Electronic Supplementary Informations

Molecular structural requirements, dye specificity, and application of anionic peptide amphiphiles that induce intense fluorescence in cationic dyes

Amphiphile preparation

Anionic amphiphiles derived from acidic α-amino acids (L-Glu and L-2-aminoadipic acid)

***N'*,*N"*-Bis(dodecylaminocarbonylethyl)-*N*$^{\alpha}$-[(4-carboxy)butanoyl]-L-glutamide** (**1**). 1-Aminododecane (3.01 g, 16.2 mmol), *N*-benzyloxycarbonyl-β-alanine (β-Ala-Z) (3.97 g, 17.8 mmol), and triethylamine (3.77 g, 37.2 mmol) were dissolved in 100 cm^3 of tetrahydrofuran (THF) and stirred with cooling to 0 ˚C. Diethylphosphoryl cyanidate (DEPC) (3.43 g, 21.0 mmol) was added to the solution and stirred in an ice bath for 30 min. After being stirred for 1 day at room temperature, the solution was concentrated *in vacuo*. The residue was dissolved in 200 cm^3 of chloroform and was washed with 5 wt% aqueous $NaHCO_3$ (200 cm^3, in twice), deionized water (20 cm^3, once), 0.3 N HCl (200 cm^3, in twice), and deionized water (20 cm^3, once). The solution was dried over Na_2SO_4. After filtration, the filtrate was concentrated *in vacuo* and recrystallized from methanol to give white solid *N*-dodecyl-3-(*N'*-benzyloxycarbonyl)aminopropanamide (**17**): yield 5.76 g (91.1 %); m.p. 124-125 ˚C; FT-IR (KBr): /cm^{-1} 3336, 3296, 2958, 2920, 2876, 2854, 1686, 1638, 1541, 1468, 1456, 1379, 733 and 694; ^{1}H-NMR ($CDCl_3$): δ 0.80-0.96 (t, 3H, C$\underline{H}_3$), 1.17-1.38 (m, 18H, $CH_3(C\underline{H}_2)_9$), 1.38-1.59 (m, 2H, $CH_3(CH_2)_9C\underline{H}_2$), 2.32-2.43 (m, 2H, C(=O)C$\underline{H}_2$), 3.14-3.26 (m, 2H, $CH_3(CH_2)_{10}C\underline{H}_2$), 3.41-3.52 (m, 2H, C$\underline{H}_2$NHC(=O)O), 5.01-5.16 (s, 2H, C$\underline{H}_2C_6H_5$), 5.43-5.60 (m, 1H, N$\underline{H}$), 5.60-5.76 (m, 1H, N$\underline{H}$), 7.29-7.40 (m, 5H, $C_6\underline{H}_5$); (Found: C, 70.42; H, 9.81; N, 7.16. Calc. for $C_{23}H_{38}N_2O_3\cdot0.9H_2O$: C, 70.42; H, 9.81; N, 7.14 %). **17** (5.50 g, 14.1 mmol) was dissolved in 200 cm^3 of ethanol with heating and Pd black (1 g) was added to the solution. H_2 gas was bubbled slowly into the solution

