washed with 5% aqueous acetonitril (15 ml), and finally liberated from the cartridge by elution with TFA (25 ml). The solvent was concentrated *in vacuo*, and the residue purified by column chromatography using a cyanopropyl column (Zorbax 300SB-CN) and a standard acetonitril/TFA system. The column was heated to 65°C and the acetonitril gradient was 0-100% in 60 minutes. The title compound (2.1 mg, 16 %) was isolated, and the product was analysed by PDMS.

Example 16

Synthesis of $Arg^{26,34}$,Lys^{23} (N^{ε}-(γ-glutamyl(N^{α}-hexadecanoyl))) GLP-1 (7-37)-OH.

To a mixture of $Arg^{26,34}$, Lys^{23} GLP-1 (7-37)-OH (11.6 mg, 3.4 μmol), EDPA (12.3 mg, 94.9 μmol), NMP (1.6 ml) and water (0.8 ml) was added a solution of Pal-Glu(ONSu)-OBu^t (5.5 mg, 10.2 μmol) in NMP (137 μl). The reaction mixture was gently shaken for 5 min. at room temperature, and then allowed to stand for an additional 90 min. at room temperature. The reaction was quenched by the addition of a solution of glycine (5.6 mg, 74.6 μmol) in water (560 μl). A 0.5 % aqueous solution of ammonium acetate (34 ml) was added, and the resulting mixture eluted onto a Varian 5g C8 Mega Bond Elut®, the immobilised compound washed with 5% aqueous acetonitril (15 ml), and finally liberated from the cartridge by elution with TFA (25 ml). The solvent was concentrated *in vacuo*, and the residue purified by column chromatography using a cyanopropyl column (Zorbax 300SB-CN) and a standard acetonitril/TFA system. The column was heated to 65°C and the acetonitril gradient was 0-100% in 60 minutes. The title compound (3.1 mg, 24 %) was isolated, and the product was analysed by PDMS.

Example 17

Synthesis of $Arg^{26,34}$,Lys^{18} (N^{ε}-(γ-glutamyl(N^{α}-hexadecanoyl))) GLP-1 (7-37)-OH

To a mixture of $Arg^{26,34}$, Lys^{18} GLP-1 (7-37)-OH (11.7 mg, 3.4 μmol), EDPA (12.2 mg, 94.6 μmol), NMP (1.6 ml) and water (0.8 ml) was added a solution of Pal-Glu(ONSu)-OBu^t (5.5 mg, 10.2 μmol) in NMP (137 μl). The reaction mixture was gently shaken for 5 min. at room temperature, and then allowed to stand for an additional 90 min. at room temperature. The reaction was quenched by the addition of a solution of glycine (5.6 mg, 74.6 μmol) in water (560 μl). A 0.5 % aqueous solution of ammonium acetate (34 ml) was added, and the resulting mixture eluted onto a Varian 5g C8 Mega Bond Elut®, the immobilised compound washed with 5% aqueous acetonitril (25 ml), and finally liberated from the cartridge by elution with TFA (25 ml). The solvent was concentrated *in vacuo*, and the residue purified by co-

lumn chromatography using a cyanopropyl column (Zorbax 300SB-CN) and a standard acetonitril/TFA system. The column was heated to 65°C and the acetonitril gradient was 0-100% in 60 minutes. The title compound (1.9 mg, 15 %) was isolated, and the product was analysed by PDMS.

Example 18

Synthesis of Arg^{34},Lys^{26} (N^{ε}-(octanoyl)) GLP-1 (7-37)-OH.

To a mixture of Arg^{34} GLP-1 (7-37)-OH (41.1 mg, 12.2 μmol), EDPA (44 mg, 341 μmol), NMP (5.76 ml) and water (2.88 ml) was added a solution of Cap-ONSu (8.8 mg, 36.5 μmol, prepared as described in example 10, in NMP (106 μl). The reaction mixture was gently shaken for 5 min. at room temperature, and then allowed to stand for an additional 115 min. at room temperature. The reaction was quenched by the addition of a solution of glycine (20 mg, 268 μmol) in water (200 μl). The solvent was concentrated *in vacuo*, and the residue purified by column chromatography using a cyanopropyl column (Zorbax 300SB-CN) and a standard acetonitril/TFA system. The column was heated to 65°C and the acetonitril gradient was 0-100% in 60 minutes. The title compound (18.8 mg, 44 %) was isolated, and the product was analysed by PDMS.

Example 19

Synthesis of Arg^{34},Lys^{26} (N^{ε}-(dodecanoyl)) GLP-1 (7-37)-OH.

