqamides A−D represent new members within the cyclic decapeptide family. The isolation of cyclic decapeptides is quite rare, and only a few examples have been reported from microorganisms including fungi,[12,13] bacteria,[14−16] and cyanobacteria.[17] These previously reported cyclic peptides have limited structural similarity to the auyuittuqamides, with all previously reported examples containing proline residues, which impart greater structural rigidity to these compounds than with the auyuittuqamides. The presence of multiple *N*-methylated amino acids within the auyuittuqamides is unique within the decapeptide family and has not been previously reported for fungal cyclic decapeptides. Within this family, only singular *N*-methylated amino acids have been reported, as is the case with calophycin[17] and the minutissamides, both isolated from a cyanobacteria.[18] The isolation of the auyuittuqamides represents the first report of fungal *N*-methylated cyclic decapeptides and highlights Canada's arctic as a resource for the discovery of new and distinct natural products.

EXPERIMENTAL SECTION

General Experimental Procedures. Optical rotations were measured on a Rudolph Autopol III polarimeter using a 50 mm microcell (1.2 mL). Infrared spectra were recorded using attenuated total reflectance, on a Thermo Nicolet 6700 FT-IR spectrometer.

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NMR spectra were obtained on a Bruker Avance III NMR spectrometer (^{1}H: 600 MHz, ^{13}C: 151 MHz) equipped with a 5 mm cryoprobe. All chemical shifts (δ) are referenced to the DMSO-d_6 residual solvent peaks [^{1}H (DMSO-d_6): 2.50 ppm; ^{13}C (DMSO-d_6): 39.51 ppm].

LC-HRMS of compounds and extracts was carried out with an ESI-HRMS Exactive (Thermo Scientific) operating in positive mode with a resolution of 30 000, monitoring a mass range from 190 to 2000 amu. Chromatography was carried out using a Core−Shell 100 Å C18 column (Phenomenex, Kinetex, 1.7 μm 50 × 2.1 mm) using a linear solvent gradient from 95% H_2O/0.1% formic acid (solvent A):5% CH_3CN/0.1% formic acid (solvent B) to 100% solvent B over 4.8 min followed by a hold for 3.2 min. A flow rate of 500 μL min^{-1} and 10 μL injection volume were used. Eluant was detected by ESIMS, ELSD, and UV 200−600 nm.

Direct infusion (MS/MS analysis) high-resolution mass spectrometry analysis was carried out on an LTQ Orbitrap Velos mass spectrometer (Thermo Scientific) using an ESI ion source operating in positive mode with a resolution of 30 000, monitoring a mass range from 150 to 1000 amu. Selected ions were fragmented using a collision-induced dissociation energy of 35 eV.

Automated flash chromatography was performed on a Teledyne Combiflash Rf200 using C18 RediSep columns (24 g). HPLC purifications were carried out on a Waters auto purification system coupled with an evaporative light-scattering detector and UV detector. All amino acid standards were purchased from Sigma-Aldrich. All reagents were purchased from commercial sources and used without further purification unless otherwise stated.

Isolation of *Sesquicillium microsporum* RKAG 186. A marine sediment core was collected using a sterile sediment sampler (LaMotte) at low tide at a depth of 30 cm in Frobisher Bay, Nunavut, Canada (63.72804° N 68.41989° W) in August 2011. The core was transferred to a sterile 50 mL conical tube, brought back to the lab on ice, and stored at −80 °C until processing. The sediment was passed through a series of sieves (104 and 51 μM) and separated based on particle size in order to increase the rate of isolation of fungi originating from vegetative propagules embedded within substrate particles as opposed to dormant spores. The separated particles were resuspended in sterile H_2O containing 0.2 g/L chloramphenicol and 18 g/L Instant Ocean and were serially diluted (100- and 1000-fold dilutions). A 10 μL aliquot from each dilution was pipetted into each well of a 48-well plate containing YM and cottonseed oil agar and incubated at 4 or 22 °C for three months. Emerging fungal colonies were purified to obtain axenic cultures of isolate RKAG 186. Identification of the fungus was performed by observation of the culture phenotype (both macro- and micromorphology) and sequence homology of the ITS1-5.8S-ITS2 region (sequence data deposited in GenBank with the accession number MW149114).

