Syntheses of analogues of the insect neuropeptide proctolin containing an oxazole ring as an amide bond replacement

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Supporting Information

General:

All solvents (p.a.) and chemicals were used without further purification. All reactions were performed under an argon atmosphere. ^{1}H-NMR studies were performed on a Bruker DRX 400 or a Bruker DRX 500. d_6-DMSO or $CDCl_3$ were used as solvents for NMR-experiments. Chemical shifts (δ) are reported in parts per million relative to tetramethylsilane (δ=0). FAB-MS, ESI-MS and HR-MS were performed using a Finnigan MAT 900, MALDI-MS were performed on a Shimadzu Compact MALDI 3.

<u>Procedure 1:</u> General procedure for the removal of Boc-protecting groups

The Boc-protected peptide was dissolved in dichloromethane (5 - 10 ml/mmol) and trifluoroacetic acid was added (1 - 2 ml/mmol). After stirring 3 h at room temperature the solvent was removed and the residue was coevaporated with toluene (3x). The product was dried and used without further purification.

Procedure 2: General procedure for the removal of Z-protecting groups, benzyl ethers and benzyl esters

The starting material was dissolved in methanol and purged with nitrogen. After addition of the catalyst (10% Pd on charcoal, 200 mg/mmol starting material) the flask was purged with hydrogen. After completion of the reaction (approx. 5 h, TLC control) the catalyst was filtered off and the filtrate was evaporated to dryness. The product was dried and used without further purification.

Procedure 3: Cyclodehydratisation of Serine- or Threonine-containing peptides with the Burgess reagent

The C- and N-terminal protected peptide was dissolved in THF (10 ml/mmol). Under an argon atmosphere 1.1 eq. Burgess reagent were slowly added and the reaction mixture was warmed up to 70°C for 2 - 3 h, until all starting material was consumed (TLC). The solvent was removed and the residue was purified by flash chromatography.

Procedure 4: Fragment condensation with BOP-Cl

The N-terminal protected peptide was dissolved in DMF (3 - 10 ml/mmol) and at 0°C 2.5 eq. N-ethyldiisopropylamine and 1.3 eq BOP-Cl were added. The C-terminal protected peptide was dissolved in DMF (3 - 5 ml/mmol) and added to the reaction mixture. After 1 h the ice-bath was removed and the mixture was allowed to warm up to room temperature overnight. The solvent was removed and the residue was dissolved in ethyl acetate. The organic layer was washed with 1 M HCl, sat. $NaHCO_3$ solution and brine, dried over Na_2SO_4 and the crude product was purified by flash chromatography.

Procedure 5: Formation of peptide bonds using EDCI x HCl / HOBt x H_2O

The N-terminal protected peptide was dissolved in DMF (3 - 5 ml/mmol), cooled to -30°C, and 1.3 eq. HOBt x H_2O and 1.3 eq. EDCI x HCl were added. After 30 minutes at this temperature 1.1 eq. N-ethyldiisopropylamine were added. A solution of the C-terminal protected peptide in DMF (2 - 3 ml/mmol) was then added over 30 minutes and the pH of the reaction mixture was adjusted with N-ethyldiisopropylamine to a value of 8-9. The mixture was kept at -30°C for 1 h and allowed to warm up to room temperature overnight. The solvent was removed, the residue was dissolved in ethyl acetate, washed with 2 x 1 N HCl, 2 x sat. $NaHCO_3$ and brine, and dried over Na_2SO_4. The solvent was removed and the crude product was purified by flash chromatography.

Boc-Arg(Boc)$_2$-Tyr(Bzl)-Leu-Ψ[oxazoline]-Ser-Pro-Thr(Bzl)-OBzl (6), ($C_{63}H_{82}O_{14}N_8$),

MG: 1175.349

1.48 g (1.24 mmol) Boc-Arg(Boc)$_2$-Tyr(Bzl)-Leu-Ser-Pro-Thr(Bzl)-OBzl was reacted with Burgess reagent according to procedure 3. The crude product was purified by flash chromatography (cyclohexane/ethyl acetate/dichloromethane/methanol 5:5:9:1).

Yield: 0.65 g (45%), white solid.