To a mixture of Arg^{34} GLP-1 (7-37)-OH (41.1 mg, 12.2 μmol), EDPA (44 mg, 341 μmol), NMP (5.76 ml) and water (2.88 ml) was added a solution of Lau-ONSu (8.8 mg, 36.5 μmol, prepared in a similar manner as described for Cap-ONSu in example 10), in NMP (271 μl). The reaction mixture was gently shaken for 5 min. at room temperature, and then allowed to stand for an additional 100 min. at room temperature. The reaction was quenched by the addition of a solution of glycine (20.1 mg, 268 μmol) in water (200 μl). The solvent was concentrated *in vacuo*, and the residue purified by column chromatography using a cyanopropyl column (Zorbax 300SB-CN) and a standard acetonitril/TFA system. The column was heated to 65°C and the acetonitril gradient was 0-100% in 60 minutes. The title compound (18 mg, 42 %) was isolated, and the product was analysed by PDMS.

Example 20

Synthesis of Pal-GABA-ONSu.

A mixture of Pal-ONSu (3 g, 8.48 mmol), γ-aminobutyric acid (0.87 g, 8.48 mmol) in DMF (200 ml) was stirred at room temperature for 60 h. The reaction mixture was filtered and the filtrate was added drop wise to 10% aqueous citric acid (500 ml). The precipitated N-acylated intermediate was collected and dried *in vacuo*. To a suspension of the dried intermediate in DMF (35 ml) was added a solution of DCC (1.45 g, 7.0 mmol) in dichloromethane (20 ml). The resulting mixture was stirred at room temperature for 20 h, and then filtered. The solvent was removed *in vacuo* to give a solid residue. The residue was recrystallised from a mixture of n-heptane (50 ml) and 2-propanol (2.5 ml) to give the title compound (2.5 g, 75 %).

Example 21

Synthesis of Arg^{34},Lys^{26} (N^{ε}-(γ-aminobutyroyl(N^{γ}-hexadecanoyl))) GLP-1 (7-37)-OH.

To a mixture of Arg^{34}, Lys^{26} GLP-1 (7-37)-OH (41.1 mg, 12.2 μmol), EDPA (44 mg, 341 μmol), NMP (5.76 ml) and water (2.88 ml) was added a solution of Pal-GABA-ONSu (16 mg, 36.5 μmol, prepared as described in example 20) in NMP (400 μl). The reaction mixture was gently shaken for 5 min. at room temperature, and then allowed to stand for an additional 100 min. at room temperature. The reaction was quenched by the addition of a solution of glycine (20 mg, 268 μmol) in water (200 μl). The solvent was concentrated *in vacuo*, and the residue purified by column chromatography using a cyanopropyl column (Zorbax 300SB-CN) and a standard acetonitril/TFA system. The column was heated to 65°C and the acetonitril gradient was 0-100% in 60 minutes. The title compound (15.8 mg, 35 %) was isolated, and the product was analysed by PDMS.

Example 22

Synthesis of N^{α}-hexadecanoyl-D-glutamic acid α-t-butyl ester-γ-2,5-dioxopyrrolidin-1-yl ester.

A mixture of Pal-ONSu (6.64 g, 18.8 mmol), D-glutamic acid α-tert-butyl ester (4.5 g, 18.8 mmol) and EDPA (4.85 g, 37.5 mmol) in DMF (538 ml) was stirred at room temperature for 60 h. The solvent was removed and the residue dissolved in ethyl acetate (175 ml). The resulting solution was extracted with 10% aqueous citric acid (2x125 ml), and the organic phase concentrated *in vacuo*. The residue was dissolved in DMF (60 ml), and the resulting mixture slowly added to 10% aqueous citric acid (500 ml). The precipitated compound was collected and dried *in vacuo*, to give the crude N-acylated glutamic acid intermediate. The crude intermediate was dissolved in DMF (35 ml), and a solution of DCC (3.5 g, 17 mmol) in dichloromethane (70 ml) was added. The resulting mixture was stirred at room

temperature for 20 h, and then filtered. The filtrate was concentrated *in vacuo*, and the solid residue recrystallised from a mixture of n-heptane (75 ml) and 2-propanol (5 ml), to give the title compound (5.2 g, 50 %)

Example 23

Synthesis of Arg^{34},Lys^{26} (N^{ε}-(γ-D-glutamyl(N^{α}-hexadecanoyl))) GLP-1 (7-37)-OH.

To a mixture of Arg^{34}, Lys^{26} GLP-1 (7-37)-OH (41.1 mg, 12.2 μmol), EDPA (44 mg, 341 μmol), NMP (5.76 ml) and water (2.88 ml) was added a solution of N^{α}-hexadecanoyl-D-glutamic acid α-t-butyl ester-γ-2,5-dioxopyrrolidin-1-yl ester (19.7 mg, 36.5 μmol) in NMP (491 μl). The reaction mixture was gently shaken for 5 min. at room temperature, and then allowed to stand for an additional 95 min. at room temperature. The reaction was quenched by the addition of a solution of glycine (20 mg, 268 μmol) in water (2 ml). A 0.5 % aqueous solution of ammonium acetate (120 ml) was added, and the resulting mixture divided into to equal portions, and each portion eluted onto a Varian 5g C8 Mega Bond Elut®, the immobilised compound washed with 5% aqueous acetonitril (25 ml), and finally liberated from the cartridge by elution with TFA (25 ml). The combined eluates were concentrated *in vacuo*, and the residue purified by column chromatography using a cyanopropyl column (Zorbax 300SB-CN) and a standard acetonitril/TFA system. The column was heated to 65°C and the acetonitril gradient was 0-100% in 60 minutes. The title compound (10.5 mg, 23 %) was isolated, and the product was analysed by PDMS.