Extraction and Purification. Isolate RKAG 186 was inoculated into 15 mL of YM liquid seed medium at 22 °C and agitated at 200 rpm for 5 days. The seed culture (200 μL) was used to inoculate the isolate onto 150, 100 × 15 mm Petri plates containing 20 mL of solid PDA agar and grown for 21 days at 22 °C. The solid agar cultures were roughly cut up, pooled, and extracted with EtOAc. The extract was evaporated to dryness and partitioned between 80% CH_3CN/H_2O and 100% hexane. The CH_3CN layer was collected and evaporated to dryness in vacuo to give a CH_3CN extract (138 mg).

The extract was fractionated using automated medium-pressure reversed-phase flash chromatography with a linear gradient from 20% aqueous MeOH to 100% MeOH over 15 min on a 15.5 g C18 column (High Performance GOLD RediSep Rf) with a flow rate of 30 mL/min. The semipure fraction eluting at 9.5 min was subjected to reversed-phase HPLC using a Gemini 110A C18 column (5 μm 250 × 10 mm, Phenomenex) and 20 min isocratic elution with 65% aqueous CH_3CN (0.1% formic acid), resulting in the purification of **1** (4.1 mg), **2** (1.5 mg), **3** (2 mg), and **4** (3 mg).

*Auyuittuqamide A (**1**).* White powder; $[\alpha]^{23}_D$ −3.6 (*c* 0.1, MeOH); UV (MeOH) λ_{max} 222 nm; IR (film) ν_{max} 3270, 2965, 1627, 1546, 1418, 1340, 1292, 1112, 1018 cm^{-1}; ^{1}H and ^{13}C NMR data, Table 1; HRESIMS *m*/*z* 1015.6201 [M + H]$^+$, (calcd for $C_{50}H_{83}N_{10}O_{12}$, 1015.6187, Δ 1.38 ppm).

*Auyuittuqamide B (**2**).* White powder; $[\alpha]^{23}_D$ −4.9 (*c* 0.1, MeOH); UV (MeOH) λ_{max} 222 nm; IR (film) ν_{max} 3282, 2960, 1632, 1547, 1470, 1417, 1386, 1350, 1205, 1138, 1026 cm^{-1}; ^{1}H and ^{13}C NMR data, Table 1; HRESIMS *m*/*z* 1001.6013 [M + H]$^+$ (calcd for $C_{49}H_{81}NO_5$, 1001.6030, Δ 1.70 ppm).

*Auyuittuqamide C (**3**).* White powder; $[\alpha]^{23}_D$ −1.6 (*c* 0.1, MeOH); UV (MeOH) λ_{max} 222 nm; IR (film) ν_{max} 3282, 2964, 1632, 1547, 1467, 1417, 1386, 1209, 1112 cm^{-1}; ^{1}H and ^{13}C NMR data, Table 1; HRESIMS *m*/*z* 1029.6342 [M + H]$^+$ (calcd for $C_{51}H_{85}NO_4$, 1029.6343, Δ 0.01 ppm).

*Auyuittuqamide D (**4**).* White powder; $[\alpha]^{23}_D$ −1.8 (*c* 0.1, MeOH); UV (MeOH) λ_{max} 222 nm; IR (film) ν_{max} 3273, 2963, 1629, 1548, 1465, 1417, 1112, 1016 cm^{-1}; ^{1}H and ^{13}C NMR data, Table 1; HRESIMS *m*/*z* 1043.6550 [M + H]$^+$ (calcd for $C_{52}H_{87}NO_5$, 1043.6500, Δ 4.79 ppm).