for 6 hours. After confirming the removal of the benzyloxycarbonyl group (Z-group) by FTIR measurement, Pd black was removed by filtration. The filtrate was concentrated and dried *in vacuo* to give white waxy solid *N*-dodecyl-3-aminopropanamide (**18**): yield 3.61 g (100 %); m.p. 84.0-85.5 ˚C; FT-IR (KBr): /cm^{-1} 3298, 2958, 2928, 2854, 1647, 1555, 1468, 1375 and 721; ^{1}H-NMR ($CDCl_3$): δ 0.72-0.95 (t, 3H, $C\underline{H}_3$), 1.12-1.40 (m, 18H, $CH_3(C\underline{H}_2)_9$), 1.40-1.77 (m, 2H, $CH_3(CH_2)_9C\underline{H}_2$), 1.77-1.87 (m, 2H, $N\underline{H}_2$), 2.27-2.35 (m, 2H, $C(=O)C\underline{H}_2$), 2.97-3.07 (m, 2H, $C\underline{H}_2NH_2$), 3.17-3.30 (m, 2H, $C\underline{H}_2NH$), 6.90-7.10 (m, 1H, N$\underline{H}$); (Found: C, 68.11; H, 12.29; N, 10.89. Calc. for $C_{15}H_{32}N_2O$: C, 72.26; H, 12.58; N, 10.92 %). **18** (3.21 g, 12.5 mmol), *N*-benzyloxycarbonyl-L-glutamic acid (L-Glu-Z) (1.60 g, 5.69 mmol), and triethylamine (2.60 g, 25.7 mmol) were dissolved in 150 cm^3 of THF and stirred with cooling to 0 ˚C. DEPC (2.32 g, 14.2 mmol) was added to the mixture and stirred for 30 min in an ice bath. After being stirred for 1 day at room temperature, the solution was concentrated *in vacuo* and the residue was recrystallized from methanol to give white solid *N',N''*-bis(dodecylaminocarbonylethyl)-N^{α}-benzyloxycarbonyl-L-glutamide (**19**): yield 3.26 g (75.6 %); m.p. 213-216 ˚C; FT-IR (KBr): /cm^{-1} 3298, 2960, 2924, 2856, 1692, 1657, 1640, 1547, 1468, 1456, 1375, 721 and 696; ^{1}H-NMR ($CDCl_3$): δ 0.79-0.97 (m, 6H, $C\underline{H}_3$ × 2), 1.00-1.41 (m, 36H, $CH_3(C\underline{H}_2)_9$ × 2), 1.41-1.57 (m, 6H, $CH_3(CH_2)_9C\underline{H}_2$ × 2, *$CHC\underline{H}_2$), 2.15-2.47 (m, 6H, $C(=O)C\underline{H}_2$ × 3), 2.98-3.13 (q, 4H, $CH_3(CH_2)_{10}C\underline{H}_2$ × 2), 3.13-3.28 (m, 4H, $C(=O)CH_2C\underline{H}_2NH$ × 2), 4.07-4.27 (m, 1H, *C$\underline{H}$), 5.02-5.14 (s, 2H, $C\underline{H}_2C_6H_5$), 5.87-6.10 (m, 2H, N$\underline{H}$ × 2), 6.50-6.70 (m, 1H, N$\underline{H}$), 6.70-6.90 (m, 1H, N$\underline{H}$), 6.96-7.10 (m, 1H, N$\underline{H}$), 7.30-7.44 (m, 5H, $C_6\underline{H}_5$); (Found: C, 66.97; H, 10.28; N, 9.00. Calc. for $C_{43}H_{75}N_5O_6{\cdot}0.7H_2O$: C, 66.97; H, 9.99; N, 9.08 %). **19** (3.10 g, 4.09 mmol) was dissolved in 200 cm^3 of *N*,*N*-dimethylformamide (DMF) with heating and Pd black (1 g) was added to the solution. H_2 gas was bubbled slowly into the solution for 6 hours. After confirming the removal of Z-group by FTIR measurement, Pd black was removed by filtration. The filtrate was concentrated and dried *in vacuo* to give white solid *N',N''*-bis(dodecylaminocarbonylethyl)-L-glutamide (**20**): yield 2.55 g (100 %); m.p. 172-

