

## Supplementary Material

# (-)-Bacillamide C: The Convergent Approach

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### Experimental

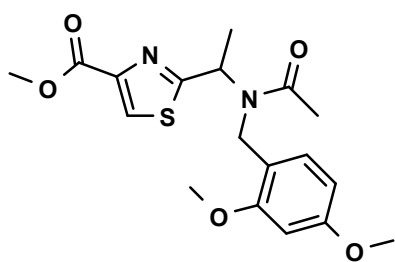
**General:** Proton and carbon NMR spectra were obtained on Bruker Avance™ 600 MHz NMR spectrometer. Chemical shifts are reported as  $\delta$  values in parts per million (ppm) as referenced to residual solvent. <sup>1</sup>H NMR spectra are tabulated as follows: chemical shift, multiplicity (s = singlet, bs = broad singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constant(s), and number of protons. All reactions were under air atmosphere. Flash column chromatography was performed using SiO<sub>2</sub> 60 (particle size 0.040-0.055 mm, 230-400 mesh, EM science distributed by Bioman), Preparative TLC was conducted using Preparative Silica gel TLC plates (1000  $\mu$ m, 20cm $\times$ 20cm). High Resolution Mass spectra were obtained at the University of Pittsburgh Mass Spectrometry facility. LC-MS analysis was performed on an SHIMADZU instrument, using an analytical C18 column (Dionex Acclaim 120 Å, 2.1  $\times$  50 mm, 3.0  $\mu$ m, 0.2 mL/min).

### Preparation of 2-{1-[Acetyl-(2,4-dimethoxy-benzyl)-amino]-ethyl}-thiazole-4-carboxylic acid methyl ester **6**

Acetaldehyde (57  $\mu$ L, 1 mmol), (2,4-dimethoxyphenyl)methanamine (150  $\mu$ L, 1 mmol), and dry methanol (1 mL) are added together at room temperature. Then the isocyanide (0.154 g, 1 mmol) and thiocarboxylic acid (71  $\mu$ L, 1 mmol) are added to the reaction mixture and stirred at room temperature for one day. The mixture is then condensed and purified with column chromatography (EtOAc: PE). Orange oil is obtained (227 mg, 60 %), white solid crystal was recrystallized in EtOAc.

### 2-{1-[Acetyl-(2,4-dimethoxy-benzyl)-amino]-ethyl}-thiazole-4-carboxylic acid methyl

### ester 6

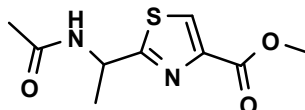


$C_{18}H_{22}N_2O_5S$ , Mw: 378.44 g/mol; HRMS (ESI-TOF)  $m/z$  (calc.): 378.1249, (found)  $[M+Na]^+$ : 401.1155; HPLC-MS  $r_t$ : 9.80,  $m/z$   $[M+H]^+$ : 379.0,  $[M+Na]^+$  400.8.  $^1H$ -NMR ( $CDCl_3$ , 600 MHz):  $\delta$  = 1.65 (d,  $J=7.2$  Hz, 3H), 2.15 (s, 3H), 3.79 (s, 3H), 3.81 (s, 3H), 3.94 (s, 3H), 4.42 (d,  $J=18$  Hz, 1H), 4.51 (d,  $J=18$  Hz, 1H), 5.90 (q,  $J=7.2$  Hz, 1H), 6.42 (s, 1H), 6.44 (d,  $J=8.4$  Hz, 1H), 7.01 (d,  $J=8.4$  Hz, 1H), 8.12 (s, 1H).  $^{13}C$ -NMR ( $CDCl_3$ , 150.92 MHz):  $\delta$  = 17.0, 22.2, 45.1, 52.4, 52.4, 55.1, 55.4, 98.4, 103.6, 117.3, 127.7, 128.5, 145.932, 157.5, 160.3, 161.9, 172.1, 172.5.

### Preparation of 2-(1-Acetylamino-ethyl)-thiazole-4-carboxylic acid methyl ester 7

1 mL TFA was added to **6** (567 mg, 1.5 mmol) and the mixture is heated at 50 °C for 12 hours. After the reaction was complete, the solution was concentrated and purified by column chromatography (EtOAc: PE). A yellow solid was obtained (200 mg, 58 %).

### 2-(1-Acetylamino-ethyl)-thiazole-4-carboxylic acid methyl ester 7

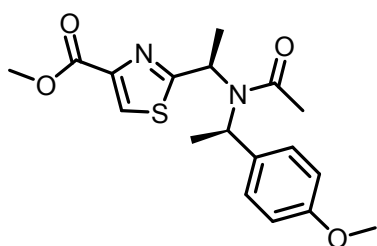


$C_9H_{12}N_2O_3S$ , Mw: 228.27 g/mol; HRMS (ESI-TOF)  $m/z$  (calc.): 228.0569, (found)  $[M]^+$ : 228.0563; HPLC-MS  $r_t$ : 1.48,  $m/z$   $[M+H]^+$ : 229.0.  $^1H$ -NMR ( $CDCl_3$ , 600 MHz):  $\delta$  = 1.59 (d,  $J=7.2$  Hz, 3H), 2.00 (s, 3H), 3.91 (s, 3H), 5.37 (q,  $J=7.2$  Hz, 1H), 6.79 (d,  $J=7.2$  Hz, 2H), 8.01 (s, 1H).  $^{13}C$ -NMR ( $CDCl_3$ , 150.92 MHz):  $\delta$  = 21.4, 23.1, 47.2, 52.4, 127.6, 146.5, 161.7, 169.8, 173.5.

### Preparation of methyl 2-((R)-1-(N-((R)-1-(4-methoxyphenyl)ethyl)acetamido)ethyl)thiazole-4-carboxylate 12

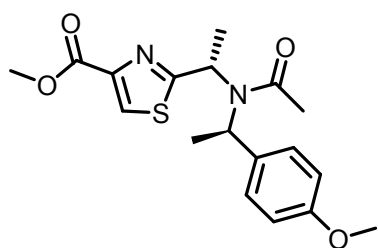
Acetaldehyde (0.45 mL, 8 mmol), (R)-1-(4-methoxyphenyl)ethylamine (1.2 mL, 8 mmol), and dry methanol (8 mL) are added together at room temperature. Then the isocyanide (1.23 g, 8 mmol) and thiocarboxylic acid (560  $\mu$ L, 8 mmol) are added to the reaction mixture and stirred at room temperature for one day. The mixture is then condensed and purified with column chromatography (EtOAc: PE). Two diastereomer were separated with 476 mg and 140 mg, and 1.2 mg of mixture.

