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The total synthesis of bistratamides F–I

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Dedicated to Professor Li-Xin Dai on the occasion of his 80th birthday

Abstract—The total synthesis of bistratamides F–I (**2**–**5**) have been achieved in overall yields of 3, 10, 13, and 27%, respectively. The thiazole substructure was prepared utilizing a MnO_2 oxidation of a thiazoline, synthesized from a Val-Cys dipeptide using bis(triphenyl)oxodiphosphonium trifluoromethanesulfonate. The serine-based oxazole substructure was prepared from a Val-Ser dipeptide using literature methods. The threonine-derived oxazole substructure was synthesized from a ketoamide dipeptide using the bisphosphonium salt employed for thiazoline preparation. Most of the amide bonds were formed using HBTU and HOBt in the presence of DIEA. The final macrocyclization step was accomplished efficiently by PyBOP and DMAP in all cases.

1. Introduction

Many oxazole and/or thiazole-containing macrocycles have been recently isolated from marine organisms.[1–2] Their activities as cytotoxic agents and multiple drug resistance inhibitors, as well as their metal binding and transport properties have led to much synthetic interest.[3] Bistratamides are a family of macrolactams isolated from *Lissoclinum bistratum* in the southern Philippines.[4] Their interesting biological activities led to total syntheses of three bistratamide family members.[5] Bistratamides E–J (**1**–**6**) were very recently isolated and exhibit moderate cytotoxic activity against a human colon tumor (HCT-116) cell line (Fig. 1).[4c] The antimicrobial, antitumor and the anti-drug resistance properties of members of this family of natural products warrant the synthetic efforts published thus far to prepare natural products related to bistratamides E–J.

Construction of the thiazoles in these macrolactams is central to their total synthesis. Commonly used methods for the preparation of thiazolines and thiazoles include (1) a modification of Hantzsch's procedure using thioamides as intermediates,[6] (2) a condensation reaction between cysteine esters and *N*-protected imino esters,[7] and (3) the cyclodehydration of β-hydroxythioamides using either Mitsunobu conditions or the Burgess reagent.[8–9] Thiazolines are readily converted into thiazoles by oxidation.[3a–d] Recently, we reported a facile and efficient biomimetic synthesis of thiazolines accomplished by treating *N*-acylated cysteines with bis(triphenyl)oxodiphosphonium trifluoromethanesulfonate.[10] Dendroamide A, as well as bistratamides E (**1**) and J (**6**) have been recently efficiently synthesized by taking advantage of this methodology.[11] In this paper, we report the synthesis of bistratamides F–I (**2**–**5**, respectively) using bis(triphenyl)-oxodiphosphonium trifluoromethanesulfonate to construct the thiazoline and threonine-derived oxazole precursors. Amide bond formation was utilized to stitch the heterocyclic amino acids together while PyBOP and DMAP were employed to facilitate the final macrolactamization.

2. Results and discussion

The retrosynthetic analysis for bistratamide F (**2**) is shown in Figure 2. Disconnections at the amide bonds result in two Fmoc-protected α-amino acids and two heterocyclic amino acids derived from dipeptides.

The thiazole-containing fragment (**7**) was synthesized as shown in Scheme 1. The synthesis commences with the protection of the carboxylic acid of *N*-Fmoc-*S*-trityl-L-cysteine as an allyl ester. Fmoc deprotection allows the resulting amine to be coupled with an activated ester of *N*-Fmoc-L-valine to afford the fully protected dipeptide **9** (84% overall, 3 steps). Bis(triphenyl)oxodiphosphonium trifluoromethanesulfonate was utilized to convert the trityl

Keywords: Bistratamide; Bis(triphenyl)oxodiphosphonium trifluoromethanesulfonate; Oxazole; Thiazole.
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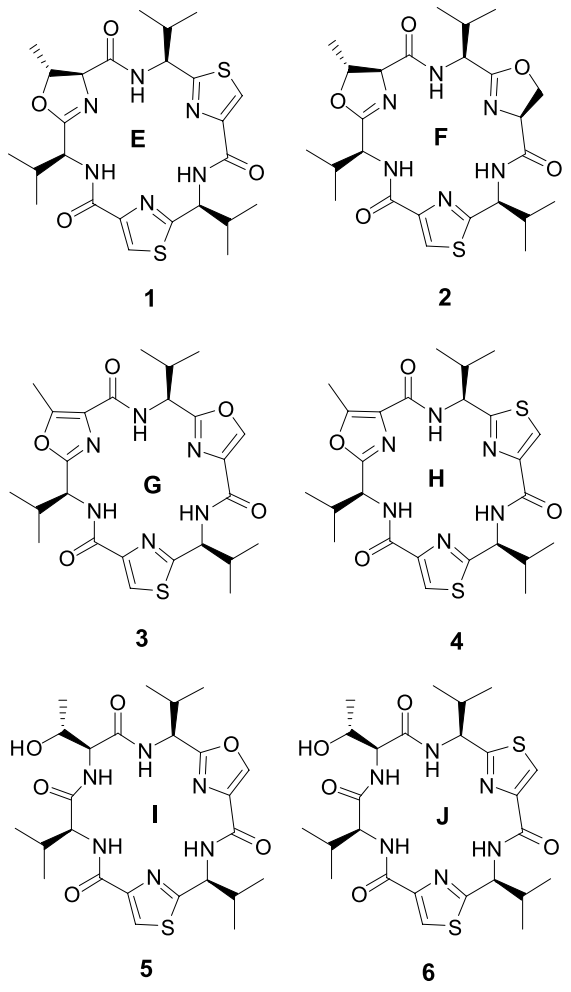


Figure 1. Bistratamides E–J (**1**–**6**).

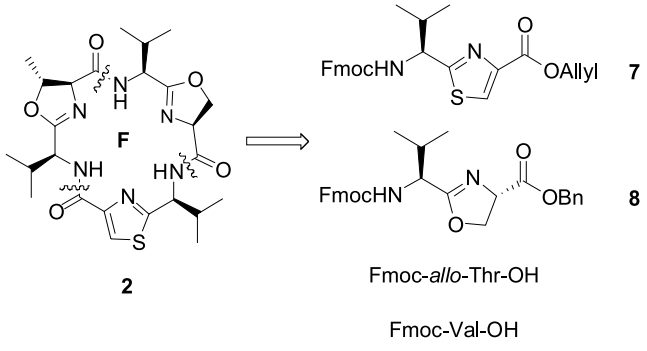
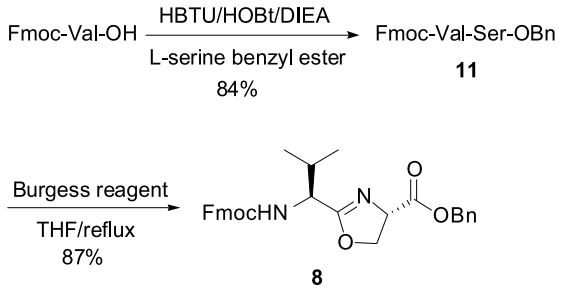


Figure 2. Retrosynthetic analysis for bistratamide F (**2**).

protected cysteine-containing dipeptide **9** into thiazoline **10** (89%). Thiazoline **10** was oxidized to a thiazole **7** employing activated manganese oxide (94%; >96% ee).[11b]

The synthesis of compound **8** is depicted in Scheme 2. Dipeptide **11** was synthesized by coupling *N*-Fmoc-L-valine and L-serine benzyl ester utilizing HBTU (2-(1H-benzotriazole-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate) and HOBt (*N*-hydroxybenzotriazole) in the presence of DIEA (*N*,*N*-diisopropylethylamine). Treating compound **11** with the Burgess reagent in refluxing THF afforded oxazoline **8** (87%).

