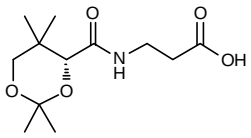
Supplementary materials and methods

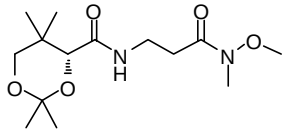
Synthesis of N5-Pan and N7-Pan

(*R*)-3-(2,2,5,5-tetramethyl-1,3-dioxane-4-carboxamido)propanoic acid (1)



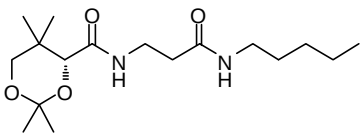
To a cooled solution (0 °C) of (R)-pantothenic acid (20.8 g, 94.0 mmol) in acetone (500 mL) were added subsequently 2-methoxyprop-1-ene (27.1 mL, 283 mmol) and pTsOH·H2O (0.89 g, 4.72 mmol). After 15 min the temperature was raised to room temperature and the mixture was stirred for another 30 min. The mixture was diluted with saturated aqueous NaHCO3 (10 mL) and concentrated in vacuo to yield **1** as a yellow solid, which was used without purification. TLC (CH2Cl2:MeOH, 9:1 v/v): Rf = 0.67. Spectral data were in correspondence with reported data in literature (Sewell *et al*. Org. Lett. **13**, 800-803 (2011).

(*R*)-*N*-{3-[methoxy(methyl)amino]-3-oxopropyl}-2,2,5,5-tetramethyl-1,3-dioxane-4-carboxamide (2)



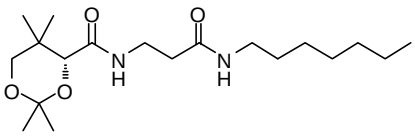
To a solution of **1** (1.80 g, 6.92 mmol) in dry CH_2Cl_2 (65 mL) at rt were added, EDC (2.09 g, 1.5 equiv), *N*,*O*-dimethylhydroxylamine hydrochloride (1.04 g, 1.5 equiv) and DIPEA (3.43 mL, 3.0 equiv), followed by DMAP (483 mg, 0.5 equiv). The reaction mixture was stirred over night at rt, quenched with saturated aqueous NH_4Cl (40 mL), extracted with CH_2Cl_2.(3 × 50 mL), dried (Na_2SO_4), and concentrated *in vacuo*. The product was purified by column chromatography (MeOH/CH_2Cl_2, 0:1→1:4) to afford **2** (1.90 g, 91% yield) as a colorless oil. R_f 0.56 (MeOH/CH_2Cl_2, 1:9). $[\alpha]_D^{20}$ +44.5 (*c* 1.32, CH_2Cl_2). IR (ATR) 3417, 3334, 2980, 2940, 2871, 1661, 1520, 1378, 1196, 1095, 873 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ 7.13 (t, *J* = 5.7 Hz, 1H), 4.07 (s, 1H), 3.68 (d, *J* = 11.7 Hz, 1H), 3.67 (s, 3H), 3.64-3.48 (m, 2H), 3.27 (d, *J* = 11.7 Hz, 1H), 3.18 (s, 3H), 2.76-2.59 (m, 2H), 1.46 (s, 3H), 1.42 (s, 3H), 1.03 (s, 3H), 0.96 (s, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 169.9, 99.1, 77.3, 71.6, 61.4, 34.2, 33.1, 32.3, 31.9, 29.6, 22.3, 19.0, 18.8. HRMS (ESI) *m/z* calcd for $C_{14}H_{26}N_2O_5$ $(M+Na)^+$: 325.1739, found: 325.1746.

(*R*)-2,2,5,5-tetramethyl-*N*-[3-oxo-3-(pentylamino)propyl]-1,3-dioxane-4-carboxamide (3)