Preparation of *N*-Me-D-Thr Standard. To a vial containing Fmoc-*N*-Me-D-Thr(tbu)-OH (18 mg, 47 μmol, 1 equiv) in CH_2Cl_2 (1 mL), TFA (1 mL) was added dropwise and the reaction was left to stir at rt for 16 h. The reaction was neutralized using 1 N NaOH and concentrated under reduced pressure before being resuspended in H_2O (5 mL) and extracted with EtOAc (3 × 5 mL). The organic layers were combined and subjected to purification through reversed phase flash chromatography, yielding Fmoc-*N*-Me-D-Thr-OH as an off-white solid (13 mg, yield 83%).

In a vial containing Fmoc-*N*-Me-D-Thr-OH (13 mg, 47 μmol, 1 equiv) in DMF (800 μL) piperidine (200 μL) was added and the reaction was left to stir at rt for 16 h. The reaction was concentrated under reduced pressure and taken forward for derivatization without further purification.

Amino Acid Configuration by Marfey's Analysis. Auyuittuqamides A−D (0.25 mg each) were hydrolyzed by stirring in 6 M HCl (60 μL) at 80 °C for 6 h and neutralized with 1 M $NaHCO_3$ solution. *N*-(5-Fluoro-2,4-dinitrophenyl-5)-L-alaninamide (FDAA, 0.4 mg in 380 μL of acetone) was added to the reaction mixture and stirred at 37 °C for 2 h. The reaction was quenched with 1 N aqueous HCl (80 μL) and dried before the addition of MeOH for analysis by LC-HRMS. LC-HRMS analyses was conducted using a Hypersil Gold 100 Å column (Thermo, 1.9 μm C18 50 mm × 2.1 mm) and a flow rate of 400 μL/min. The following method was used: 0−55 min 95% H_2O/0.1% formic acid (solvent A):5% CH_3CN/0.1% formic acid (solvent B) to 60% solvent A:40% solvent B, 55−57 min 60% solvent A:40% solvent B to 100% solvent B, 57−60 min 100% solvent B. Retention times were compared to derivatized amino acid standards to determine the amino acid configurations. Chromatograms of derivatized standards and hydrolysates are located within the Supporting Information.

Antimicrobial Assays. Compounds **1**−**4** were tested for antimicrobial activity according to Clinical Laboratory Standards Institute testing standards in a 96-well plate microbroth dilution assay as previously described.[19] Compounds were tested against the human microbial pathogens methicillin-resistant *Staphyloccocus aureus* ATCC 33591, vancomycin-resistant *Enterococcus faecium* EF379, *Staphylococcus warneri* ATCC 17917, *Pseudomonas aeruginosa* ATCC 14210, and *Candida albicans* ATCC 14035. Optical density was recorded at T_{zero} and T_{final} using a Thermo Scientific Varioskan Flash plate reader at 600 nm to determine growth inhibition after incubation for 22 h (37 °C).

Cytotoxicity Assays. Compounds **1**−**4** were tested for cytotoxicity against adult human epidermal keratinocytes (HEKa), human breast adenocarcinoma cells (ER −) (ATCC HTB-26), and human breast adenocarcinoma cells (ER +) (ATCC MCF-7) in triplicate in a 96-well cell culture plate as described previously.[19] Cell viability was determined 24 h after treatment using the redox dye Alamar Blue to extrapolate cell viability. Fluorescence was monitored using a Thermo Scientific Varioskan Flash plate reader at 560/12 excitation, 590 nm emission both at time zero and 4 h after Alamar Blue addition.

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■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.jnatprod.0c00966.

^{1}H and ^{13}C NMR data of **2**−**4**, NMR spectra, LC-HRMS profiles, MS/MS fragmentation analysis, and Marfey's analysis chromatograms (PDF)

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Notes

The authors declare no competing financial interest.

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