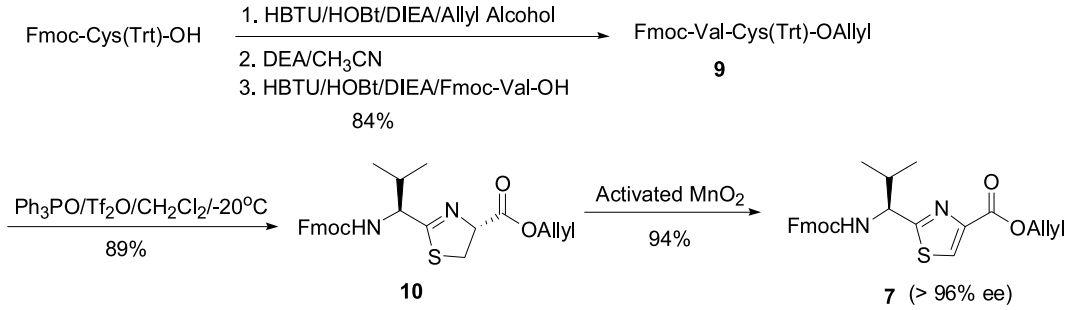


Scheme 2. Synthesis of the oxazoline-containing amino acid **8**.

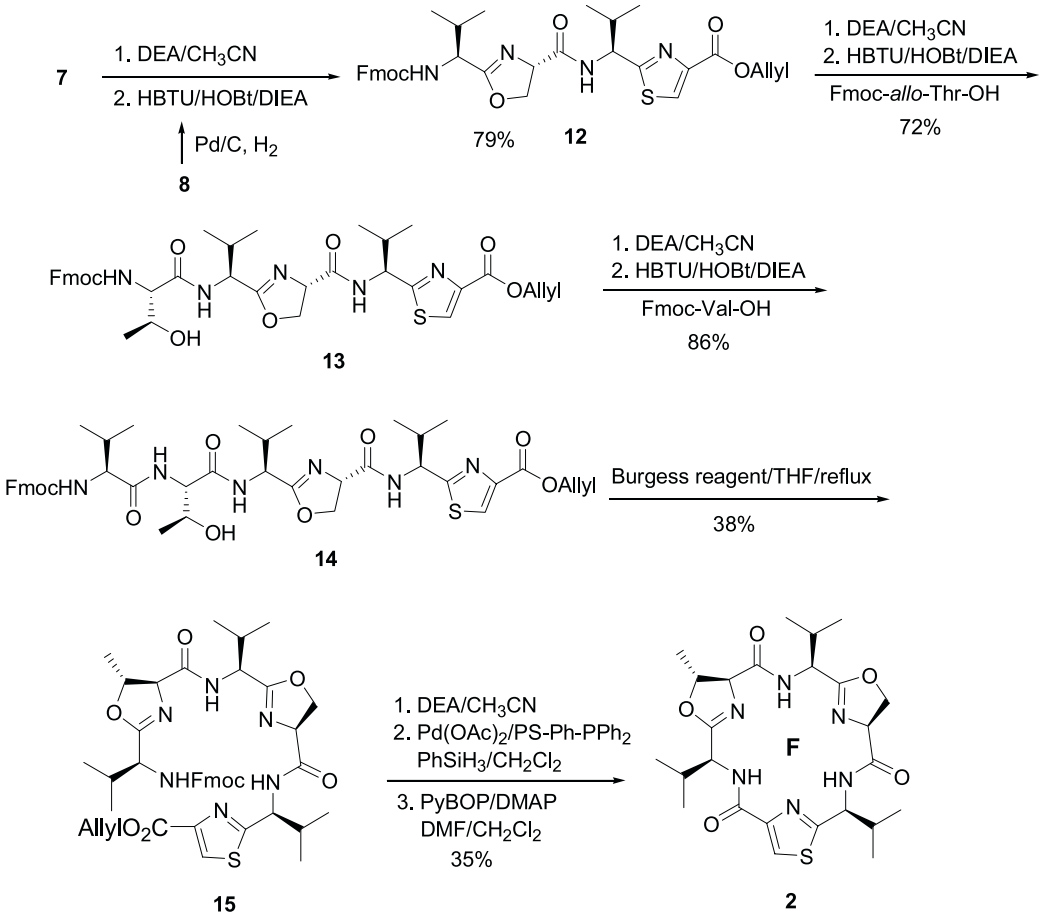
Thiazole **7** was coupled with the carboxylic acid resulting from removal of the benzyl protecting group from oxazoline **8** (using a Pd/C mediated hydrogenation) utilizing HBTU and HOBt in the presence of DIEA (Scheme 3). The resulting amide-linked bisheterocycle **12** was obtained in 79% yield. Compound **12** was coupled sequentially with *N*-Fmoc-*allo*-threonine and *N*-Fmoc-L-valine employing HBTU/HOBt/DIEA affording **13** (72%) and **14** (86%), respectively. Treating compound **14** with the Burgess reagent in refluxing THF afforded **15** (38%).

Removal of the Fmoc group in **15** using diethylamine followed by cleavage of the allyl ester using a palladium catalyst,[12] generated from $Pd(OAc)_2$ and polymer-supported triphenylphosphine, gave the amino acid macrolide precursor. The final cyclization mediated by PyBOP (benzotriazole-1-yl-oxy-tris-pyrrolidino-phosphonium hexafluorophosphate) and DMAP (4-dimethylaminopyridine) yielded **2** (35%). Bistratamide F (**2**) was obtained as a white semisolid having identical ^{1}H and ^{13}C NMR spectra to those reported in the literature.[4c]

The retrosynthetic analysis for bistratamide G (**3**) is outlined



Scheme 1. Synthesis of the thiazole-containing amino acid **7**.



Scheme 3. Completion of the synthesis of bistratamide F (**2**).

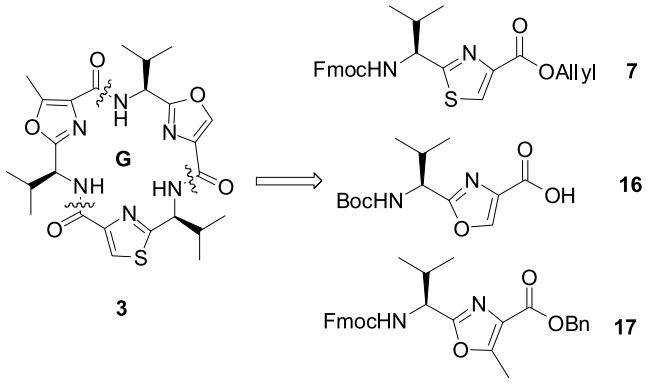
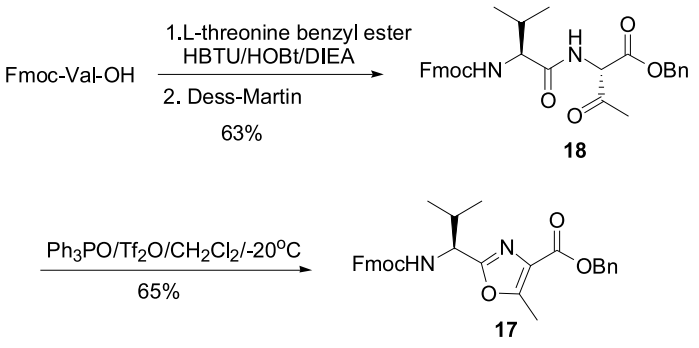