175 ˚C; FT-IR (KBr): /cm^{-1} 3298, 2960, 2920, 2854, 1638, 1547, 1468, 1379 and 721; ^{1}H-NMR ($CDCl_3$): δ 0.83-0.93 (t, 6H, C$\underline{H}_3$ × 2), 1.13-1.37 (m, 36H, $CH_3(C\underline{H}_2)_9$ × 2), 1.43-1.57 (m, 4H, $CH_3(CH_2)_9C\underline{H}_2$ × 2), 1.57-1.80 (m, 2H, N$\underline{H}_2$), 1.87-2.01 (m, 2H, *CHC$\underline{H}_2$), 2.17-2.28 (m, 2H, *$CHCH_2C\underline{H}_2$), 2.37-2.46 (m, 4H, C(=O)C$\underline{H}_2CH_2$NH × 2), 3.16-3.29 (m, 4H, $CH_3(CH_2)_{10}C\underline{H}_2$ × 2), 3.46-3.60 (m, 4H, C(=O)$CH_2C\underline{H}_2$NH × 2), 6.09-6.33 (m, 1H, N$\underline{H}$), 7.70-7.83 (m, 1H, N$\underline{H}$); (Found: C, 67.33; H, 11.01; N, 11.01. Calc. for $C_{35}H_{69}N_5O_4$·0.7H_2O: C, 67.33; H, 11.15; N, 10.22 %). **20** (0.80 g, 1.3 mmol) was dissolved in 80 cm^3 of DMF. Glutaric anhydride (0.18 g, 1.5 mmol) and triethylamine (0.13 g, 1.3 mmol) were added to the solution and stirred in an ice bath. After being stirred for 1 day at room temperature, the solution was concentrated *in vacuo*. The residue was recrystallized from methanol and dried *in vacuo* to give a white solid (**1**): yield 0.65 g (69 %); m.p. 205-210 ˚C; FT-IR (KBr): /cm^{-1} 3296, 2960, 2924, 2856, 1709, 1638, 1549, 1468, 1456, 1377 and 721; ^{1}H-NMR ($CDCl_3$): δ 0.79-0.95 (t, 6H, C$\underline{H}_3$ × 2), 1.03-1.38 (m, 36H, $CH_3(C\underline{H}_2)_9$ × 2), 1.42-1.53 (m, 4H, $CH_3(CH_2)_9C\underline{H}_2$ × 2), 1.59-2.11 (m, 4H, *CHC$\underline{H}_2$, C$\underline{H}_2CH_2$(C=O)O), 2.37-2.62 (m, 10H, (C=O)C$\underline{H}_2$ × 5), 3.08-3.28 (m, 4H, $CH_3(CH_2)_{10}C\underline{H}_2$ × 2), 3.38-3.63 (m, 4H, (C=O)$CH_2C\underline{H}_2$NH × 2); (Found: C, 63.98; H, 10.11; N, 9.81. Calc. for $C_{40}H_{75}N_5O_7$·0.7H_2O: C, 63.98; H, 10.26; N, 9.33 %).

***N'*,*N"*-Bis(dodecylaminocarbonylethyl)-N^{α}-[(3-carboxy)propanoyl]-L-glutamide** (**2**). **2** was prepared as described above using succinic anhydride instead of glutaric anhydride: yield 1.10 g (72.8 %); m.p. 199.5-200.5 ˚C; FT-IR (KBr): /cm^{-1} 3300, 2960, 2924, 2856, 1719, 1638, 1551, 1468 and 721; ^{1}H-NMR ($CDCl_3$): δ 0.79-0.94 (m, 6H, C$\underline{H}_3$ × 2), 1.13-1.42 (m, 36H, $CH_3(C\underline{H}_2)_9$ × 2), 1.42-1.92 (m, 6H, $CH_3(CH_2)_9C\underline{H}_2$ × 2, *CHC$\underline{H}_2$), 2.35-2.60 (m, 10H, C(=O)C$\underline{H}_2$ × 5), 3.12-3.30 (m, 4H, $CH_3(CH_2)_{10}C\underline{H}_2$ × 2), 3.43-3.66 (m, 4H, C(=O)$CH_2C\underline{H}_2$NH × 2), 4.09-4.23 (m, 1H, *C$\underline{H}$), 6.95-7.03 (m, 1H, N$\underline{H}$), 7.49-7.55 (m, 1H, N$\underline{H}$), 7.95-8.08 (m, 2H, N$\underline{H}$ × 2); (Found: C, 64.17; H, 10.90; N, 9.68. Calc. for $C_{39}H_{73}N_5O_7$·0.7H_2O: C, 64.17; H, 10.17; N, 9.59 %).