### methyl 2-((R)-1-(N-((R)-1-(4-methoxyphenyl)ethyl)acetamido)ethyl)thiazole-4-carboxylate (R,R)12



$C_{18}H_{22}N_2O_4S$ , Mw: 362.44 g/mol; HRMS (ESI-TOF)  $m/z$  (calc.): 362.13, (found)  $[M]^+$ : 362.1307; HPLC-MS  $r_t$ : 10.13,  $m/z$   $[M+H]^+$ : 363.2,  $[M+Na]^+$  385.0.  $[\alpha]_D^{24}$  -17.2 (c 0.215, MeOH).  $^1H$ -NMR ( $CDCl_3$ , 600 MHz):  $\delta$  = 1.21 (t,  $J=6.6$  Hz, 3H), 1.42 (t,  $J=6.6$  Hz, 3H), 2.25 (s, 3H), 3.78 (s, 3H), 3.88 (s, 3H), 4.66 (s, 1H), 5.08 (m, 1H), 6.87 (d,  $J=9$  Hz, 2H), 7.26 (d,  $J=9$  Hz, 2H), 8.07 (s, 1H).  $^{13}C$ -NMR ( $CDCl_3$ , 150.92 MHz):  $\delta$  = 14.2 (rotamer), 16.9 (rotamer), 18.0, 18.9, 23.4, 42.3, 52.2, 52.3, 53.5, 55.3, 56.3, 62.8, 114.0, 128.5, 128.9, 131.1, 144.8, 146.0 (rotamer), 159.2, 162.0, 173.3, 177.9.

**methyl 2-((S)-1-(N-((R)-1-(4-methoxyphenyl)ethyl)acetamido)ethyl)thiazole-4-carboxylate (S,R)12**



$C_{18}H_{22}N_2O_4S$ , Mw: 362.44 g/mol; HRMS (ESI-TOF) m/z (calc.): 362.13, (found)  $[M]^+$ : 362.1307; HPLC-MS  $r_t$ : 9.77, m/z:  $[M+Na]^+$  384.9.  $[\alpha]_D^{24} +2.14$  (c 0.14, MeOH).  $^1H$ -NMR ( $CDCl_3$ , 600 MHz):  $\delta$  = 1.48 (d,  $J=7.2$  Hz, 20% 3H), 1.60 (d,  $J=7.2$  Hz, 3H), 1.84 (t,  $J=3.6$  Hz, 80%, 3H), 1.86 (t,  $J=3.6$  Hz, 80%, 3H), 2.29 (m, 3H), 3.75 (m, 3H), 3.90 (m, 3H), 4.80 (m, 1H), 5.14 (m, 1H), 6.75 (d,  $J=8.4$  Hz, 80% 2H), 6.86-6.93 (m, 20% 2H), 7.13 (d,  $J=8.4$  Hz, 2H), 7.24-7.38 (m, 20% 2H), 7.96 (s, 80% 1H), 8.11 (s, 20% 1H).  $^{13}C$ -NMR ( $CDCl_3$ , 150.92 MHz):  $\delta$  = 18.0, 19.5, 23.5, 48.2, 52.2, 53.2, 55.2, 55.3, 56.2, 113.8, 114.0, 127.4, 128.4, 128.5, 129.0, 130.8, 144.6, 159.2, 161.9, 170.3, 172.6.

**Preparation of 2-(1-Acetylamino-ethyl)-thiazole-4-carboxylic acid methyl ester (R)7**

100  $\mu$ L TFA was added to (R,R)12 (50 mg, 0.138 mmol) and the mixture is stirred at r.t for 24 hours. After the reaction was complete, the solution was concentrated and purified by preparative TLC (EtOAc: PE). A yellow solid was obtained (30 mg, 98 %).  $[\alpha]_D^{24} -19.4$  (c 0.11, MeOH).

**HPLC condition:**

Chiral Column: DAICEL CHIRALPAK IB, Mobile Phase: 15% EtOH and 85% Hexane, Retention time of two enantiomers: 5.4 mins and 6.2 mins

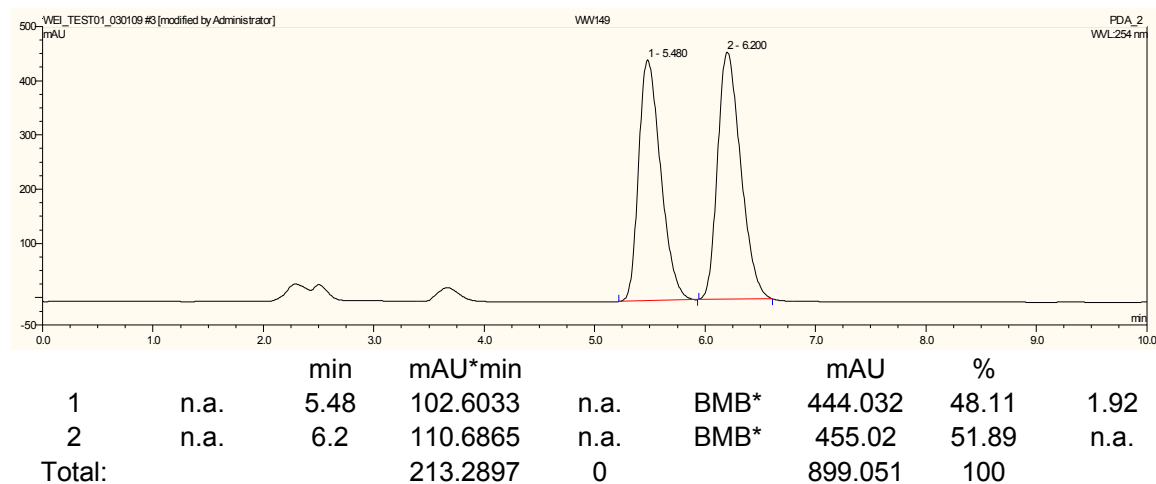
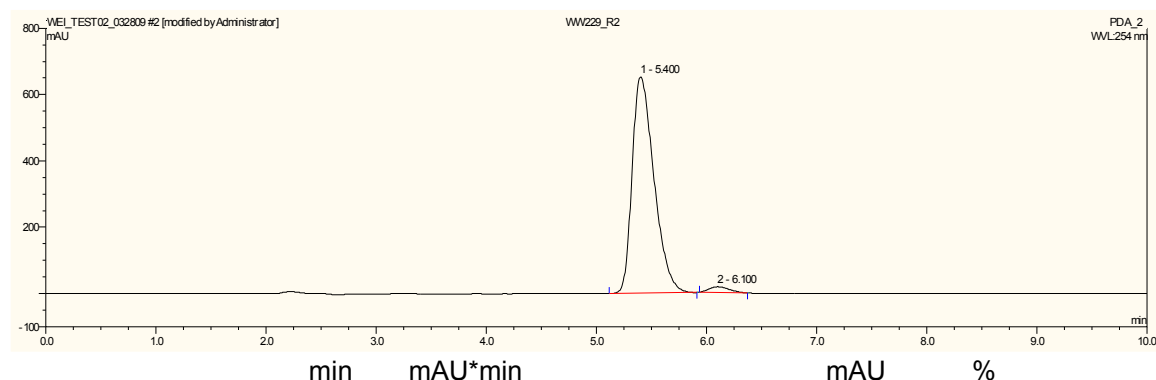