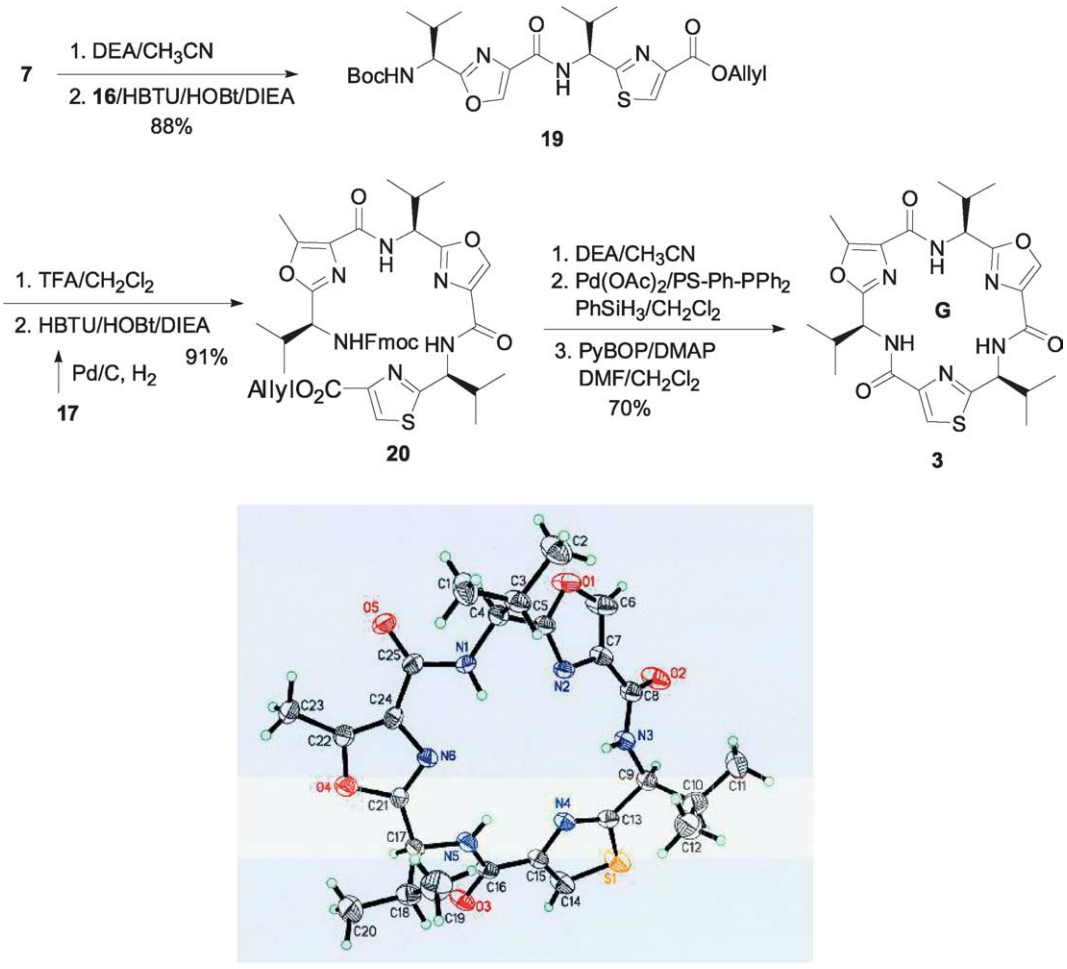
Figure 3. Retrosynthetic analysis for bistratamide G (**3**).

in Figure 3. Disconnections at the amide bonds result in three heterocyclic amino acids derived from dipeptides. The synthesis of compound **16** was performed following a known procedure.[5b,13] The synthesis of oxazole **17** is shown in Scheme 4. Coupling *N*-Fmoc-L-valine to L-threonine benzyl ester gave a dipeptide, which afforded ketone **18** when the dipeptide was subjected to a Dess–Martin oxidation.[14] Bis(triphenyl)oxodiphosphonium trifluoromethanesulfonate was used to convert the β-ketodipeptide **18** to the protected oxazole amino acid **17** (65%) without compromising the valine-derived stereocenter.

The carboxylic acid **16** was coupled with the free amine generated by removing the Fmoc group from **7** (diethylamine) utilizing HBTU and HOBt in the presence of DIEA



Scheme 4. Synthesis of the oxazole-containing amino acid **17**.



Scheme 5. Completion of the synthesis of bistratamide G (**3**) and an ORTEP diagram of the X-ray structure of bistratamide G (**3**).

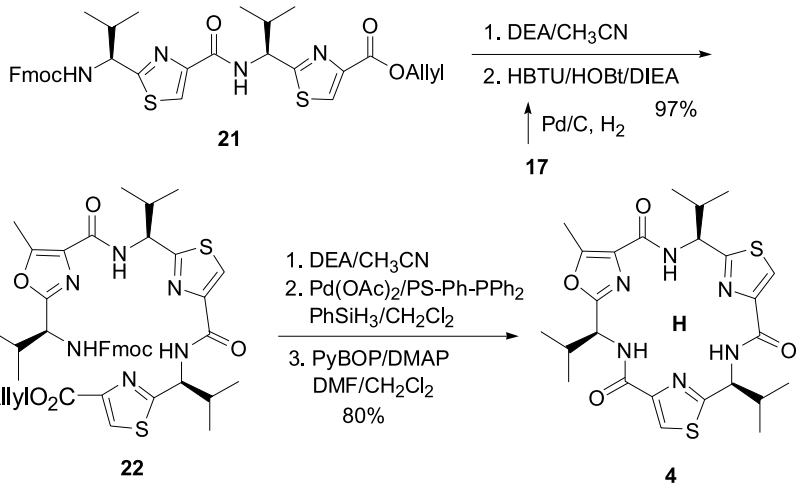
(Scheme 5). The bisheterocyclic amino acid **19** was thus obtained in 88% yield. The Boc group in **19** was removed by a TFA treatment. The resulting free amine was coupled with the amino acid generated from **17** by removal of the benzyl group (using a Pd/C mediated hydrogenation), yielding **20** (91%). Removal of the Fmoc and allyl groups in **20** as described above for **15** gave the amino acid macrolide precursor. The final macrolactamization was mediated by PyBOP and DMAP yielding **3** (70%). Bistratamide G (**3**) was obtained as a white solid having identical ^{1}H and ^{13}C NMR spectra to those reported in the literature.[4c] The structure of **3** was also verified by X-ray crystallography (Scheme 5).[15]

Bistratamide H (**4**) was synthesized from oxazole **17** and the bisheterocyclic amino acid **21** (Scheme 6), which was easily prepared from the coupling of two differentially protected molecules derived from thiazole **7**.[11b] The bisheterocyclic amino acid **21** was coupled with the carboxylic acid resulting from deprotection of **17**, affording **22** in 97% yield. Removal of the Fmoc and allyl groups in **22**, as described above, afforded the amino acid macrolide precursor. PyBOP and DMAP promoted the final macrolactamization yielding bistratamide H (**4**) (80%), which exhibited identical ^{1}H and ^{13}C NMR spectra to those reported in the literature.[4c]

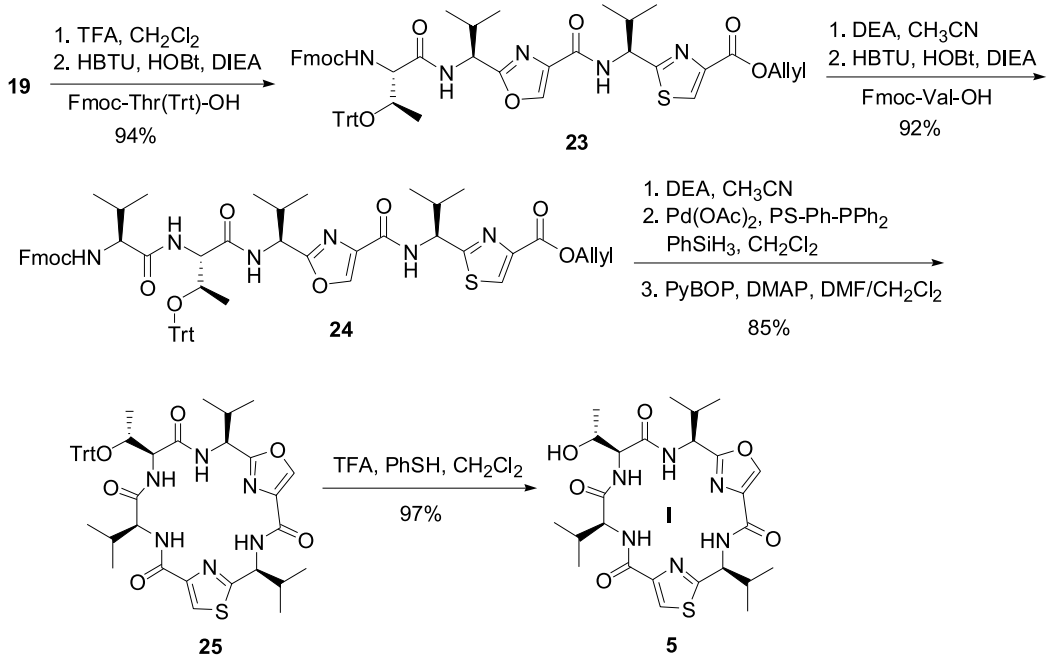
The synthesis of bistratamide I (**5**) is outlined in Scheme 7. The Boc-protected amine within **19**, liberated by TFA treatment, was coupled sequentially to *N*-Fmoc-*O*-trityl-L-threonine and *N*-Fmoc-L-valine employing HBTU/HOBt/DIEA affording **23** (94%) and **24** (92%), respectively. Removal of the Fmoc and allyl groups within **24** yielded the amino acid macrolide precursor. The final macrolactamization mediated by PyBOP and DMAP afforded **25** (85%). Bistratamide I (**5**) was obtained as a white semisolid after removing the trityl group from **25** utilizing 2% TFA in CH_2Cl_2 in the presence of 1 equiv of PhSH. Its ^{1}H and ^{13}C NMR spectra are identical to those reported in the literature.[4c]