***N',N"*-Didodecyl-L-2-N^{α}-[(4-carboxy)butanoyl]aminoadipamide** (**3**). L-2-aminoadipic acid (1.00 g, 6.21 mmol) and sodium hydroxide (0.898 g, 22.5 mmol) were dissolved in 50 cm^3 of deionized water with cooling in an ice bath. Benzyl chloroformate (Z-Cl) (1.60 g, 9.31 mmol) was added dropwise to the solution and the solution was stirred vigorously for 2 hours in an ice bath. The solution was washed with 50 cm^3 of diethylether to remove excess Z-Cl. The pH of aqueous layer was lowered to 2 to give turbid solution. The solution was stored in refrigerator. The solid precipitated was filtered and collected to obtain white powder *N*-benzyloxycarbonyl-L-2-aminoadipic acid (**21**): yield 1.58 g (86.3 %); m.p. 138 ˚C; FT-IR (KBr): /cm^{-1} 3326, 1711, 1698, 1537, 1462 and 698; (Found: C, 56.95; H, 6.50; N, 4.71. Calc. for $C_{14}H_{17}NO_6$: C, 56.95; H, 5.80; N, 4.74 %). 1-Aminododecane (1.04 g, 5.59 mmol), **21** (0.750 g, 2.54 mmol), and triethylamine (1.16 g, 11.4 mmol) were dissolved in 100 cm^3 of THF and stirred with cooling to 0 ˚C. DEPC (1.05 g, 6.44 mmol) was added to the mixture and stirred for 30 min in an ice bath. After being stirred for 1 day at room temperature, the solution was concentrated *in vacuo* and the residue was dissolved in 250 cm^3 of chloroform. The solution was washed with 5 wt% aqueous $NaHCO_3$ (200 cm^3, in twice), deionized water (20 cm^3, once), 0.3 N HCl (200 cm^3, in twice), and deionized water (20 cm^3, once). The solution was dried over Na_2SO_4. After filtration, the filtrate was concentrated *in vacuo* and recrystallized from methanol to give white solid *N',N"*-didodecyl-L-2-N^{α}-(benzyloxycarbonyl)aminoadipamide (**22**): yield 0.626 g (39.1 %); m.p. 156-158 ˚C; FT-IR (KBr): /cm^{-1} 3298, 2958, 2922, 2854, 1684, 1653, 1545, 1468, 721 and 696; ^{1}H-NMR ($CDCl_3$): δ 0.72-1.00 (m, 6H, $C\underline{H}_3 \times 2$), 1.00-1.60 (m, 42H, $CH_3(C\underline{H}_2)_{10} \times 2$, *$CHCH_2C\underline{H}_2$), 1.66-1.87 (m, 2H, *$CHC\underline{H}_2$), 2.10-2.52 (m, 2H, $C(=O)C\underline{H}_2$), 3.02-3.38 (m, 4H, $C\underline{H}_2NH \times 2$), 3.91-4.25 (m, 1H, *C<u>H</u>), 4.95-5.15 (s, 2H, $C\underline{H}_2C_6H_5$), 5.60-5.89 (m, 2H, N<u>H</u> × 2), 6.48-6.80 (m, 1H, N<u>H</u>), 7.23-7.49 (m, 5H, $C_6\underline{H}_5$); (Found: C, 72.21; H, 10.67; N, 6.64. Calc. for $C_{38}H_{67}N_3O_4 \cdot 0.1H_2O$: C, 72.21; H, 10.72; N, 6.65 %). **22** (0.576 g, 0.914 mmol) was dissolved in 200 cm^3 of ethanol with heating and Pd black (1 g) was added to the solution. H_2 gas was bubbled slowly into the solution for 6