Figure 1 Chiral HPLC Separation of the two enantiomers of 7



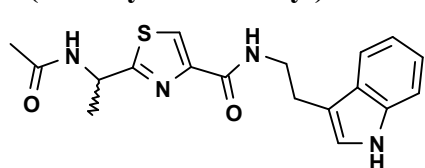
1	n.a.	5.4	149.8549	n.a.	BMB*	652.612	97.61	1.97
2	n.a.	6.1	3.6731	n.a.	BMB*	17.256	2.39	n.a.
Total:			153.528	0		669.868	100	

Figure 2 Chiral HPLC Separation of the one enantiomers of **(R)7**

### General Procedure for Amidation:

0.1 mmol of thiazole ester, 30% TBD, 0.2-0.3 mmol of amine were mixed in 0.5 mL of anhydrous THF, stirred for 1hr at r.t.. Then purified by preparative TLC to give the corresponding amide product.

### 2-(1-Acetylamino-ethyl)-thiazole-4-carboxylic acid [2-(1H-indol-3-yl)-ethyl]-amide ((±)1)



$C_{18}H_{20}N_4O_2S$ , Mw: 356.44 g/mol; HRMS (ESI-TOF) m/z (calc.): 356.1307, (found)  $[M+Na]^+$ : 379.1209; HPLC-MS  $r_t$ : 1.48, m/z  $[M+H]^+$ : 357.1.  $^1H$ -NMR ( $CDCl_3$ , 600 MHz):  $\delta$  = 1.54 (d, J=7.2 Hz, 3H), 2.02 (s, 3H), 3.09 (t, J=6.6 Hz, 2H), 3.74 (m, 1H), 3.79 (m, 1H), 5.35 (q, J=7.2

Hz, 1H), 6.40(d, J=9.6 Hz, 1H), 7.06 (d, J= 2.4 Hz, 1H), 7.12 (dd, J= 6.6 Hz, 1H), 7.21 (dd, J= 9.6 Hz, 1H), 7.39 (d, J= 8.4 Hz, 1H), 7.46 (t, J=6 Hz, 1H), 7.65 (d, J= 8.4 Hz, 1H), 8.51 (s, 1H).  $^{13}C$ -NMR ( $CDCl_3$ , 150.92 MHz):  $\delta$  =21.3, 23.3, 25.4, 39.8, 47.0, 111.3, 112.8, 118.8, 119.3, 122.1, 122.3, 123.0, 127.4, 136.4, 149.8, 161.0, 169.7, 172.6.

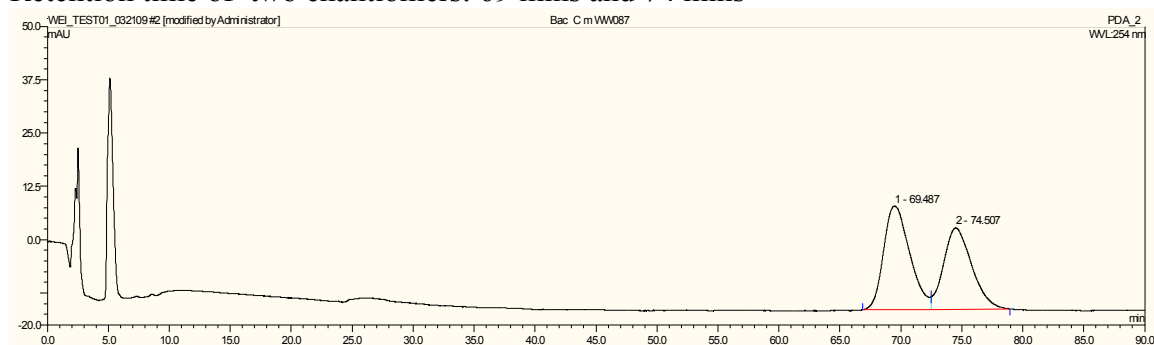
### Preparation of Amide (-)1 by Using coupling condition:

23 mg of **(R)7** was dissolved in 1 mL of THF, 200  $\mu$ l of 0.5 mol/L LiOH solution (1:1 THF:H<sub>2</sub>O) was added. The solution was stirred overnight under 0°C. Then 100  $\mu$ l of 4M HCl dioxane was added to neutralize the solution. All solvent was evaporated to give the acid for the next coupling reaction.

20 mg of EDCI, 14 mg of HOBt, 100  $\mu$ l of DIPEA, 20 mg of tryamine was mixed with prepared acid in 1 mL of dichloromethane under 0°C. Stirred overnight and monitored by TLC, then diluted with dichloromethane and washed with water, dried, evaporation. The crude sample was separated by preparative TLC to give the final compound **(-)-1** (retention time:74 min).  $[\alpha]_D^{24}$  -15.5 (c 0.155, MeOH).