3. Conclusions

The total synthesis of bistratamides F–I (**2**–**5**) have been accomplished for the first time. The thiazoles were prepared by oxidation of thiazolines. The latter were synthesized from cysteine containing amides wherein a Val-Cys dipeptide was converted to a thiazoline amino acid by bis(triphenyl)oxodiphosphonium trifluoromethanesulfonate. The oxazole substructure was synthesized from a ketoamide dipeptide derived from a Val-Thr dipeptide (Dess–Martin oxidation) using the same bisphosphonium salt. The serine-derived oxazole amino acid, a known compound, was



Scheme 6. Completion of the synthesis of bistratamide H (**4**).



Scheme 7. Completion of the synthesis of bistratamide I (**5**).

prepared as described previously.[5b] PyBOP and DMAP efficiently promoted the final macrolactamizations in all cases.

4. Experimental

4.1. General methods

Unless stated otherwise, all reactions were carried out in flame-dried glassware under a dry argon atmosphere. All solvents were purchased from Fisher and were dried prior to use. 'Regular workup' was as follows: the reaction mixture was diluted with EtOAc, washed with water, 10% $NaHCO_3$ (aq), and brine, the organic layer was dried over anhydrous Na_2SO_4 and then filtered and concentrated under reduced pressure to yield the crude product. ^1H NMR spectra were recorded at 600 MHz on a Bruker DRX spectrometer. ^{13}C NMR spectra were recorded at 150 MHz on a Bruker DRX-600 spectrometer. The chemical shift assignments for major diastereomers, not for minor diastereomers, were reported. Flash chromatography was performed on silica gel 60 (230–400 mesh, E. Merck no. 9385). Procedures for synthesis of compounds **7**, **9**, **10**, **21** were described elsewhere.[11b]

4.1.1. Compound 8. Compound **11** (413 mg, 0.8 mmol) and the Burgess reagent (214 mg, 0.9 mmol) were suspended in THF (10 mL). The mixture was refluxed for 2 h. After regular workup, the resulting crude product was purified by flash chromatography (EtOAc/hexanes = 1/2) to afford compound **8** (347 mg, 87%) as a white foam: $[\alpha]_D^{24} = +22.6$ (c 0.74, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$, 25 °C,

TMS) δ 0.91 (d, J=6.6 Hz, 3H), 0.96 (d, J=6.6 Hz, 3H), 2.12–2.15 (m, 1H), 4.21 (t, J=7.0 Hz, 1H), 4.36–4.45 (m, 4H), 4.52 (t, J=7.5 Hz, 1H), 4.78 (t, J=8.8 Hz, 1H), 5.16–5.23 (m, 2H), 5.53 (m, 1H), 7.24–7.39 (m, 9H), 7.60 (dd, J=8.3, 8.8 Hz, 2H), 7.75 (d, J=7.5 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 17.2, 18.7, 31.6, 47.1, 54.2, 66.9, 67.3, 67.7, 70.3, 119.9, 125.1, 127.0, 127.6, 128.4, 128.5 (2C), 135.1, 141.2, 143.7, 143.9, 156.1, 169.9, 170.7; HRMS (MALDI-FTMS) calcd for $C_{30}H_{30}N_2O_5$ ($M+Na^+$) 521.2047, found 521.2048.

4.1.2. Compound 11. To a solution of *N*-Fmoc-L-valine (339 mg, 1 mmol), HBTU (417 mg, 1.1 mmol) and $HOBt\cdot H_2O$ (168 mg, 1.1 mmol) in DMF (4 mL), DIEA (0.54 mL, 3.1 mmol) and L-serine benzyl ester hydrochloride (232 mg, 1 mmol) were sequentially added. The reaction mixture was stirred at 25 °C for 8 h. After regular workup, the resulting crude product was purified by flash chromatography (EtOAc/hexanes=1/1) to afford compound **11** (433 mg, 84%) as a white foam: $[\alpha]_D^{24}=-14.0$ (c 0.25, DMSO); ^{1}H NMR (600 MHz, DMSO-d_6, 25 °C) δ 0.85 (d, J=7.0 Hz, 3H), 0.88 (d, J=6.6 Hz, 3H), 1.97–2.03 (m, 1H), 3.67–3.71 (m, 1H), 3.76–3.79 (m, 1H), 4.02 (dd, J=7.0, 8.8 Hz, 1H), 4.20–4.23 (m, 2H), 4.27–4.31 (m, 1H), 4.44 (d, J=4.8, 11.8 Hz, 1H), 5.13–5.15 (m, 3H), 7.31–7.36 (m, 7H), 7.41 (t, J=7.5 Hz, 2H), 7.45 (d, J=9.2 Hz, 1H), 7.76 (d, J=7.5 Hz, 2H), 7.89 (d, J=7.5 Hz, 2H), 8.37 (d, J=7.5 Hz, 1H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 18.1, 19.1, 30.5, 46.7, 54.8, 59.7, 61.2, 65.7, 65.9, 120.1, 125.4, 127.1, 127.6, 127.7, 127.9, 128.3, 135.9, 140.7 (2C), 143.8, 143.9, 156.1, 170.3, 171.5; HRMS (MALDI-FTMS) calcd for $C_{30}H_{32}N_2O_6$ ($M+Na^+$) 539.2152, found 539.2144.

4.1.3. Compound 12 (general procedure for Pd/C mediated hydrogenation, diethylamine-mediated deprotection of Fmoc group and HBTU, HOBt-mediated peptide coupling). Pd on activated carbon (30 mg) was added to a flask containing **8** (329 mg, 0.66 mmol) in MeOH (5 mL) and THF (5 mL). The reaction flask was fitted with H_2 balloon, and evacuated and purged with H_2 three times. The reaction progress was monitored by TLC and was complete in 1 h. After removing the solvent, the residue was passed through a short silica gel column and eluted with MeOH. The carboxylic acid was used in next step without further purification. In another flask, diethylamine (3 mL) was added to a solution of **7** (277 mg, 0.6 mmol) in CH_3CN (3 mL) and the resulting mixture was stirred at 25 °C for 30 min to ensure complete removal of the Fmoc protecting group. After concentration in vacuo, the reaction mixture was azeotroped to dryness with CH_3CN (2×3 mL) and the residue was dissolved in DMF (3 mL). This amine solution was added to a solution of above carboxylic acid, HBTU (277 mg, 0.73 mmol), $HOBt\cdot H_2O$ (112 mg, 0.73 mmol) and DIEA (0.24 mL, 1.4 mmol) in DMF (3 mL). The reaction mixture was stirred at 25 °C for 8 h. After regular workup, the resulting crude product was purified by flash chromatography (EtOAc/hexanes=1/2) to afford compound **12** (299 mg, 79%) as a white foam: $[\alpha]_D^{24}=-16.8$ (c 0.77, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$, 25 °C, TMS) δ 0.90 (d, J=6.6 Hz, 3H), 0.93 (d, J=7.0 Hz, 3H), 0.98 (d, J=7.0 Hz, 3H), 1.00 (d, J=6.6 Hz, 3H), 2.14–2.18 (m, 1H), 2.44–2.50 (m, 1H), 4.25 (t, J=7.0 Hz, 1H), 4.35–4.38 (m, 1H), 4.42–4.47 (m, 2H), 4.52–4.59 (m, 2H), 4.74 (d, J=8.8, 10.5 Hz, 1H), 4.83 (d, J=5.3 Hz, 2H), 5.19 (dd, J=7.0, 8.3 Hz, 1H), 5.27 (d, J=10.5 Hz, 1H), 5.38 (d, J=17.1 Hz, 1H), 5.57 (d, J=8.8 Hz, 1H), 5.99–6.03 (m, 1H), 7.29–7.32 (m, 2H), 7.35 (d, J=8.8 Hz, 1H), 7.39 (t, J=7.5 Hz, 2H), 7.61 (d, J=7.9 Hz, 1H), 7.63 (d, J=7.5 Hz, 1H), 7.76 (d, J=7.5 Hz, 2H), 8.11 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 17.7 (2C), 18.8, 19.3, 31.3, 32.9, 47.1, 54.6, 56.1, 65.9, 67.0, 68.2, 70.8, 118.9, 119.9, 125.0, 127.0, 127.6, 131.7, 141.2, 143.7, 143.8, 146.9, 156.1, 160.7, 169.7, 171.2; HRMS (MALDI-FTMS) calcd for $C_{34}H_{38}N_4O_6S$ ($M+H^+$) 631.2585, found 631.2566.