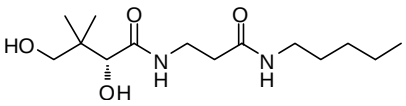
Prepared as described for **2**, starting from **1** (3.40 g, 13.1 mmol) and *n*-amylamine (2.30 mL, 1.5 equiv). Column chromatography (EtOAc/heptane, 0:1→4:1) afforded **3** (1.89 g, 44% yield) as a white solid. R_f 0.56 (MeOH/CH_2Cl_2, 1:9). Mp 81.5 °C. $[\alpha]_D^{20}$ +41.6 (*c* 1.01, CH_2Cl_2). IR (ATR) 3430, 3317, 3300, 2954, 2931, 2868, 1649, 1526, 1463, 1377, 1197, 1098, 873 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ 7.02 (t, *J* = 5.2 Hz, 1H), 5.88-5.84 (m, 1H), 4.07 (s, 1H), 3.68 (d, *J* = 11.7 Hz, 1H), 3.64-3.46 (m, 2H), 3.28 (d, *J* = 11.7 Hz, 1H), 3.26-3.21 (m, 2H), 2.43 (t, *J* = 6.2 Hz, 2H), 1.49 (dt, *J* = 7.3, 14.6 Hz, 2H), 1.46 (s, 3H), 1.42 (s, 3H), 1.38-1.24 (m, 4H), 1.04 (s, 3H), 0.97 (s, 3H), 0.90 (t, *J* = 6.8 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 170.9, 170.3, 99.2, 77.3, 71.6, 39.7, 36.4, 35.1, 33.1, 29.6, 29.4, 29.2, 22.5, 22.3, 19.0, 18.8, 14.1. HRMS (ESI) *m/z* calcd for $C_{17}H_{33}N_2O_4$ $(M+H)^+$: 329.2440, found: 329.2426.

(*R*)-*N*-[3-(heptylamino)-3-oxopropyl]-2,2,5,5-tetramethyl-1,3-dioxane-4-carboxamide (4)



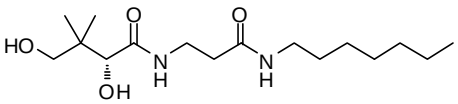
Prepared as described for **2**, starting from **1** (4.50 g, 17.4 mmol) and *n*-heptylamine (3.90 mL, 1.5 equiv). Column chromatography (EtOAc/heptane, 1:2→1:0) afforded **4** (3.15 g, 51% yield) as a colorless oil. R_f 0.56 (MeOH/CH_2Cl_2, 1:9). $[\alpha]_D^{20}$ +39.4 (*c* 1.00, CH_2Cl_2). IR (ATR) 3425, 3321, 2927, 2863, 1650, 1526, 1459, 1377, 1196, 1098, 875 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ 7.04 (t, *J* = 5.9 Hz, 1H), 6.03 (t, *J* = 4.9 Hz, 1H), 4.06 (s, 1H), 3.68 (d, *J* = 11.7 Hz, 1H), 3.63-3.46 (m, 2H), 3.28 (d, *J* = 11.7 Hz, 1H), 3.26-3.20 (m, 2H), 2.42 (t, *J* = 6.2 Hz, 2H), 1.53-1.47 (m, 2H), 1.46 (s, 3H), 1.41 (s, 3H), 1.32-1.24 (m, 8H), 1.03 (s, 3H), 0.97 (s, 3H), .88 (t, *J* = 6.9 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 170.8, 170.2, 99.1, 77.1, 71.5, 39.6, 36.2, 35.0, 33.0, 31.7, 29.6, 29.5, 29.0, 26.9, 22.6, 22.2, 18.9, 18.7, 14.1. HRMS (ESI) *m/z* calcd for $C_{19}H_{37}N_2O_4$ $(M+H)^+$: 357.2753, found: 357.2747.

(*R*)-2,4-dihydroxy-3,3-dimethyl-*N*-[3-oxo-3-(pentylamino)propyl]butanamide (N5-Pan, 5)



To a solution of **3** (30 mg, 0.10 mmol) in MeCN (1.0 mL) was added, $BiCl_3$ (6.5 mg, 20 mol%), followed by distilled H_2O (36 µL, 20 equiv). The reaction was stirred at rt for 4 h, then filtered and concentrated *in vacuo*. After dilution with EtOAc (10 mL), the reaction mixture was washed with saturated aqueous $NaHCO_3$ (2 × 8 mL) and the aqueous layer was extracted with EtOAc (3 × 8 mL). The organic layers were combined, dried (Na_2SO_4), and concentrated *in vacuo*. The product was purified by column chromatography (EtOAc/heptane, 1:1→1:0) to afford **5** (1.22 g, 75% yield) as a white solid. R_f 0.46 (MeOH/CH_2Cl_2, 1:9). Mp 89.4 °C. $[\alpha]_D^{20}$ +29.7 (*c* 1.00, MeOH). IR (ATR) 3330, 3280, 3088, 2937, 2872, 1642, 1546, 1089, 1033, 691 cm^{-1}. ^1H NMR (CD_3OD, 400 MHz): δ 3.88 (s, 1H), 3.54-3.37 (m, 4H), 3.17-3.13 (m, 2H), 2.41 (t, *J* = 6.7 Hz, 2H), 1.53-1.46 (m, 2H), 1.40-1.27 (m, 4H), 0.94-0.90 (m, 9H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 174.1, 171.6, 77.5, 70.9, 39.8, 39.4, 35.9, 35.4, 29.2, 22.4, 21.4, 20.6, 14.1 HRMS (ESI) *m/z* calcd for $C_{14}H_{28}N_2O_4Na$ $(M+Na)^+$: 311.1947, found: 311.1933.