NMR(d$_6$-DMSO, 400 MHz): 9.08 [b, 2 H, N*H*], 8.27, 8.08 [2 d, 2 H, N*H*], 7.20-7.44 [m, 15 H, arom.], 7.09 [d, 2 H, Tyr-arom.], 6.86 [d, 2 H, Tyr-arom.], 6.80 [d, 1 H, N*H*], 5.11, 5.03 [2 s, 4 H, CO_2-C*H*$_2$-Ph, C-O-C*H*$_2$-Ph(Tyr)], 4.88 [m, 1 H, oxazoline-(C4)-C*H*], 4.50-4.63, 4.28-4.35, 4.10 [3 m, 8 H, C-O-C*H*$_2$-Ph(Thr), oxazoline-(C5)-C*H*$_2$, Tyr-α-C*H*, Pro-α-C*H*, Thr-α-C*H*, Thr-β-C*H*], 3.62-3.90 [m, 5 H, Arg-α-C*H*, Arg-δ-C*H*$_2$, Pro-δ-C*H*$_2$], 2.96, 2.78 [2 m, 2 H, Tyr-β-C*H*$_2$], 2.01 [m, 1 H, Pro-β-C*H*], 1.75-1.95 [m, 3 H, Pro-β-C*H*, Pro-γ-C*H*$_2$], 1.47, 1.39, 1.35 [3 s, 27 H, Boc-C*H*$_3$], 1.2-1.5 [m, 4 H, Arg-β-C*H*$_2$, Arg-γ-C*H*$_2$], 1.16 [m, 3 H, Thr-γ-C*H*$_3$].

MALDI-MS: 1188 $[M + NH_4]^+$

C,H,N-Anal.: C: 63.3 (calc.: 64.38); H: 7.1 (calc.: 7.03); N: 9.3 (calc.: 9.53).

HR-MS: 1175.60282 ($[M + H]^+$, calc.: 1175.60287).

H-Arg-Tyr-Leu-Pro-*allo*-Thr-OH x 3 TFA (7), ($C_{30}H_{48}O_8N_8$), MG: 648.738

97 mg (0.083 mmol) Boc-Arg(Boc)$_2$-Tyr(Bzl)-Ψ[oxazoline]-Ser-Pro-Thr(Bzl)-OBzl (**6**). The benzyl groups were removed according to procedure 2 and the Boc-groups according to procedure 1.

Yield: 82 mg (98%), white solid.

NMR (d$_6$-DMSO, 500 MHz, H,H-COSY): 9.23 [b, 1 H, Tyr-O*H*], 8.54 [d, 1 H, Tyr-N*H*], 8.36 [d, 1 H, Leu-α-C*H*], 8.13 [b, 3 H, Arg-N*H*$_3^+$], 7.98 [d, 1 H, Thr-N*H*], 7.76 [m, 1 H, Arg-ε-N*H*], 7.05 [d, 2 H, Tyr-arom.], 6.66 [d, 2 H, Tyr-arom.], 4.56 [m, 1 H, Leu-α-C*H*], 4.54 [m, 1 H, Tyr-α-C*H*], 4.45 [m, 1 H, Pro-α-CH], 4.12 [m, 1 H, Thr-α-C*H*], 3.85 [m, 1 H, Thr-β-C*H*], 3.80 [m, 1 H, Arg-α-C*H*], 3.58 [m, 2 H, Pro-δ-C*H*$_2$], 3.08 [m, 2 H, Arg-δ-C*H*$_2$], 2.88, 2.68 [2 m, 2 H, Tyr-β-C*H*$_2$], 2.02, 1.85 [2 m, 2 H, Pro-β-C*H*$_2$], 1.90, 1.84 [2 m, 2 H, Pro-γ-C*H*$_2$], 1.72 [m, 2 H, Arg-β-C*H*$_2$], 1.63 [m, 1 H, Leu-γ-C*H*], 1.51 [m, 2 H, Arg-γ-C*H*$_2$], 1.49, 1.45 [2 m, 2 H, Leu-β-C*H*$_2$], 1.12 [d, 3 H, Thr-γ-C*H*$_3$], 0.90, 0.86 [2 d, 6 H, Leu-δ-C*H*$_3$].

MALDI-MS: 649 $[M + H]^+$

C,H,N-Anal.: C: 44.9 (calc.: 44.45); H: 5.2 (calc.: 5.08); N: 11.1 (calc.: 11.52).

HR-MS: 649.36821 ($[M + H]^+$, calc.: 649.36734).