hours. After confirming the removal of Z-group by FTIR measurement, Pd black was removed by filtration. The filtrate was concentrated *in vacuo* to give white solid *N',N''*-didodecyl-L-2-aminoadipamide (**23**): yield 0.426 g (94.0 %); m.p. 97-104 ˚C; FT-IR (KBr): /cm^{-1} 3308, 2960, 2922, 2854, 1636, 1543, 1470, 1376 and 721; ^{1}H-NMR ($CDCl_3$): δ 0.70-0.98 (m, 6H, C$\underline{H}_3$ × 2), 1.07-1.61 (m, 42H, $CH_3(C\underline{H}_2)_{10}$ × 2, *$CHCH_2C\underline{H}_2$), 1.87-2.17 (m, 2H, *$CHC\underline{H}_2$), 2.25-2.50 (m, 2H, C(=O)$C\underline{H}_2$), 2.50-2.81 (m, 2H, $N\underline{H}_2$), 3.01-3.50 (m, 4H, $C\underline{H}_2NH$ × 2), 3.87-4.16 (m, 1H, *C$\underline{H}$), 6.32-6.73 (m, 1H, N$\underline{H}$), 6.73-6.92 (m, 1H, N$\underline{H}$); (Found: C, 71.31; H, 12.10; N, 7.94. Calc. for $C_{30}H_{61}N_3O_2{\cdot}0.6H_2O$: C, 71.31; H, 12.38; N, 8.32 %). **23** (0.381 g, 0.768 mmol) was dissolved in 80 cm^3 of THF. Glutaric anhydride (0.132 g, 1.15 mmol) and triethylamine (0.160 g, 1.54 mmol) were added to the solution and stirred in an ice bath. After being stirred for 1 day at room temperature, the solution was concentrated *in vacuo*. The residue was recrystallized from methanol and dried *in vacuo* to give a white solid (**3**): yield 0.373 g (76.3 %); m.p. 147-153 ˚C; FT-IR (KBr): /cm^{-1} 3296, 2958, 2922, 2854, 1705, 1640, 1547, 1466, 1379 and 721; ^{1}H-NMR ($CDCl_3$): δ 0.75-1.01 (m, 6H, C$\underline{H}_3$ × 2), 1.01-1.61 (m, 36H, $CH_3(C\underline{H}_2)_9$ × 2), 1.61-1.90 (m, 10H, $CH_3(CH_2)_9C\underline{H}_2$ × 2, *$CHCH_2C\underline{H}_2$, $C\underline{H}_2CH_2C$(=O)O), 1.90-2.11 (m, 2H, *$CHC\underline{H}_2$), 2.11-2.58 (m, 6H, C(=O)$C\underline{H}_2$ × 3), 3.00-3.40 (m, 4H, $C\underline{H}_2NH$ × 2), 4.32-4.59 (m, 1H, *C$\underline{H}$), 6.17-6.39 (m, 1H, N$\underline{H}$), 7.37-8.23 (m, 2H, N$\underline{H}$ × 2); (Found: C, 67.85; H, 10.87; N, 7.18. Calc. for $C_{35}H_{67}N_3O_5{\cdot}0.7H_2O$: C, 67.85; H, 10.37; N, 6.60 %).

***N',N''*-Bis(dodecylaminocarbonylpropyl)-N^{α}-[(4-carboxy)butanoyl]-L-glutamide** (**5**). **5** was prepared as described above using γ-aminobutyric acid (GABA) instead of β-Ala. *N*-benzyloxycarbonyl-γ-aminobutyric acid (GABA-Z) (**24**) was prepared according to the method for **21**: yield 10.05 g (87.4 %); m.p. 64-65 ˚C; FT-IR (KBr): /cm^{-1} 3334, 3064, 2964, 2924, 1690, 1549, 1454, 1274, 723 and 698; ^{1}H-NMR ($CDCl_3$): δ 1.75-1.89 (m, 2H, C(=O)$CH_2C\underline{H}_2$), 2.32-2.45 (t, 2H, C(=O)$C\underline{H}_2$), 3.16-3.30 (q, 2H, $C\underline{H}_2NH$), 4.91-5.04 (s, 1H, N$\underline{H}$), 5.04-5.18 (m, 2H, $C\underline{H}_2C_6H_5$), 7.28-7.41 (m, 5H, $C_6\underline{H}_5$), 9.90 (br, 1H, O$\underline{H}$). *N*-Dodecyl-4-(*N'*-benzyloxycarbonyl)aminobutanamide (**25**): yield 4.46 g (81.7 %); m.p. 112