Example 24

Synthesis of Lys^{34} (N^{ε}-(γ-glutamyl(N^{α}-tetradecanoyl))) GLP-1 (7-37).

To a mixture of GLP-1 (7-37)-OH (33.6 mg, 8.9 μmol), EDPA (32.4 mg, 250 μmol), NMP (2.1 ml) and water (2.1 ml) was added a solution of Myr-Glu(ONSu)-OBu^t (9.1 mg, 17.9 μmol), prepared as described in PCT application no. PCT/DK97/00340, in NMP (228 μl). The reaction mixture was gently shaken for 5 min., and then allowed to stand for an additional 80 min. at room temperature. The reaction was quenched by the addition of a solution of glycine (14.8 mg, 197 μmol) in water (1.47 ml). A 0.5% aqueous solution of ammonium acetate (100 ml) was added, and the resulting mixture divided into two equal portions, and each portion eluted onto a Varian 5g C8 Mega Bond Elut®, the immobilised compound washed with 5% aqueous acetonitril (2x25 ml), and finally liberated from the cartridge by elution with TFA (2x25 ml). The combined eluates were concentrated *in vacuo*, and the residue purified by column chromatography using a cyanopropyl column (Zorbax 300SB-CN) and a standard

acetonitril/TFA system. The column was heated to 65°C and the acetonitril gradient was 0-100% in 60 minutes. The title compound (0.19 mg, 0.6%) was isolated, and the product was analysed by PDMS. The m/z value for the protonated molecular ion was found to be 3693 ± 3. The resulting molecular weight is thus 3692 ± 3 amu (theoretical value 3695 amu).

Example 25

Synthesis of $Arg^{26,34}$,Lys^{8}(N^{ε}-(γ-glutamyl(N^{α}-hexadecanoyl))) GLP-1 (7-37).

To a mixture of $Arg^{26,34}$, Lys^{8}-GLP-1 (7-37)-OH (10.3 mg, 3 μmol), EDPA (10.8 mg, 83 μmol), NMP (1.44 ml) and water (0.72 ml) was added a solution of Pal-Glu(ONSu)-OBu^{t} (4.8 mg, 8.9 μmol), prepared as described in PCT application no. PCT/DK97/00340, in NMP (120 μl). The reaction mixture was gently shaken for 5 min., and then allowed to stand for an additional 70 min. at room temperature. The reaction was quenched by the addition of a solution of glycine (4.9 mg, 65.3 μmol) in water (490 μl). A 0.5% aqueous solution of ammonium acetate (30 ml) was added, and the resulting mixture eluted onto a Varian 5g C8 Mega Bond Elut®, the immobilised compound washed with 5% aqueous acetonitril (25 ml), and finally liberated from the cartridge by elution with TFA (25 ml). The eluate was concentrated *in vacuo*, and the residue purified by column chromatography using a cyanopropyl column (Zorbax 300SB-CN) and a standard acetonitril/TFA system. The column was heated to 65°C and the acetonitril gradient was 0-100% in 60 minutes. The title compound (3.2 mg, 28%) was isolated, and the product was analysed by PDMS. The m/z value for the protonated molecular ion was found to be 3836 ± 3. The resulting molecular weight is thus 3835 ± 3 AMU (theoretical value 3836 AMU).

Example 26

Synthesis of Lau-Glu(ONSu)-OBu^{t}.

To a solution of H-Glu-OBu^{t} (3 g, 15 mmol) in DMF (344 ml) was added EDPA (2.58 ml, 15 mmol) and a solution of Lau-ONSu (4.5 g, 15 mmol), prepared in a similar manner as described for Cap-ONSu in example 10, in DMF (74 ml). The resulting mixture was stirred at ambient temperature for 18 h, and the solvent removed *in vacuo*. The oily residue was partitioned between ethyl acetate (150 ml) and 5% aqueous citric acid (250 ml). The organic phase was concentrated *in vacuo*. The residue was dissolved in DMF (40 ml) and the solution added drop by drop to a 10% aqueous citric acid solution (350 ml). The precipitated product was collected, washed with water and dried *in vacuo* for 18 h to give the intermediate free acid. To solution of the free acid intermediate in DMF (25 ml) was added N-

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