4.1.4. Compound 13. Compound **13** was synthesized from **12** in a 72% yield as a white foam by following the procedure used for the synthesis of **12**: $[\alpha]_D^{24}=-23.2$ (c 0.34, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$, 25 °C, TMS) δ 0.88 (d, J=6.6 Hz, 3H), 0.93 (d, J=6.6 Hz, 3H), 0.96 (d, J=7.0 Hz, 3H), 1.01 (d, J=6.6 Hz, 3H), 1.27 (d, J=6.1 Hz, 3H), 2.28–2.31 (m, 1H), 2.35–2.40 (m, 1H), 3.92 (dd, J=6.1, 6.6 Hz, 1H), 4.21 (m, 2H), 4.33–4.41 (m, 2H), 4.60–4.62 (m, 2H), 4.68 (m, 1H), 4.73–4.75 (m, 1H), 4.86 (d, J=5.7 Hz, 2H), 4.96 (br, 1H), 5.16 (dd, J=6.1, 8.3 Hz, 1H), 5.30 (d, J=10.5 Hz, 1H), 5.41 (d, J=17.1 Hz, 1H), 5.91 (d, J=8.3 Hz, 1H), 6.01–6.05 (m, 1H), 7.27–7.30 (m, 3H), 7.39 (t, J=7.5 Hz, 2H), 7.51 (d, J=8.3 Hz, 1H), 7.58 (t, J=7.5 Hz, 2H), 7.75 (d, J=7.5 Hz, 2H), 8.10 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 17.2, 17.7, 18.9 (2C), 19.7, 30.0, 33.4, 38.5, 47.0, 52.9, 56.3, 59.6, 66.1, 67.1, 67.6, 69.3, 71.8, 119.0, 119.9, 125.0 (2C), 127.0, 127.3, 127.6, 131.6, 141.2, 143.6, 143.7, 146.4, 156.3, 160.8, 170.3, 170.7, 171.5; HRMS (MALDI-FTMS) calcd for $C_{38}H_{45}N_5O_8S$ ($M+H^+$) 732.3061, found 732.3045.

4.1.5. Compound 14. Compound **14** was synthesized from **13** in a 86% yield as a white foam by following the procedure used for the synthesis of **12**: $[\alpha]_D^{24}=-23.1$ (c 0.85, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$, 25 °C, TMS) δ 0.87 (d, J=6.6 Hz, 3H), 0.92–0.95 (m, 12H), 0.97 (d, J=6.6 Hz, 3H), 1.24 (d, J=6.1 Hz, 3H), 2.09–2.12 (m, 1H), 2.21–2.23 (m, 1H), 2.36–2.41 (m, 1H), 3.98 (t, J=6.1 Hz, 1H), 4.15–4.20 (m, 2H), 4.30 (dd, J=7.0, 10.5 Hz, 1H), 4.40 (dd, J=7.5, 10.5 Hz, 1H), 4.51 (dd, J=7.9, 8.8 Hz, 1H), 4.54–4.59 (m, 2H), 4.65–4.70 (m, 2H), 4.85 (t, J=5.7 Hz, 2H), 4.93 (br, 1H), 5.16 (dd, J=6.1, 8.3 Hz, 1H), 5.28 (d, J=10.5 Hz, 1H), 5.40 (d, J=17.5 Hz, 1H), 5.74 (d, J=9.2 Hz, 1H), 5.98–6.04 (m, 1H), 7.26–7.30 (m, 3H), 7.36–7.39 (m, 2H), 7.41 (d, J=8.8 Hz, 1H), 7.51 (d, J=8.3 Hz, 1H), 7.57 (dd, J=7.0, 7.5 Hz, 2H), 7.74 (d, J=7.9 Hz, 2H), 8.10 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 17.4, 17.7, 17.8, 18.8, 18.9, 19.1, 19.8, 30.3, 31.4, 33.4, 47.0, 52.9, 56.3, 57.9, 60.1, 66.1, 67.0, 67.7, 68.9, 71.5, 119.0, 119.9, 125.0, 127.0, 127.3, 127.6, 131.7, 141.2, 143.7, 143.8, 146.5, 156.3, 160.8, 170.2, 170.4, 170.7, 170.0, 171.6; HRMS (MALDI-FTMS) calcd for $C_{43}H_{54}N_6O_9S$ ($M+H^+$) 831.3746, found 831.3756.

4.1.6. Compound 15. Compound **15** was synthesized from **14** in a 38% yield as a white foam by following the procedure used for the synthesis of **8**: $[\alpha]_D^{24}=-7.1$ (c 0.31, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$, 25 °C, TMS) δ 0.89 (d, J=7.0 Hz, 3H), 0.92–0.94 (m, 9H), 0.98 (d, J=8.3 Hz, 3H), 1.00 (d, J=7.5 Hz, 3H), 1.51 (d, J=6.1 Hz, 3H), 2.15–2.17 (m, 1H), 2.47–2.49 (m, 2H), 4.21–4.22 (m, 2H), 4.34–

4.44 (m, 3H), 4.55–4.59 (m, 2H), 4.67 (dd, J=5.7, 8.8 Hz, 1H), 4.73–4.77 (m, 1H), 4.78–4.80 (m, 3H), 5.19 (dd, J=6.6, 8.8 Hz, 1H), 5.26 (d, J=10.1 Hz, 1H), 5.36 (dd, J=17.1 Hz, 1H), 5.57 (d, J=8.8 Hz, 1H), 5.96–6.00 (m, 1H), 7.11 (d, J=9.2 Hz, 1H), 7.27–7.29 (m, 2H), 7.37–7.42 (m, 3H), 7.58 (t, J=6.6 Hz, 2H), 7.76 (d, J=7.5 Hz, 2H), 8.04 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 17.6, 17.7, 17.9, 18.8, 18.9, 19.4, 21.8, 31.2, 31.4, 33.0, 47.1, 52.2, 54.8, 56.2, 65.9, 67.0, 68.3, 70.8, 74.5, 80.7, 118.9, 120.0, 125.0 (2C), 127.0, 127.2, 127.7, 131.7, 141.2, 143.7, 143.8, 146.9, 156.0, 160.7, 168.9, 169.1, 171.0, 171.3, 171.5; HRMS (MALDI-FTMS) calcd for $C_{43}H_{52}N_6O_8S$ ($M+H^+$) 813.3640, found 813.3633.