### HPLC condition:

Chiral Column: DAICEL CHIRALPAK IB, Mobile Phase: 6% EtOH and 94% Hexane, Retention time of two enantiomers: 69 mins and 74 mins



		min	mAU*min			mAU	%	
1	n.a.	69.487	61.1197	n.a.	BM *	24.351	54.33	1.23
2	n.a.	74.507	51.3832	n.a.	MB*	19.143	45.67	n.a.
Total:			112.5029	0		43.494	100	

Figure 3 Chiral HPLC Separation of the two Bacillamide C enantiomers

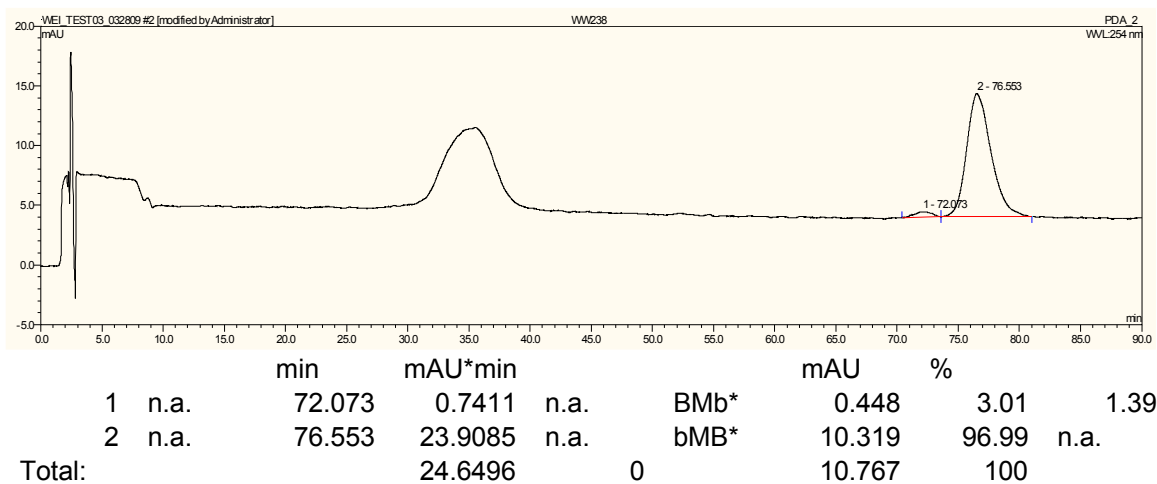


Figure 4 Chiral HPLC Separation of the one Bacillamide C enantiomers

### The HNMR comparison of the reported Natural Bacillamide C and the synthesized one

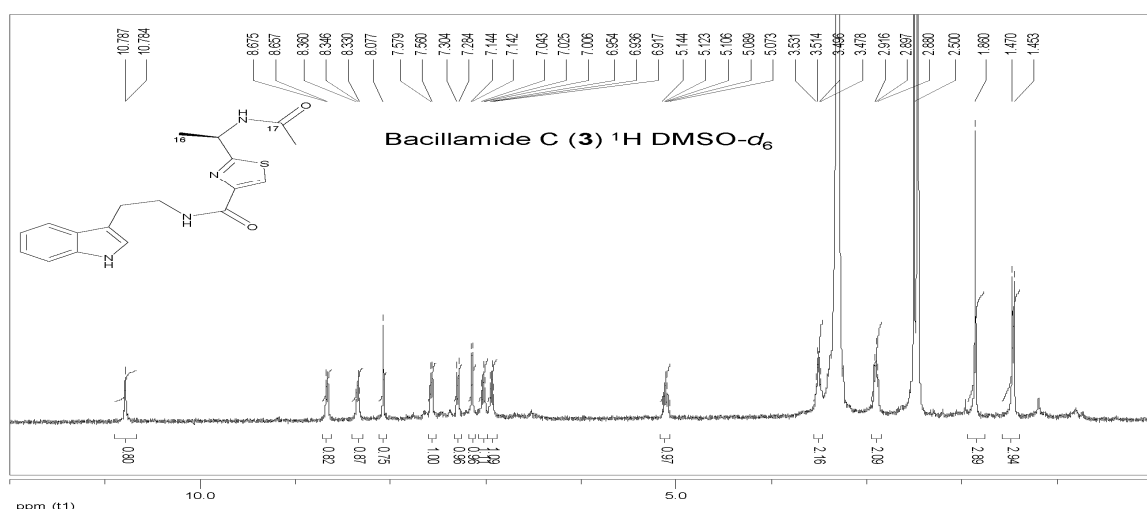


Figure 5 <sup>1</sup>H-NMR of the reported Natural Bacillamide C<sup>1</sup>

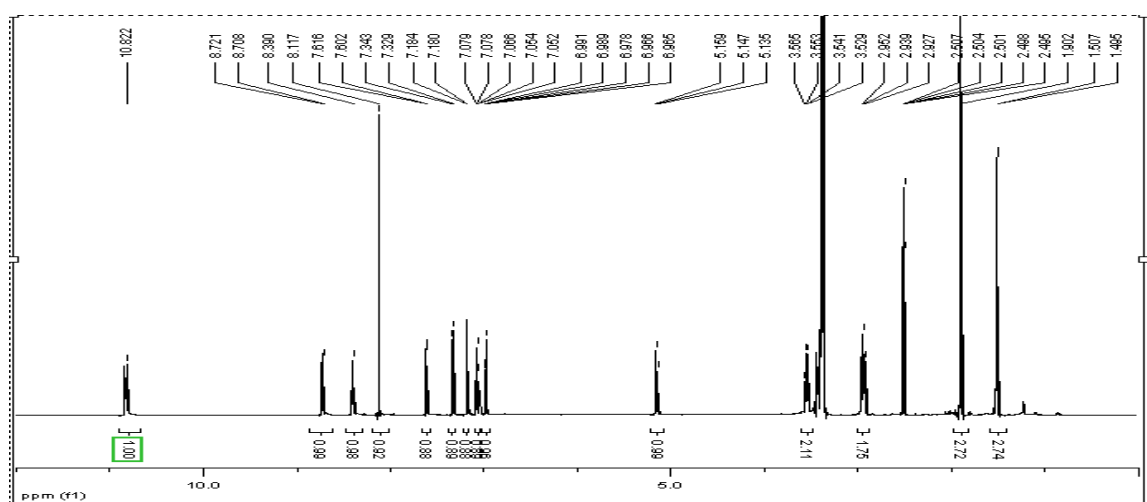


Figure 6 <sup>1</sup>H-NMR of synthesized Bacillamide C

<sup>1</sup> Socha, A. M.; Long, R. A.; Rowley, D. C. *J. Nat. Prod.* **2007**, *70*, 1793-1795.