˚C; FT-IR (KBr): /cm^{-1} 3344, 3308, 2960, 2920, 2854, 1688, 1634, 1543, 1468, 1456, 1381, 733 and 694; ^{1}H-NMR ($CDCl_3$): δ 0.85-0.92 (t, 3H, C$\underline{H}_3$), 1.19-3.36 (m, 18H, $CH_3(C\underline{H}_2)_9$), 1.43-1.53 (m, 2H, $CH_3(CH_2)_9C\underline{H}_2$), 1.78-1.88 (m, 2H, $C(=O)CH_2C\underline{H}_2$), 2.15-2.23 (t, 2H, $C(=O)C\underline{H}_2$), 3.16-3.29 (m, 4H, $C\underline{H}_2NH \times 2$), 5.06-5.12 (s, 2H, $C\underline{H}_2C_6H_5$), 5.12-5.20 (s, 1H, N$\underline{H}$), 5.94-6.01 (t, 1H, N$\underline{H}$), 7.28-7.38 (m, 5H, $C_6\underline{H}_5$); (Found: C, 68.49; H, 9.61; N, 6.45. Calc. for $C_{24}H_{40}N_2O_3{\cdot}0.9H_2O$: C, 68.49; H, 10.01; N, 6.66 %). *N*-Dodecyl-4-aminobutanamide (**26**): yield 2.90 g (100 %); m.p. 74-83 ˚C; FT-IR (KBr): /cm^{-1} 3302, 2960, 2920, 2854, 1636, 1551, 1470, 1379 and 721; ^{1}H-NMR ($CDCl_3$): δ 0.84-0.94 (t, 3H, C$\underline{H}_3$), 1.17-1.36 (m, 18H, $CH_3(C\underline{H}_2)_9$), 1.43-1.56 (m, 2H, $CH_3(CH_2)_9C\underline{H}_2$), 1.71-1.91 (m, 4H, $C\underline{H}_2CH_2N\underline{H}_2$), 2.18-2.33 (t, 2H, $C(=O)C\underline{H}_2$), 2.71-2.81 (t, 2H, $C\underline{H}_2NH_2$), 3.16-3.30 (q, 2H, $C\underline{H}_2NH$), 5.92-6.07 (s, 1H, N$\underline{H}$); (Found: C, 65.87; H, 11.48; N, 7.66. Calc. for $C_{16}H_{34}N_2O{\cdot}1.1H_2O$: C, 65.87; H, 12.65; N, 8.63 %). *N',N''*-bis(dodecylaminocarbonylpropyl)-N^{α}-benzyloxycarbonyl-L-glutamide (**27**): yield 2.46 g (73.4%); m.p. 179-181 ˚C; FT-IR (KBr): /cm^{-1} 3322, 3290, 2960, 2924, 2856, 1690, 1651, 1636, 1543, 1468, 1460, 1379, 719 and 700; ^{1}H-NMR ($CDCl_3$): δ 0.84-0.92 (t, 6H, $C\underline{H}_3 \times 2$), 1.17-1.35 (m, 36H, $CH_3(C\underline{H}_2)_9 \times 2$), 1.43-1.54 (m, 4H, $CH_3(CH_2)_9C\underline{H}_2 \times 2$), 1.78-1.94 (m, 4H, $(C=O)CH_2C\underline{H}_2CH_2 \times 2$), 1.94-2.10 (m, 2H, $*CHC\underline{H}_2$), 2.13-2.22 (t, 2H, $*CHCH_2C\underline{H}_2$), 2.22-2.39 (m, 4H, $C(=O)C\underline{H}_2CH_2CH_2 \times 2$), 3.12-3.50 (m, 8H, $NHC\underline{H}_2 \times 4$), 4.16-4.26 (q, 1H, *C$\underline{H}$), 5.06-5.13 (s, 2H, $C\underline{H}_2C_6H_5$), 6.10-6.20 (d, 2H, N$\underline{H} \times 2$), 6.22-6.30 (m, 1H, N$\underline{H}$), 6.72-6.81 (s, 1H, N$\underline{H}$), 7.30-7.40 (m, 5H, $C_6\underline{H}_5$), 7.45-7.53 (m, 1H, N$\underline{H}$); (Found: C, 67.73; H, 10.02; N, 8.53. Calc. for $C_{45}H_{79}N_5O_6{\cdot}0.7H_2O$: C, 67.73; H, 10.15; N, 8.78 %). *N',N''*-bis(dodecylaminocarbonylpropyl)-L-glutamide (**28**): yield 1.51 g (77.0 %); m.p. 168-173 ˚C; FT-IR (KBr): /cm^{-1} 3312, 2960, 2922, 2854, 1638, 1543, 1470, 1452, 1369 and 719; ^{1}H-NMR ($CDCl_3$): δ 0.83-0.94 (t, 6H, $C\underline{H}_3 \times 2$), 1.18-1.38 (m, 36H, $CH_3(C\underline{H}_2)_9 \times 2$), 1.43-1.55 (m, 4H, $CH_3(CH_2)_9C\underline{H}_2 \times 2$), 1.57-1.72 (s, 6H, $C(=O)CH_2C\underline{H}_2CH_2 \times 2$, $N\underline{H}_2$), 1.77-1.90 (q, 2H, $*CHC\underline{H}_2$), 2.14-2.28 (m, 4H, $C(=O)C\underline{H}_2(CH_2)_2 \times 2$), 2.28-2.36 (m, 2H, $*CHCH_2C\underline{H}_2$), 3.15-3.40 (m, 8H, $C\underline{H}_2NH \times 4$),