(*R*)-*N*-[3-(heptylamino)-3-oxopropyl]-2,4-dihydroxy-3,3-dimethylbutanamide (N7-Pan, 6)



Prepared as described for **5**, starting from **4** (2.90 g, 8.13 mmol). Column chromatography (MeOH/CH_2Cl_2, 0:1→1:9) afforded **6** (2.21 g, 86% yield) as a white solid. R_f 0.47 (MeOH/CH_2Cl_2, 1:9). Mp 78.2 °C. $[\alpha]_D^{20}$ +26.9 (*c* 1.01, MeOH). IR (ATR) 3352, 2483, 2068, 1119, 973 cm^{-1}. ^1H NMR (CD_3OD, 400 MHz): δ 3.89 (s, 1H), 3.54-3.37 (m, 4H), 3.15 (dt, *J* = 1.2, 6.9 Hz, 2H), 2.41 (t, *J* = 6.7 Hz, 2H), 1.53-1.46 (m, 2H), 1.32-1.31 (m, 8H), 0.92-0.89 (m, 9H). ^{13}C NMR (CD_3OD, 75 MHz): δ 176.1, 173.6, 77.3, 70.4, 40.5, 40.4, 36.4, 32.9, 30.4, 30.1, 28.0, 23.7, 21.3, 20.9, 14.4. HRMS (ESI) *m/z* calcd for $C_{16}H_{33}N_2O_4$ $(M+H)^+$: 317.2440, found: 317.2429.

Table S1. Structure and anti-vanin properties of N5-Pan, N7-Pan and RR6

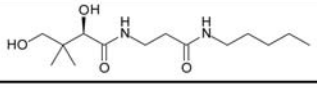
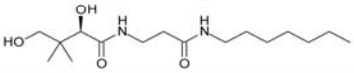
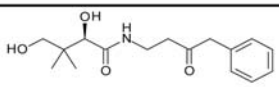
Name	Structure	IC_{50} (μM)		
		Rec. VNN1	Human serum	Fetal bovine serum
N5-Pan		-	-	-
N7-Pan		-	-	-
RR6		0.54	0.040	0.041

Table S2. Complete list of MIC values of N5-Pan and N7-Pan against various bacterial strains

Species	Gram staining	Strain	N5-Pan	N7-Pan
S. aureus	positive	Xen8.1	8	0.5
		ATCC6538	8	0.5
		MRSA	8	0.5
S. pneumoniae	positive	R6	0.25	2
		D39	0.5	16
		TIGR4	0.5	8
		G54	1	32
		PMEN-1	4	16
		PMEN-3	2	32
		PMEN-4	0.5	8
		PMEN-9	2	16
		PMEN-13	2	32
		PMEN-14	1	16
		PMEN-15	0.5	8
		PMEN-18	1	16
		PMEN-19	0.5	16
		PMEN-20	1	32
		PMEN-21	1	16
		PMEN-23	0.5	16
		PMEN-24	0.5	16
		PMEN-25	1	8
S. epidermidis	positive	ATCC12228	32	1
S. agalactiae	positive	RIVM861352	>256	>256
		RIVM801284	>256	>256
		RIVM861167	>256	>256
		RIVM821256	>256	>256
		RIVM782651	>256	>256
S. pyogenes	positive	SS410	1	16
		SS91	0,5	8
		SS799	1	32
E. coli	negative	BL21	64	256
		ATCC25922	64	128
		C-1	128	>256
		DH5alpha	32	>256
K. pneumoniae	negative	ATCC43816	32	>256
M. catarrhalis	negative	RH4	>256	128
		BBH18	>256	256
P. aeruginosa	negative	ATCC15692	>256	>256
		ATCC9027	>256	>256
		Xen41	>256	>256