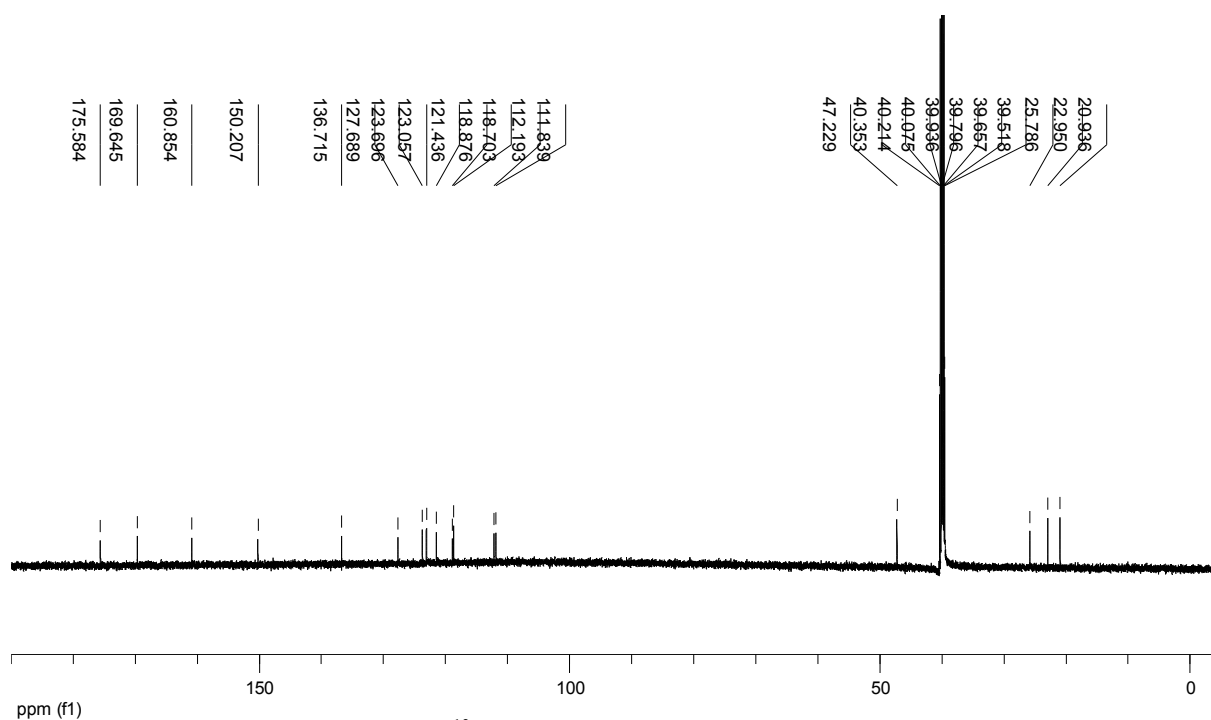


Figure 7  $^{13}\text{C}$ -NMR of synthesized Bacillamide C

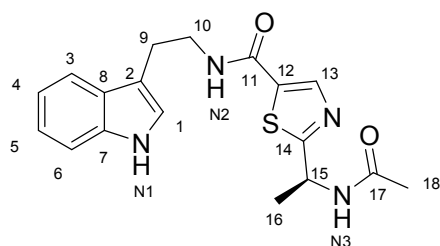
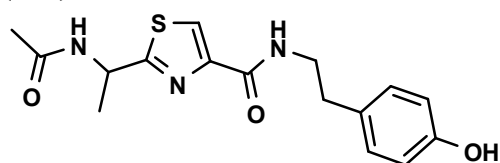


Table 1: The NMR data comparison between the reported natural Bacillamide C and the synthesized product

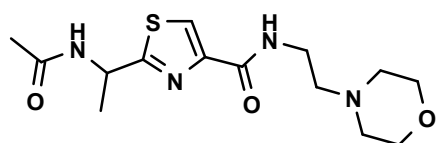
	$\delta_{\text{C}}$ (reported natural)	$\delta_{\text{C}}$ (synthesized)	$\delta_{\text{H}}$ (reported natural)	$\delta_{\text{H}}$ (synthesized)
1	122.6	123.0	7.14(d, 1.0)	7.14(d, 2.4)
2	111.7	112.2		
3	118.2	118.9	7.57(d, 7.8)	7.60(d, 8.4)
4	118.2	118.7	6.94(dd, 7.6, 7.8)	6.97(dd, 7.2, 1.2)
5	121	121.4	7.03(dd, 7.6, 7.8)	7.07(dd, 7.2, 1.2)
6	111.4	111.8	7.29(d, 7.8)	7.33(d, 8.4)
7	136	136.7		
8	127.2	127.7		
9	25.4	25.8	2.90(t, 7.4)	2.50(t, 1.8)
10	40.4	40.4(overlapped)	3.51(dt, 6.6, 7.4)	3.55(dt, 6.6, 1.8)
11	160.4	160.8		
12	149.8	150.2		
13	123.2	123.7	8.08(s)	8.12(s)
14	176.5	175.6		
15	46.8	47.2	5.11(dq, 6.8, 7.2)	5.15(m)
16	20.5	20.9	1.46(d, 6.8)	1.50(d, 7.2)
17	169.1	169.6		
18	22.5	22.9	1.86(s)	1.90(s)
NH-1			10.76(d, 1.0)	10.82(s, 1.0)
NH-2			8.35(t, 6.6)	8.39(t, 6.0)
NH-3			8.66(d, 7.2)	8.71(d, 7.8)