4.1.7. Bistratamide F (2) (general procedure for removal of the allyl ester protecting group, PyBOP and DMAP-mediated macrocyclization). Deprotection of the Fmoc group in **15** (81.3 mg, 0.1 mmol) followed the procedure described in the synthesis of **12**. To remove the allyl group, $Pd(OAc)_2$ (1.12 mg, 5 μmol) and polystyrene-triphenylphosphine (25.2 mg, 1.59 mol/g, 0.04 mmol) were added to a flask containing CH_2Cl_2 (5 mL). After stirring for 10 min, the above amino ester in CH_2Cl_2 (2 mL) and $PhSiH_3$ (0.025 mL, 0.2 mmol) were added separately. The reaction progress was monitored by TLC and completed in 15 min. After removing the solvent, the residue was passed through a short silica gel column and eluted with $CHCl_3$/EtOH (1/2). After removing the solvents, the macrolide precursor was redissovled in CH_2Cl_2/DMF (5 mL, v/v: 2/1). This solution was added to a flask containing PyBOP (104 mg, 0.2 mmol) and DMAP (24.4 mg, 0.2 mmol) in CH_2Cl_2/DMF (20 mL, v/v: 2/1) over 8 h using a syringe pump. After the completion of addition, the mixture was stirred for 2 h. Regular workup and purification by flash chromatography (EtOAc/hexanes=4/1) gave **2** (18.6 mg, 35%) as a white foam: $[\alpha]_D^{24}=+25.3$ (c 0.30, MeOH) {lit[4c] $[\alpha]_D^{25}=+23.2$ (c 1.0, MeOH)}; ^{1}H NMR (600 MHz, DMSO-d_6, 25 °C) δ 0.76 (d, J=7.0 Hz, 3H), 0.80 (d, J=6.6 Hz, 3H), 0.81 (d, J=6.6 Hz, 3H), 0.84 (d, J=6.9 Hz, 3H), 0.85 (d, J=7.0 Hz, 3H), 0.89 (d, J=7.0 Hz, 3H), 1.48 (d, J=6.1 Hz, 3H), 2.12 (m, 1H), 2.21 (m, 1H), 2.33 (m, 1H), 4.31 (dd, J=2.2, 8.3 Hz, 1H), 4.38 (t, J=7.5 Hz, 1H), 4.60 (br, d, J=8.8 Hz, 1H), 4.78–4.85 (m, 4H), 5.30 (dd, J=4.8, 7.9 Hz, 1H), 7.64 (d, J=8.8 Hz, 1H), 7.73 (d, J=7.5 Hz, 1H), 7.99 (d, J=9.2 Hz, 1H), 8.37 (s, 1H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 15.9, 16.0, 17.2, 17.8, 18.5, 18.7, 21.4, 30.7, 30.8, 33.7, 51.1, 51.3, 54.7, 66.7, 72.4, 72.7, 81.8, 124.9, 147.9, 159.0, 160.4, 167.6, 168.9, 169.7, 169.8; HRMS (MALDI-FTMS) calcd for $C_{25}H_{36}N_6O_5S$ ($M+H^+$) 533.2541, found 533.2519.

4.1.8. Compound 17. To a solution of triphenylphosphine oxide (835 mg, 3 mmol) in dry CH_2Cl_2 (10 mL), trifluoromethanesulfonic anhydride (0.24 mL, 1.5 mmol) was added slowly at 0 °C. The reaction mixture was stirred for 10 min at 0 °C and then adjusted to −20 °C using a brine-ice bath. Then **18** (528 mg, 1 mmol) was added. The reaction progress was monitored by TLC and completed in 2 h. After regular workup, the resulting crude product was purified by flash chromatography (EtOAc/hexanes=1/3) to afford compound **17** (332 mg, 65%) as a white foam: $[\alpha]_D^{24}=+31.1$ (c 0.72, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$, 25 °C, TMS) δ 0.92 (d, J=7.0 Hz, 3H), 0.95 (d, J=6.6 Hz, 3H), 2.18–2.23 (m, 1H), 2.57 (s, 3H), 4.21 (t, J=7.0 Hz, 1H), 4.36–4.43 (m, 2H), 4.79 (dd, J=6.1, 6.8 Hz, 1H), 5.35 (AB, J_{AB}=12.3 Hz, 1H), 5.38 (AB, J_{AB}=12.3 Hz, 1H), 5.57 (d, J=8.8 Hz, 1H), 7.28–7.40 (m, 9H), 7.60 (dd, J=7.5, 7.9 Hz, 2H), 7.75 (d, J=7.5 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 12.2, 18.0, 18.7, 32.7, 47.1, 54.6, 66.6, 67.0, 119.9, 125.0, 127.0, 127.4, 127.6, 128.3, 128.4, 128.5, 135.6, 141.2, 143.6, 143.8, 156.0, 156.3, 161.7, 161.9; HRMS (MALDI-FTMS) calcd for $C_{31}H_{30}N_2O_5S$ ($M+Na^+$) 533.2047, found 533.2060.

4.1.9. Compound 18. *N*-Fmoc-L-valine and L-threonine benzyl ester oxalate were coupled by following the procedure used for the synthesis of **12** to give the dipeptide (5 mmol scale). The resulting dipeptide was suspended in 150 mL CH_2Cl_2, then Dess–Martin periodinane (3.06 g, 97%, 7 mmol) was added. The resulting reaction mixture was stirred at 25 °C for 1 h. After regular workup, the resulting crude product was purified by flash chromatography (EtOAc/hexanes=1/3) to afford compound **18** (1.66 g, 63%) as a gel: $[\alpha]_D^{24}=-12.9$ (c 0.38, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$, 25 °C, TMS) δ 0.85–0.98 (m, 6H), 2.10–2.13 (m, 1H), 2.28 (s, 3H), 4.19–4.21 (m, 2H), 4.35–4.43 (m, 2H), 5.16–5.29 (m, 3H), 5.50–5.57 (m, 1H), 7.16–7.34 (m, 10H), 7.37–7.39 (m, 2H), 7.58–7.76 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 17.7, 19.1, 28.1, 31.3, 47.1, 59.8, 63.2, 67.1, 68.3, 119.9, 125.1, 127.0, 127.7, 128.5 (2C), 128.7, 128.8 (2C), 133.0, 134.4, 141.2, 141.6, 143.7, 143.8, 156.3, 165.5, 171.2, 197.7; HRMS (MALDI-FTMS) calcd for $C_{31}H_{32}N_2O_6$ ($M+Na^+$) 551.2152, found 551.2146.

4.1.10. Compound 19. Compound **19** was synthesized from **7** and **16** in a 88% yield as a white foam by following the procedure used for the synthesis of **12**: $[\alpha]_D^{24}=-57.1$ (c 0.28, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$, 25 °C, TMS) δ 0.94 (d, J=6.6 Hz, 3H), 0.95 (d, J=8.3 Hz, 3H), 0.99 (d, J=7.0 Hz, 3H), 1.05 (d, J=6.6 Hz, 3H), 1.46 (s, 9H), 2.19–2.21 (m, 1H), 2.59–2.63 (m, 1H), 4.78 (dd, J=8.3, 6.1 Hz, 1H), 4.86 (d, J=5.7 Hz, 2H), 5.17 (d, J=8.3 Hz, 1H), 5.29–5.31 (m, 2H), 5.41 (d, J=17.1 Hz, 1H), 6.01–6.07 (m, 1H), 7.55 (d, J=9.2 Hz, 1H), 8.12 (s, 1H), 8.15 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 17.9, 18.1, 18.6, 19.6, 28.3, 32.7, 33.0, 54.2, 56.0, 65.9, 80.1, 118.8, 127.3, 131.8, 135.4, 141.2, 147.1, 155.3, 160.2, 160.8, 163.9, 171.3; HRMS (MALDI-FTMS) calcd for $C_{24}H_{34}N_4O_6S$ ($M+Na^+$) 529.2091, found 529.2093.