Boc-Pro-Ψ[oxazole]-Thr-OBzl (9), ($C_{21}H_{26}O_5N_2$), MG: 386.433

1.41 g (4.40 mmol) Boc-Pro-Ψ[oxazoline]-Thr-OBzl (**8**), 0.70 g (4.84 mmol) CuBr and 0.88 g (4.84 mmol) $Cu(OAc)_2$ were suspended in 30 ml benzene and stirred at 60°C. 1.28 g (6.60 mmol) peroxybenzoic acid tert.-butylester was added over 15 min and refluxed for 8 h. After cooling 15 ml ethyl acetate was added and washed with 10% NH_4OH-solution. The aqueous layer was reextracted 3 times with ethyl acetate. The organic layers were combined and dried over Na_2SO_4 the solvent was removed and the crude product was purified by flash chromatography (cyclohexane/ethyl acetate 3:2).

Yield: 0.73 g (43 %), off-white solid.

NMR(d_6-DMSO, 400 MHz): 2 rotamers, 7.32-7.45 [m, 5 H, arom.], 5.29 [s, 2 H, CO_2-C*H*$_2$-Ph], 4.79 [m, 1 H, Pro-α-C*H*], 3.28-3.48 [m, 2 H, Pro-δ-C*H*$_2$], 2.55 [s, 3 H, oxazole-(C5)-C-C*H*$_3$], 2.27 [m, 1 H, Pro-γ-C*H*], 1.81-2.00 [m, 3 H, Pro-β-C*H*$_2$, Pro-γ-C*H*], 1.20, 1.38 [2 s (2 rotamers), 9 H, Boc-C*H*$_3$].

ESI-MS: 387.3 $[M + H]^+$, 409.3 $[M + Na]^+$, 773.4 $[2M + H]^+$, 795.5 $[2M + Na]^+$

C,H,N-Anal.: C: 65.4 (calc.: 65.27); H: 6.8 (calc.: 6.78); N: 6.9 (calc.: 7.25).

HR-MS: 409.17335 ($[M + Na]^+$, calc.: 409.17394).

H-Pro-Ψ[oxazole]-Thr-OBzl x TFA (11), ($C_{16}H_{18}O_3N_1$), MG: 286.322

10.15 g (25 mmol) Boc-Pro-Thr-OBzl (**10**) was dissolved in 90 ml dichloromethane and 13.75 g (32.5 mmol) Dess-Martin-Periodane was added under stirring. After 4 h at room temperature the solvent was removed and the crude product was purified by flash chromatography (cyclohexane/ethyl acetate 1:1, 7.88 g of a colourless oil).

In a separate flask 13.62 g (52 mmol) PPh_3 and 11.94 g (47 mmol) I_2 were dissolved in 70 ml THF and 9.09 g (90 mmol) NEt_3 was added. The mixture was cooled to -78°C and 7.88 g (19.5 mmol) of the β-ketoester prepared above dissolved in 20 ml THF were added drop wise. After warming up to room temperature 200 ml water were added and this mixture was extracted with 3 x 120 ml dichloromethane. The combined organic layers were washed with water, $Na_2S_2O_3$ solution, 1 N HCl and brine. After drying over Na_2SO_4 the solvent was removed and the crude product was purified by flash chromatography (cyclohexane/ethyl acetate 1:1).

Finally, the Boc-protecting group was removed according procedure 1.

Yield: 5.75 g(57%), dark green oil.

NMR(d_6-DMSO, 400 MHz): 9.95, 9.45 [2 b, 2 H, Pro-NH_2^+], 7.34-7.46 [m, 5 H, arom.], 5.32 [s, 2 H, CO_2-CH_2-Ph], 4.88 [m, 1 H, Pro-α-C*H*], 3.32 [m, 2 H, Pro-δ-CH_2], 2.61 [s, 3 H, oxazole-(C5)-CH_3], 2.38 [m, 1 H, Pro-β-C*H*], 1.95-2.25 [m, 3 H, Pro-β-C*H*, Pro-γ-CH_2].