### 2-(1-Acetylamino-ethyl)-thiazole-4-carboxylic acid [2-(4-hydroxy-phenyl)-ethyl]-amide (10a)



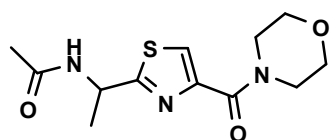
$C_{16}H_{19}N_3O_3S$ , Mw: 333.11 g/mol; HRMS (ESI-TOF)  $m/z$  (calc.): 333.1147, (found)  $[M]^+$ : 333.1146; HPLC-MS  $r_t$ : 8.34,  $m/z$   $[M+H]^+$ : 333.9.  $^1H$ -NMR ( $CDCl_3$ , 600 MHz):  $\delta$  = 1.60 (d,  $J=7.2$  Hz, 3H), 2.07 (s, 3H), 2.86 (t,  $J=6.6$  Hz, 2H), 3.66 (t,  $J=6.6$  Hz, 2H), 5.39 (q,  $J=7.2$  Hz, 1H), 6.21 (d,  $J=9.6$  Hz, 1H), 6.82 (d,  $J=10.8$  Hz, 2H), 7.09 (d,  $J=10.8$  Hz, 2H), 7.28 (t,  $J=6$  Hz, 1H), 8.01 (s, 1H).  $^{13}C$ -NMR ( $CDCl_3$ , 150.92 MHz):  $\delta$  = 21.4, 23.2, 34.9, 40.8, 47.1, 114.8, 115.6, 123.2, 130.0, 130.3, 149.6, 154.8, 161.0, 169.8, 172.4.

### 2-(1-Acetylamino-ethyl)-thiazole-4-carboxylic acid (2-morpholin-4-yl-ethyl)-amide (10b)



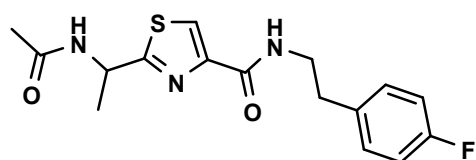
$C_{14}H_{22}N_4O_3S$ , Mw: 326.41 g/mol; HRMS (ESI-TOF)  $m/z$  (calc.): 326.1413, (found)  $[M]^+$ : 326.1423; HPLC-MS  $r_t$ : 1.58,  $m/z$   $[M+H]^+$ : 327.3.  $^1H$ -NMR ( $CDCl_3$ , 600 MHz):  $\delta$  = 1.64 (d,  $J=7.2$  Hz, 3H), 2.08 (s, 3H), 2.53 (s, 4H), 2.61 (t,  $J=6$  Hz, 2H), 3.56 (t,  $J=6$  Hz, 2H), 3.74 (t,  $J=4.2$  Hz, 4H), 5.42 (q,  $J=7.2$  Hz, 1H), 6.27 (d,  $J=9.6$  Hz, 1H), 7.72 (s, 1H), 8.01 (s, 1H).  $^{13}C$ -NMR ( $CDCl_3$ , 150.92 MHz):  $\delta$  = 21.3, 23.3, 35.7, 47.1, 53.4, 57.0, 67.1, 123.1, 149.8, 161.0, 169.5, 172.7.

### N-{1-[4-(Morpholine-4-carbonyl)-thiazol-2-yl]-ethyl}-acetamide (10c)



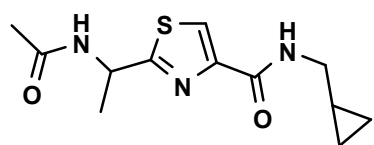
$C_{12}H_{17}N_3O_3S$ , Mw: 283.1 g/mol; HRMS (ESI-TOF)  $m/z$  (calc.): 283.0991, (found)  $[M]^+$ : 283.0982; HPLC-MS  $r_t$ : 6.96,  $m/z$   $[M+H]^+$ : 284.  $^1H$ -NMR ( $CDCl_3$ , 600 MHz):  $\delta$  = 1.61 (d,  $J=7.2$  Hz, 3H), 2.06 (s, 3H), 3.71-3.89 (w, 8H), 5.41 (q,  $J=7.2$  Hz, 1H), 6.28 (d,  $J=7.2$  Hz, 1H), 7.83 (s, 1H).  $^{13}C$ -NMR ( $CDCl_3$ , 150.92 MHz):  $\delta$  = 21.4, 23.2, 43.1, 47.2, 47.9, 66.9, 67.0, 124.6, 149.7, 162.621, 169.6, 172.0.

### 2-(1-Acetylamino-ethyl)-thiazole-4-carboxylic acid [2-(4-fluoro-phenyl)-ethyl]-amide (10d)



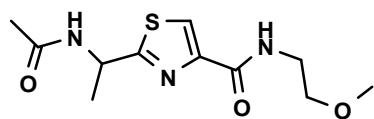
$C_{16}H_{18}FN_3O_2S$ , Mw: 335.11g/mol; HRMS (ESI-TOF)  $m/z$  (calc.): 335.1104, (found)  $[M]^+$ : 335.1102; HPLC-MS  $r_t$ : 9.37,  $m/z$   $[M+H]^+$ : 336.0.  $^1H$ -NMR ( $CDCl_3$ , 600 MHz):  $\delta$  = 1.60 (d,  $J=7.2$  Hz, 3H), 2.06 (s, 3H), 2.91 (t,  $J=7.2$  Hz, 2H), 3.66 (m, 2H), 5.39 (q,  $J=7.2$  Hz, 1H), 6.25 (d,  $J=9.6$  Hz, 1H), 7.01 (m, 2H), 7.20 (m, 2H), 7.34 (t,  $J=6$  Hz, 1H), 8.00 (s, 1H).  $^{13}C$ -NMR ( $CDCl_3$ , 150.92 MHz):  $\delta$  = 21.3, 23.2, 34.1, 40.6, 47.1, 115.4, 115.5, 123.1, 130.2, 130.3, 134.4, 134.5, 149.6, 160.9, 160.9, 162.483, 169.5, 172.8.