4.1.11. Compound 20. To a solution of **19** (507 mg, 1 mmol) in CH_2Cl_2 (10 mL), TFA (2.5 mL) was added. After stirring for 20 min, the solvent was removed. The residue was azeotroped with toluene to remove TFA. The resulting oil was dissolved in DMF (4 mL) and DIEA was added to neutralize. This amine was coupled with **17** yielding **20** (736 mg, 91%) as a white foam by following the procedure used for the synthesis of **12**: $[\alpha]_D^{24}=-37.6$ (c 1.0, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$, 25 °C, TMS) δ 0.95 (d, J=6.6 Hz, 3H), 0.96–0.99 (m, 9H), 1.02 (d, J=7.0 Hz, 3H), 1.04 (d, J=6.6 Hz, 3H), 2.21–2.25 (m, 1H), 2.30–2.34 (m, 1H), 2.46 (br, 1H), 2.55–2.59 (m, 1H), 2.62 (s, 3H), 4.22 (dd, J=6.6, 7.0 Hz, 1H), 4.40–4.49 (m, 2H), 4.77 (dd, J=7.0, 8.8 Hz, 1H), 4.82 (m, 2H), 5.20 (dd, J=7.0, 9.2 Hz, 1H), 5.26–5.31 (m, 2H), 5.38 (d, J=17.1 Hz, 1H), 5.51 (d,

J=9.2 Hz, 1H), 5.98–6.02 (m, 1H), 7.26–7.29 (m, 2H), 7.36–7.39 (m, 3H), 7.58 (dd, J=7.5, 12.7 Hz, 2H), 7.61 (d, J=9.7 Hz, 1H), 7.75 (d, J=7.5 Hz, 2H), 8.06 (s, 1H), 8.10 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 11.6, 17.9, 18.0, 18.3, 18.8, 18.9, 19.5, 32.2 (2C), 32.9, 47.1, 52.1, 54.7, 56.0, 65.8, 66.8, 118.7, 119.9, 124.8 (2C), 126.9, 127.2, 127.6, 128.4, 131.7, 135.4, 141.2 (2C), 141.4, 143.5, 143.7, 146.9, 153.6, 155.9, 160.2, 160.4, 160.7, 161.4, 163.1, 171.4; HRMS (MALDI-FTMS) calcd for $C_{43}H_{48}N_6O_8S$ ($M+H^+$) 809.3327, found 809.3318.

4.1.12. Bistratamide G (3). Compound **3** was synthesized from **20** in a 70% yield as a white solid by following the procedure used for the synthesis of **2**: mp 224–226 °C; $[\alpha]_D^{24}=-84.4$ (c 0.97, MeOH) {lit[4c] $[\alpha]_D^{25}=-73.8$ (c 1.0, MeOH)}; ^{1}H NMR (600 MHz, DMSO-d_6, 25 °C) δ 0.88 (d, J=6.6 Hz, 3H), 0.91 (d, J=6.6 Hz, 3H), 0.93 (d, J=7.0 Hz, 3H), 0.94 (d, J=7.0 Hz, 3H), 0.96 (d, J=6.6 Hz, 3H), 0.97 (d, J=7.0 Hz, 3H), 2.15–2.22 (m, 2H), 2.27–2.31 (m, 1H), 2.54 (s, 3H), 5.01 (dd, J=4.4, 7.5 Hz, 1H), 5.09 (dd, J=5.7, 8.8 Hz, 1H), 5.39 (dd, J=6.1, 8.8 Hz, 1H), 8.30 (d, J=7.0 Hz, 1H), 8.32 (d, J=9.2 Hz, 1H), 8.35 (s, 1H), 8.44 (d, J=8.8 Hz, 1H), 8.78 (s, 1H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 11.1, 18.0, 18.1, 18.2, 18.3, 18.6, 32.6, 32.9, 34.6, 52.1, 52.7, 54.8, 125.2, 128.0, 134.5, 142.9, 147.9, 152.8, 158.4, 159.3, 160.2, 160.5, 163.2, 168.3; HRMS (MALDI-FTMS) calcd for $C_{25}H_{32}N_6O_5S$ ($M+H^+$) 529.2228, found 529.2221.

4.1.13. Compound 22. Compound **22** was synthesized from **21** and **17** in a 97% yield as a white foam by following the procedure used for the synthesis of **12**: $[\alpha]_D^{24}=-27.1$ (c 0.77, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$, 25 °C, TMS) δ 0.94 (d, J=6.6 Hz, 3H), 0.97 (d, J=7.0 Hz, 3H), 1.00 (d, J=7.0 Hz, 3H), 1.03 (d, J=7.5 Hz, 6H), 1.05 (d, J=7.9 Hz, 3H), 2.20–2.23 (m, 1H), 2.52–2.55 (m, 1H), 2.62–2.65 (m, 1H), 2.63 (s, 3H), 4.21 (dd, J=6.6, 7.0 Hz, 1H), 4.40–4.49 (m, 2H), 4.77 (dd, J=6.6, 9.2 Hz, 1H), 4.83 (m, 2H), 5.28 (d, J=10.1 Hz, 1H), 5.31 (dd, J=6.1, 9.2 Hz, 1H), 5.34 (dd, J=6.6, 9.2 Hz, 1H), 5.39 (d, J=17.1 Hz, 1H), 5.45 (m, 1H), 5.99–6.04 (m, 1H), 7.24–7.28 (m, 2H), 7.37 (t, J=7.5 Hz, 2H), 7.46 (d, J=8.8 Hz, 1H), 7.57 (dd, J=7.9, 8.3 Hz, 2H), 7.75 (d, J=7.5 Hz, 2H), 7.99 (d, J=9.2 Hz, 1H), 8.01 (s, 1H), 8.06 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 11.7, 17.8 (2C), 18.0, 18.9, 19.4, 19.6, 32.3, 32.8, 33.0, 47.1, 54.7, 55.8, 56.4, 65.8, 66.8, 118.7, 119.9, 123.5, 124.8, 124.9, 126.9, 127.2, 127.7, 128.4, 131.8, 141.2 (2C), 143.5, 143.7, 147.0, 149.3, 153.7, 155.9, 160.5, 160.7, 160.8, 161.6, 171.8, 171.9; HRMS (MALDI-FTMS) calcd for $C_{43}H_{48}N_6O_7S_2$ ($M+H^+$) 825.3098, found 825.3084.

4.1.14. Bistratamide H (4). Compound **4** was synthesized from **22** in a 80% yield as a gel-like solid by following the procedure used for the synthesis of **2**: $[\alpha]_D^{24}=-106.2$ (c 1.1, MeOH) {lit[4c] $[\alpha]_D^{25}=-92.9$ (c 1.0, MeOH)}; ^{1}H NMR (600 MHz, DMSO-d_6, 25 °C) δ 0.90 (d, J=6.6 Hz, 3H), 0.93 (d, J=7.0 Hz, 6H), 0.94 (d, J=8.3 Hz, 3H), 0.96 (d, J=7.0 Hz, 3H), 0.98 (d, J=7.0 Hz, 3H), 2.16–2.25 (m, 3H), 2.58 (s, 3H), 5.07 (dd, J=5.3, 8.3 Hz, 1H), 5.35 (dd, J=5.3, 8.3 Hz, 1H), 5.45 (dd, J=7.0, 9.6 Hz, 1H), 8.33 (s, 1H), 8.35 (s, 1H), 8.36 (d, J=9.2 Hz, 1H), 8.49 (d, J=8.3 Hz, 1H), 8.52 (d, J=9.7 Hz, 1H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 12.2, 18.9, 19.0, 19.1, 19.2, 19.4, 33.7, 35.3, 35.5, 53.2, 55.5, 55.7, 125.7, 126.2, 128.7, 148.7, 149.2, 154.2, 159.9, 160.4, 160.6, 161.4, 169.4, 169.9; HRMS (MALDI-FTMS) calcd for $C_{25}H_{32}N_6O_4S_2$ ($M+Na^+$) 567.1819, found 567.1810.