FAB-MS: 287 $[M + H]^+$**,** 309 $[M + Na]^+$, 573 $[2M + H]^+$

H-Arg-Tyr-Leu-Pro-Ψ[oxazole]-Thr-OH x 3 TFA (2), ($C_{44}H_{58}O_{11}N_4$), MG: 818.932

236 mg (0.59 mmol) H-Pro-Ψ[oxazole]-Thr-OBzl x TFA (**11**) and 233 mg (0.59 mmol) Boc-Tyr-Leu-OH were reacted according procedure 4. The crude product was purified by flash chromatography (cyclohexane/ethyl acetate 1:2). The Boc-protecting groups were removed according procedure 1. 185 mg (0.28 mmol) Boc-Arg$(Boc)_2$-OH was reacted with the modified tetrapeptide H-Tyr-Leu-Pro-Ψ[oxazole]-Thr-OBzl according to procedure 5. The crude product was purified by flash chromatography (cyclohexane/ethyl acetate/dichloromethane/methanol 5:5:9:1). Hydrogenolytic removal of the benzyl groups according to procedure 2 and cleavage of the Boc groups according procedure 1 afforded the desired product **2**.

Yield: 246 mg (36%), white solid.

NMR(d_6-DMSO, 500 MHz, H,H-COSY): main conformer (approx. 80%): 8.59 [d, 1 H, Tyr-N*H*], 8.36 [d, 1 H, Leu-N*H*], 8.16 [b, 3 H, Arg-NH_3^+], 7.76, [m, 1 H, N*H*], 7.05 [m, 2 H, Tyr-arom.], 6.66 [m, 2 H, Tyr-arom.], 4.96 [m, 1 H, Pro-α-C*H*], 4.56 [m, 1 H, Leu-α-C*H*], 4.53 [m, 1 H, Tyr-α-C*H*], 3.80 [m, 1 H, Arg-α-C*H*], 3.67, 3.61 [m, 2 H, Pro-δ-CH_2], 3.08 [m, 2 H, Arg-δ-CH_2], 2.88, 2.70 [2 m, 2 H, Tyr-β-CH_2], 2.50 [s, 3 H, oxazole-(C5)-CH_3], 2.20, 1.94 [m, 1 H, Pro-β-CH_2], 2.04, 1.95 [2 m, 2 H, Pro-γ-CH_2], 1.72 [m, 2 H, Arg-β-CH_2], 1.60 [m, 1 H, Leu-γ-C*H*], 1.52 [m, 2 H, Arg-γ-CH_2], 1.44 [m, 2 H, Leu-β-CH_2], 0.89, 0.85 [2 d, 6 H, Leu-δ-CH_3].

MALDI-MS: 629.5 $[M + H]^+$, 651.4 $[M + Na]^+$

C,H,N-Anal.: C: 45.0 (calc.: 44.54); H: 5.4 (calc.: 4.88); N: 12.2 (calc.: 11.54).

HR-MS: 629.34112 ($[M+H]^+$, calc.: 629.34112).

Boc-Tyr(Bzl)-Ψ[oxazole]-Ser-OH (13), ($C_{24}H_{26}O_6N_2$), MG: 438.462

7.55 g (18.5 mmol) Boc-Tyr(Bzl)-Ser-OMe (**12**) was reacted with Burgess Reagent according to procedure 3. The crude oxazoline was purified by flash chromatography

(cyclohexane/ethyl acetate 1:1). The pure oxazoline was dissolved in 25 ml acetonitrile; 25 ml pyridine and 18 ml tetrachloromethane and 8.1 g (52.5 mmol) DBU were added under stirring. The reaction was stirred until all starting material was consumed. The mixture was evaporated to dryness; the residue was dissolved in ethyl acetate and washed with 0.5 M HCl. The aqueous layer was reextracted with ethyl acetate and the combined organic layers were washed with brine, dried over Na_2SO_4 and the solvent was removed. The crude product was purified by flash chromatography (cyclohexane/ethyl acetate 1:1). The methyl ester was saponified by dissolving the ester in 50 ml dioxane and under stirring 20 ml 1 N NaOH was added. The reaction was stopped after all starting material was consumed. The mixture was evaporated to dryness, the residue was dissolved in 50 ml water and a pH of 2-3 was adjusted with 1 N HCl. The solution was extracted with 3 x 50 ml ethyl acetate, the combined organic layers were washed with brine, dried over Na_2SO_4 and the solvent was removed.

Yield: 4.30 g (53%), white solid.

NMR(d_6-DMSO, 400 MHz): 8.4 [s, 1 H, oxazole-(C5)-C*H*], 7.56 [d, 1 H, N*H*], 7.25-7.45 [m, 5 H, arom.], 7.12 [d, 2 H, Tyr-arom.], 6.89 [d, 2 H, Tyr-arom.], 5.06 [s, 2 H, C-O-CH_2-Ph(Tyr)], 4.79 [m, 1 H, Tyr-α-C*H*], 3.09, 2.95 [2 m, 2 H, Tyr-β-CH_2], 1.31 [s, 9 H, Boc-CH_3].