### 2-(1-Acetylamino-ethyl)-thiazole-4-carboxylic acid cyclopropylmethyl-amide (10e)



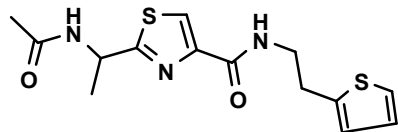
$C_{12}H_{17}N_3O_2S$ , Mw: 267.35 g/mol; HRMS (ESI-TOF) m/z (calc.): 267.1041, (found)  $[M]^+$ : 267.1043; HPLC-MS r<sub>t</sub>: 8.32, m/z  $[M+H]^+$ : 268.1.  $^1H$ -NMR ( $CDCl_3$ , 600 MHz):  $\delta$  = 0.28 (m, 2H), 0.58 (m, 2H), 1.07 (m, 1H), 1.64 (d, J=7.2 Hz, 3H), 2.08 (s, 3H), 3.30 (m, 2H), 5.42 (q, J=7.2 Hz, 1H), 6.33(d, J=8.4 Hz, 1H), 7.39 (t, J=6 Hz, 1H), 7.99 (s, 1H).  $^{13}C$ -NMR ( $CDCl_3$ , 150.92 MHz):  $\delta$  = 3.6, 10.8, 21.4, 23.3, 44.2, 47.1, 123.1, 149.9, 160.9, 169.5, 172.7.

### 2-(1-Acetylamino-ethyl)-thiazole-4-carboxylic acid (2-methoxy-ethyl)-amide (10f)



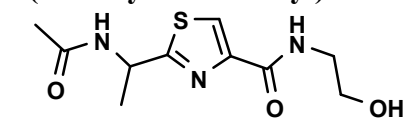
$C_{11}H_{17}N_3O_3S$ , Mw: 271.34 g/mol; HRMS (ESI-TOF) m/z (calc.): 271.0991, (found)  $[M]^+$ : 271.09803; HPLC-MS r<sub>t</sub>: 7.42, m/z  $[M+H]^+$ : 272.1.  $^1H$ -NMR ( $CDCl_3$ , 600 MHz):  $\delta$  = 1.61 (d, J=7.2 Hz, 3H), 2.07 (s, 3H), 3.41 (s, 3H), 3.58 (m, 2H), 3.63 (t, J=5.4 Hz, 2H), 5.40 (q, J=7.2 Hz, 1H), 6.50(d, J=9.6 Hz, 1H), 7.65 (s, 1H), 7.97 (s, 1H).  $^{13}C$ -NMR ( $CDCl_3$ , 150.92 MHz):  $\delta$  = 21.4, 23.2, 34.9, 40.8, 47.1, 114.8, 115.6, 123.2, 129.9, 130.3, 149.6, 154.8, 161.2, 169.8, 172.4.

### 2-(1-Acetylamino-ethyl)-thiazole-4-carboxylic acid (2-thiophen-2-yl-ethyl)-amide (10g)



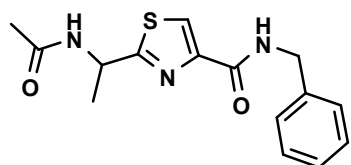
$C_{14}H_{17}N_3O_2S_2$ , Mw: 323.43 g/mol; HRMS (ESI-TOF) m/z (calc.): 323.0762, (found)  $[M]^+$ : 323.0762; HPLC-MS r<sub>t</sub>: 9.06, m/z  $[M+H]^+$ : 324.0.  $^1H$ -NMR ( $CDCl_3$ , 600 MHz):  $\delta$  = 1.60 (d, J=7.2 Hz, 3H), 2.06 (s, 3H), 3.15 (t, J=7.2 Hz, 2H), 3.72 (m, 2H), 5.39 (q, J=7.2 Hz, 1H), 6.36(d, J=6.6 Hz, 1H), 6.89(d, J=3 Hz, 1H), 6.97(dd, J=3.6 Hz, J=4.8 Hz, 1H), 6.97(dd, J=1.2 Hz, J=4.8 Hz, 1H), 7.49 (s, 1H), 7.99 (s, 1H).  $^{13}C$ -NMR ( $CDCl_3$ , 150.92 MHz):  $\delta$  = 21.3, 23.2, 30.0, 40.7, 47.1, 123.2, 124.0, 125.4, 127.1, 141.1, 149.6, 161.0, 169.5, 172.7.

### 2-(1-Acetylamino-ethyl)-thiazole-4-carboxylic acid (2-hydroxy-ethyl)-amide (10h)



$C_{10}H_{15}N_3O_3S$ , Mw: 257.31 g/mol; HRMS (ESI-TOF) m/z (calc.): 257.0834, (found)  $[M]^+$ : 257.0831; HPLC-MS r<sub>t</sub>: 1.50, m/z  $[M+Na]^+$ : 280.2.  $^1H$ -NMR ( $CDCl_3$ , 600 MHz):  $\delta$  = 1.61 (d, J=7.2 Hz, 3H), 2.07 (s, 3H), 3.62 (m, 2H), 3.84 (t, J=4.8 Hz, 2H), 5.38 (q, J=7.2 Hz, 1H), 6.54(d, J=6.6 Hz, 1H), 7.77 (t, J=2.4 Hz, 1H), 7.98(s, 1H).  $^{13}C$ -NMR ( $CDCl_3$ , 150.92 MHz):  $\delta$  = 21.2, 23.2, 42.4, 47.0, 62.2, 123.5, 149.3, 162.0, 169.7, 172.8.

### 2-(1-Acetylamino-ethyl)-thiazole-4-carboxylic acid benzylamide (10i)

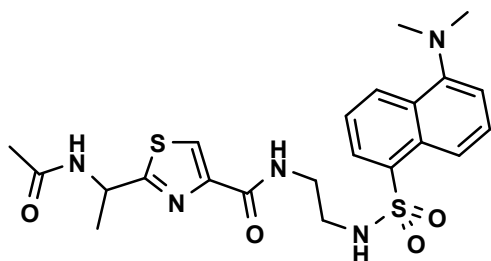


$C_{15}H_{17}N_3O_2S$ , Mw: 303.38 g/mol; HRMS (ESI-TOF) m/z (calc.): 303.1041, (found)  $[M]^+$ : 303.1047; HPLC-MS r<sub>t</sub>: 8.93, m/z  $[M+H]^+$ : 304.0.  $^1H$ -NMR ( $CDCl_3$ , 600 MHz):  $\delta$  = 1.59 (d,



J=7.2 Hz, 3H), 2.05 (s, 3H), 4.64 (d, J=6 Hz, 2H), 5.38 (q, J=7.2 Hz, 1H), 7.31(m, 1H), 7.36(m 4H), 7.63 (m, 1H), 8.04(s, 1H). <sup>13</sup>C-NMR (CDCl<sub>3</sub>, 150.92 MHz): δ =21.4, 23.2, 42.3, 47.0, 123.4, 127.6, 127.9, 128.8, 138.1, 149.6, 16.9, 169.5, 172.8.