4.1.15. Compound 23. Compound **23** was synthesized from **19** and *N*-Fmoc-*O*-trityl-threonine in a 94% yield as a white foam by following the procedure used for the synthesis of **12**: $[\alpha]_D^{24}=-15.0$ (c 0.50, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$, 25 °C, TMS) δ 0.80 (d, J=7.0 Hz, 3H), 0.88 (d, J=6.6 Hz, 3H), 0.97 (d, J=6.6 Hz, 3H), 1.00 (d, J=7.0 Hz, 3H), 1.17 (d, J=6.1 Hz, 3H), 2.21–2.27 (m, 1H), 2.56–2.62 (m, 1H), 3.44 (br, 1H), 4.13 (t, J=7.5 Hz, 1H), 4.22–4.29 (m, 2H), 4.35 (br, 1H), 4.82 (d, J=5.7 Hz, 2H), 5.08 (dd, J=8.8, 6.6 Hz, 1H), 5.26 (d, J=10.5 Hz, 1H), 5.37 (d, J=17.1 Hz, 1H), 5.41 (dd, J=8.8, 6.6 Hz, 1H), 5.73 (d, J=4.8 Hz, 1H), 5.97–6.02 (m, 1H), 7.23–7.30 (m, 12H), 7.35–7.38 (m, 2H), 7.52–7.57 (m, 9H), 7.72–7.74 (m, 2H), 8.09 (s, 1H), 8.22 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 16.1, 17.6, 18.2, 19.0, 19.5, 31.8, 33.0, 47.0, 53.1, 56.1, 65.9, 66.7, 69.8, 88.6, 118.9, 119.9, 125.0, 125.1, 126.9 (2C), 127.2, 127.5, 127.6, 128.2, 128.7, 131.8, 135.6, 141.2, 141.6, 143.7 (d), 147.2, 155.0, 160.3, 160.8, 163.7, 169.6, 171.9; HRMS (MALDI-FTMS) calcd for $C_{57}H_{57}N_5O_8S$ ($M+Na^+$) 994.382, found 994.3805.

4.1.16. Compound 24. Compound **24** was synthesized from **23** in a 92% yield as a white foam by following the procedure used for the synthesis of **12**: $[\alpha]_D^{24}=-25.6$ (c 1.21, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$, 25 °C, TMS) δ 0.79 (d, J=6.6 Hz, 3H), 0.84 (d, J=6.6 Hz, 3H), 0.87 (d, J=6.6 Hz, 3H), 0.88 (d, J=6.6 Hz, 3H), 0.94 (d, J=6.6 Hz, 3H), 0.98 (d, J=6.6 Hz, 3H), 1.13 (d, J=6.1 Hz, 3H), 2.04–2.06 (m, 1H), 2.20–2.22 (m, 1H), 2.55–2.58 (m, 1H), 3.62 (br, 1H), 4.01 (t, J=6.1 Hz, 1H), 4.19 (m, 1H), 4.32 (dd, J=10.5, 7.0 Hz, 1H), 4.37–4.42 (m, 2H), 4.82 (d, J=5.7 Hz, 2H), 5.04 (dd, J=8.3, 6.6 Hz, 1H), 5.26 (d, J=10.5 Hz, 1H), 5.37 (d, J=17.1 Hz, 1H), 5.40 (dd, J=9.2, 6.1 Hz, 1H), 5.45 (d, J=8.8 Hz, 1H), 5.96–6.01 (m, 1H), 6.81 (d, J=4.8 Hz, 1H), 7.22–7.29 (m, 11H), 7.38 (t, J=7.0 Hz, 2H), 7.54–7.58 (m, 10H), 7.60 (d, J=9.2 Hz, 1H), 7.75 (d, J=7.5 Hz, 1H), 8.07 (s, 1H), 8.20 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 16.3, 17.5, 17.6, 18.2, 18.9, 19.1, 19.5, 31.3, 31.7, 33.0, 47.1, 53.2, 55.4, 56.0, 60.0, 65.9, 66.9, 69.2, 88.6, 118.8, 119.9, 125.0, 127.0, 127.2, 127.5, 127.6, 128.1, 128.7, 131.8, 135.5, 141.2, 141.6, 143.6, 143.7, 143.9, 147.1, 156.2, 160.3, 160.8, 163.6, 169.5, 170.2, 171.8; HRMS (MALDI-FTMS) calcd for $C_{62}H_{66}N_6O_9S$ ($M+Na^+$) 1093.4504, found 1093.4547.

4.1.17. Compound 25. Compound **25** was synthesized from **24** in a 85% yield as a white foam by following the procedure used for the synthesis of **2**: $[\alpha]_D^{24}=-115.5$ (c 0.27, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$, 25 °C, TMS) δ 0.75 (d, J=6.6 Hz, 3H), 0.90 (d, J=7.0 Hz, 3H), 0.92 (d, J=6.6 Hz, 3H), 0.98 (d, J=6.6 Hz, 3H), 1.00 (d, J=7.0 Hz, 3H), 1.09 (d, J=7.0 Hz, 3H), 1.46 (d, J=6.6 Hz, 3H), 2.17–2.22 (m, 1H), 2.35–2.38 (m, 1H), 2.54–2.56 (m, 1H), 3.65 (dd, J=5.3, 4.4 Hz, 1H), 4.53–4.55 (m, 1H), 4.63 (dd, J=10.5, 3.5 Hz, 1H), 4.76 (dd, J=6.1, 4.4 Hz, 1H), 5.22 (dd, J=9.7, 7.0 Hz, 1H), 6.84 (d, J=5.3 Hz, 1H), 7.26–7.29 (m, 3H), 7.33–7.35 (m, 6H), 7.45 (d, J=10.1 Hz,

1H), 7.55–7.57 (m, 7H), 7.95 (s, 1H), 8.09 (s, 1H), 8.11 (d, $J=6.6$ Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 16.1, 16.8, 18.0, 18.6, 18.7, 18.8, 19.9, 30.3, 30.4, 34.1, 54.5, 55.0, 56.4, 57.6, 68.8, 89.5, 122.8, 127.6, 128.1, 128.2, 128.8, 135.5, 143.6, 149.7, 160.0, 160.1, 162.5, 168.8, 169.9, 170.1; HRMS (MALDI-FTMS) calcd for $C_{44}H_{50}N_6O_6S$ ($M+Na^+$) 813.3405, found 813.3376.

4.1.18. Bistratamide I (5). To a flask containing **25** (158 mg, 0.2 mmol) in CH_2Cl_2 (5 mL), TFA (0.1 mL) and PhSH (21 μL, 0.2 mmol) were added. TLC showed that **25** disappeared in 5 min. After removing all of the solvents, the residue was purified by flash chromatography. Bistratamide I (**5**) was obtained as a white semisolid (106 mg, 97%): $[\alpha]_D^{24}=-129.4$ (*c* 0.36, MeOH){lit[4c] $[\alpha]_D^{25}=-122$ (*c* 0.5, MeOH)}; ^{1}H NMR (600 MHz, DMSO-d_6, 25 °C) δ 0.86 (d, $J=6.6$ Hz, 3H), 0.91 (d, $J=6.6$ Hz, 3H), 0.96 (d, $J=7.0$ Hz, 3H), 0.99 (d, $J=6.6$ Hz, 3H), 1.00 (d, $J=6.6$ Hz, 3H), 1.03 (d, $J=6.6$ Hz, 3H), 1.11 (d, $J=6.1$ Hz, 3H), 2.10–2.24 (m, 3H), 4.08–4.11 (m, 1H), 4.31 (dd, $J=10.1$, 3.1 Hz, 1H), 4.37 (t, $J=11.0$ Hz, 1H), 5.06 (dd, $J=8.8$, 6.1 Hz, 1H), 5.30 (dd, $J=9.2$, 7.0 Hz, 1H), 5.36 (d, $J=7.0$ Hz, 1H), 8.04 (d, $J=8.8$ Hz, 1H), 8.31 (s, 1H), 8.32 (d, $J=9.2$ Hz, 1H), 8.40 (d, $J=10.1$ Hz, 1H), 8.56 (d, $J=10.5$ Hz, 1H), 8.67 (s, 1H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 18.2, 18.3, 18.4, 18.9, 19.2, 19.8, 21.1, 30.9, 33.2, 34.7, 52.2, 55.3, 59.1, 61.2, 67.3, 125.6, 135.0, 141.9, 148.0, 159.4, 159.6, 163.2, 169.4, 170.1, 170.3; HRMS (MALDI-FTMS) calcd for $C_{25}H_{36}N_6O_6S$ ($M+Na^+$) 571.2309, found 571.2324.

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References and notes

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15. Crystallographic data for the structure **3** in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 246784. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44 1223 336033 or e-mail: deposit@ccdc.cam.ac.uk].