ESI-MS: 437 $[M - H]^-$, 461 $[M + Na]^+$

C,H,N-Anal.: C: 64.7 (calc.: 65.74); H: 6.2 (calc.: 5.98); N: 5.7 (calc.: 6.39).

HR-MS: 461.16931 ($[M + Na]^+$, calc.: 461.16886).

H-Arg-Tyr-Ψ[oxazole]-Ser-Pro-Thr-OH x 3 TFA (3), ($C_{27}H_{38}O_8N_8$), MG: 602.625

877 mg (2 mmol) Boc-Tyr(Bzl)-Ψ[oxazole]-Ser-OH (**13**) and 840 mg (2 mmol) H-Pro-Thr-OBzl x TFA were reacted according to procedure 4. The crude product was purified by flash chromatography (ethyl acetate). The Boc groups were removed according to procedure 1. 1.09 g (1.48 mmol) of the N-terminal deprotected modified tetrapeptide H-Tyr(Bzl)-Ψ[oxazole]-Ser-Pro-Thr-OBzl x TFA was reacted with 947 mg (1.48 mmol) Boc-Arg$(Boc)_2$-OH according to procedure 5. The crude product was purified by flash chromatography (cyclohexane/ethyl acetate/dichloromethane/methanol 5:5:9:1). The benzyl groups were removed according to procedure 2 and the Boc groups were removed according to procedure 1.

Yield: 574 mg (36%), white solid.

NMR(d_6-DMSO, 500 MHz, H-H-COSY): 2 rotamers (80:20), 9.32 [b, 1 H, Tyr-O*H*], 9.23 [d, 1 H, Tyr-N*H*], 8.53 [s, 1 H, oxazole-(C5)-C*H*], 7.82 [m, 1 H, Arg-ε-N*H*], 7.80 [d, 1 H, Thr-N*H*], 7.00 [d, 2 H, Tyr-arom.], 6.66 [d, 2 H, Tyr-arom.], 5.15 [m, 1 H, Tyr-α-C*H*], 4.67 [m, 1 H, Pro-

α-C*H*], 4.17 [m, 1 H, Thr-α-C*H*], 4.17 [m, 1 H, Thr-β-C*H*], 3.83 [m, 1 H, Arg-α-C*H*], 3.80 [m, 2 H, Pro-δ-CH_2], 3.10 [m, 2 H, Arg-δ-CH_2] 3.13, 3.04 [2 m, 2 H, Tyr-β-CH_2], 2.12, 1.88 [2 m, 2 H, Pro-β-CH_2], 1.90, 1.84 [2 m, 2 H, Pro-γ-CH_2], 1.72 [m, 2H, Arg-β-CH_2], 1.47 [m, 2H, Arg-γ-CH_2], 1.09 [d, 3 H, Thr-γ-CH_3].

MALDI-MS: 603.4 $[M + H]^+$, 625.4 $[M + Na]^+$

C,H,N-Anal.: C: 42.5 (calc.: 41.96); H: 4.6 (calc.: 4.37); N: 11.8 (calc.: 11.86).

HR-MS: 603.28941 ($[M + H]^+$, calc.: 603.28908).

Boc-Tyr(Bzl)-Ψ[oxazole]-Ser-Pro-Ψ[oxazole]-Thr-OBzl (14), ($C_{40}H_{42}O_8N_4$), MG: 706.772

2.19 g (5 mmol) Boc-Tyr(Bzl)-Ψ[oxazole]-Ser-OH (**13**) was reacted with 2.72 g (5 mmol) H-Pro-Ψ[oxazole]-Thr-OBzl x TFA (**11**) according to procedure 4. The product was purified by flash chromatography (cyclohexane/ethyl acetate 1:2).

Yield: 1.68 g (71%), white solid.