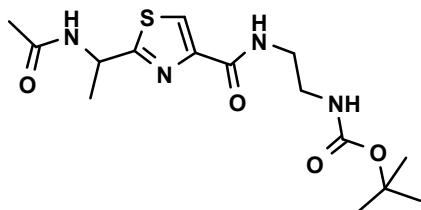
**2-(1-Acetylamino-ethyl)-thiazole-4-carboxylic acid [2-(5-dimethylamino-naphthalene-1-sulfonylamino)-ethyl]-amide (10j)**



C<sub>22</sub>H<sub>27</sub>N<sub>5</sub>O<sub>4</sub>S<sub>2</sub>, Mw: 489.61 g/mol; HRMS (ESI-TOF) m/z (calc.): 489.1504, (found) [M]<sup>+</sup>: 489.1501; HPLC-MS r<sub>t</sub>: 9.44, m/z [M+H]<sup>+</sup>: 490.0. <sup>1</sup>H-NMR (CDCl<sub>3</sub>, 600 MHz): δ =1.61 (d, J= 6.6 Hz, 3H), 2.09 (s, 3H), 2.89 (s, 6H), 3.15(t, J=6Hz, 2H), 3.52 (m, 2H), 5.39 (q, J=7.2 Hz, 1H), 5.83(t, J=6Hz, 1H), 6.61(d, J=8.4Hz, 1H), 7.16(d, J=8.4Hz, 1H), 7.52 (m, 2H), 7.84(t, J=6Hz, 1H), 8.25(d, J=6.6 Hz, 1H), 8.28(d, J=8.4Hz, 1H), 8.84(d, J=9Hz, 1H). <sup>13</sup>C-

NMR (CDCl<sub>3</sub>, 150.92 MHz): δ = 21.8, 23.2, 39.5, 43.2, 45.4, 47.1, 115.2, 118.6, 123.1, 123.5, 128.5, 129.5, 129.6, 129.9, 130.6, 134.3, 149.0, 152.0, 161.8, 169.8, 172.4.

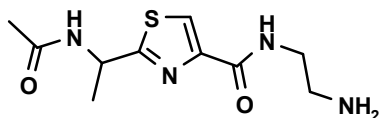
**(2-([2-(1-Acetylamino-ethyl)-thiazole-4-carbonyl]-amino)-ethyl)-carbamic acid tert-butyl ester (Boc-10k)**



C<sub>15</sub>H<sub>24</sub>N<sub>4</sub>O<sub>4</sub>S, Mw: 356.44 g/mol; HRMS (ESI-TOF) m/z (calc.): 356.1518, (found) [M]<sup>+</sup>: 356.1518; HPLC-MS r<sub>t</sub>: 8.32, m/z [M+H]<sup>+</sup>: 268.1. <sup>1</sup>H-NMR (CDCl<sub>3</sub>, 600 MHz): δ =1.42 (s, 9H), 1.62 (d, J= 6.6 Hz, 3H), 2.08 (s, 3H), 3.40 (m, 2H), 3.51(t, J=5.4Hz, 2H), 5.07(s, 1H), 5.39 (q, J=7.2 Hz, 1H), 6.48 (d, J=6.6 Hz, 1H), 7.76 (s, 1H), 7.77(s, 1H). <sup>13</sup>C-NMR (CDCl<sub>3</sub>, 150.92 MHz): δ = 21.4,

23.2, 42.3, 47.1, 123.5, 127.6, 127.9, 128.8, 138.1, 149.6, 16.9, 169.5, 172.8.

**2-(1-Acetylamino-ethyl)-thiazole-4-carboxylic acid (2-amino-ethyl)-amide TFA Salt (10k)**



C<sub>10</sub>H<sub>16</sub>N<sub>4</sub>O<sub>2</sub>S, Mw: 256.32 g/mol; HRMS (ESI-TOF) m/z (calc.): 256.0994, (found) [M]<sup>+</sup>: 256.0998; HPLC-MS r<sub>t</sub>: 1.60, 2.63, m/z [M+H]<sup>+</sup>: 257.1. <sup>1</sup>H-NMR (MeOD, 600 MHz): δ = 1.63 (d, J= 6.6 Hz, 3H), 2.05 (s, 3H), 3.20 (t,

J=6Hz, 2H), 3.70(m, 2H), 5.31 (q, J=7.2 Hz, 1H), 8.17(s, 1H). <sup>13</sup>C-NMR (CDCl<sub>3</sub>, 150.92 MHz): δ = 23.4, 25.0, 40.7, 43.5, 127.7, 152.8, 167.1, 175.6, 179.0.

**Procedure for confocal microscope:**

HCT116 cancer cell lines were grown in medium on a LAB\_TEK II 8-chamber coverglass plate for 4 days in an incubator at 37°C. After the 4 day the medium was removed and 200µL of fresh medium was added. **9j** dissolved in DMSO, was then added to the chamber to afford a medium with 100µM **9j** with 1% DMSO.

The plate was viewed under the Olympus FV1000 confocal microscope system equipped with an inverter scope, 4 lasers and differential interface contrast (DIC) microscope. The fluorescent images were captured using a laser emitting at 488nm and DIC images were captured using a laser emitting at 408nm. The cells were incubated while on the microscope (using an incubation plate) at 37°C.

The video images were taken 10 seconds apart from one another for about half hour.

Picture images the compound was allowed to incubate for a half hour before images were taken.

A control well with no **9j** was also viewed to make sure there was no background fluorescence in the cells.