NMR(d_6-DMSO, 400 MHz): 8.55 [s, 1 H, oxazole-(C5)-C*H*], 7.58 [d, 1 H, N*H*], 7.29-7.45 [m, 10 H, arom.], 7.13 [d, 2 H, Tyr-arom.], 6.91 [m, 2 H, Tyr-arom.], 5.28 [s, 1 H, CO_2-CH_2-Ph], 5.15 [m, 1 H, Pro-α-C*H*], 5.06 [s, 2 H, C-O-CH_2-Ph(Tyr)], 4.82 [m, 1 H, Tyr-α-C*H*], 3.82-4.02 [m, 1 H, Pro-δ-CH_2], 2.92-3.18 [m, 2 H, Tyr-β-CH_2], 2.50 [s, 3 H, oxazole-(C5)-C-CH_3], 2.30 [m, 1 H, Pro-β-C*H*], 1.88-2.15 [m, 3 H, Pro-β-C*H*, Pro-γ-CH_2], 1.32 [s, 9 H, Boc-CH_3].

MALDI-MS: 729.1 $[M + H]^+$

H-Arg-Tyr-Ψ[oxazole]-Ser-Pro-Ψ[oxazole]-Thr-OH x 3 TFA (4), ($C_{27}H_{34}O_7N_8$), MG: 582.597

The N-terminal protecting group of Boc-Tyr(Bzl)-Ψ[oxazole]-Ser-Pro-Ψ[oxazole]-Thr-OBzl (**14**) was removed according procedure 1. 816 mg (1.13 mmol) of the N-terminal deprotected modified tetrapeptide H-Tyr(Bzl)-Ψ[oxazole]-Ser-Pro-Ψ[oxazole]-Thr-OBzl x TFA was reacted with 723 mg (1.13 mmol) Boc-Arg$(Boc)_2$-OH according to procedure 5. The crude product was purified by flash chromatography (cyclohexane/ethyl acetate/dichloromethane/methanol 5:5:9:1). The benzyl groups were removed according to procedure 2 and the Boc groups were removed according to procedure 1.

Yield: 660 mg (63%), white solid.

NMR (d_6-DMSO, 500 MHz, H-H-COSY): 2 conformers (70:30), trans-conformer: (70%): 9.32 [b, 1 H, Tyr-O*H*], 9.23 [d, 1 H, Tyr-N*H*], 8.55 [s, 1 H, oxazole-(C5)-C*H*], 7.90 [m, 1 H, Arg-ε-

N*H*], 7.01 [d, 2 H, Tyr-arom.], 6.67 [d, 2 H, Tyr-arom.], 5.17 [m, 1 H, Tyr-α-C*H*], 5.16 [m, 1 H, Pro-α-C*H*], 3.97, 3.86 [2 m, 2 H, Pro-δ-CH_2], 3.84 [m, 1 H, Arg-α-C*H*], 3.10 [m, 2 H, Arg-δ-CH_2] 3.14, 3.06 [2 m, 2 H, Tyr-β-CH_2], 2.53 [s, 3 H, oxazole-(C5)-CH_3], 2.26, 1.95 [2 m, 2 H, Pro-β-CH_2], 2.07, 2.00 [2 m, 2 H, Pro-γ-CH_2], 1.72 [m, 2H, Arg-β-CH_2], 1.48 [m, 2H, Arg-γ-CH_2];

cis-conformer (30%): 9.32 [b, 1 H, Tyr-O*H*], 9.13 [d, 1 H, Tyr-N*H*], 8.45 [s, 1 H, oxazole-(C5)-C*H*], 7.98 [m, 1 H, Arg-ε-N*H*], 6.73 [d, 2 H, Tyr-arom.], 6.59 [d, 2 H, Tyr-arom.], 5.81 [m, 1 H, Pro-α-C*H*], 4.93 [m, 1 H, Tyr-α-C*H*], 3.84 [m, 1 H, Arg-α-C*H*], 3.72, 3.59 [2 m, 2 H, Pro-δ-CH_2], 3.10 [m, 2 H, Arg-δ-CH_2] 2.95, 2.85 [2 m, 2 H, Tyr-β-CH_2], 2.50 [s, 3 H, oxazole-(C5)-CH_3], 2.32, 2.12 [2 m, 2 H, Pro-β-CH_2], 1.93, 1.81 [2 m, 2 H, Pro-γ-CH_2], 1.72 [m, 2H, Arg-β-CH_2], 1.48 [m, 2H, Arg-γ-CH_2].

MALDI-MS: 583.4 $[M + H]^+$

C,H,N-Anal.: C: 44.1 (calc.: 42.87); H: 4.7 (calc.: 4.03); N: 12.7 (calc.: 12.12).

HR-MS: 583.26294 ($[M + H]^+$, calc. 583.26287).