4.07-4.16 (m, 1H, *CH), 6.17-6.26 (m, 2H, NH × 2), 6.74-6.79 (t, 1H, NH), 7.60-7.67 (t, 1H, NH); (Found: C, 67.15; H, 11.05; N, 9.22. Calc. for $C_{37}H_{73}N_5O_4 \cdot 0.5H_2O$: C, 67.15; H, 10.28; N, 10.58 %). **5**, yield 0.227 g (64.3 %); m.p.168-172 ˚C; FT-IR (KBr): /cm^{-1} 3302, 2960, 2924, 2854, 1702, 1638, 1551, 1468, 1379 and 721; δ 0.80-0.96 (s, 6H, CH_3 × 2), 1.06-1.41 (m, 36H, $CH_3(CH_2)_9$ × 2), 1.41-1.57 (s, 4H, $CH_3(CH_2)_9CH_2$ × 2), 1.61-2.09 (m, 8H, $C(=O)CH_2CH_2$ × 4), 2.09-2.46 (m, 10H, $C(=O)CH_2$ × 5), 3.07-3.44 (m, 8H, CH_2NH × 4), 4.07-4.17 (m, 1H, *CH), 6.17-6.46 (m, 2H, NH × 2), 6.87-7.02 (m, 1H, NH), 7.10-7.20 (m, 1H, NH), 7.42-4.57 (m, 1H, NH); (Found: C, 65.09; H, 9.82; N, 9.07. Calc. for $C_{42}H_{79}N_5O_7$: C, 65.84; H, 10.39; N, 9.14 %).

***N',N"*-Dihexadecyl-N^{α}-[(4-carboxy)butanoyl]-L-glutamide** (**6**). **6** was prepared by coupling of glutaric anhydride and *N',N"*-dihexadecyl-L-glutamide (**30**) prepared according to the previously described method[1] using 1-aminohexadecane instead of 1-aminododecane. *N',N"*-Dihexadecyl-N^{α}-benzyloxycarbonyl-L-glutamide (**29**): yield 3.6 g (87 %); m.p. 129.5 ˚C; FT-IR (KBr): /cm^{-1} 3296, 2920, 2854, 1688, 1649 and 1560; ^{1}H-NMR ($CDCl_3$): δ 0.70-1.03 (t, 6H, CH_3 × 2), 1.03-1.72 (m, 56H, $CH_3(CH_2)_{14}$ × 2), 1.72-2.63 (m, 4H, $*CH(CH_2)_2$), 2.63-3.42 (m, 4H, CH_2NH × 2), 4.03-4.40 (m, 1H, *CH), 4.98-5.20 (s, 2H, $CH_2C_6H_5$), 6.29 (br, 1H, NH), 6.90 (br, 1H, NH), 7.23-7.50 (s, 5H, C_6H_5). **30**, yield 6.5 g (95 %); m.p. 88-102 ˚C; FT-IR (KBr): /cm^{-1} 3326, 2922, 2854, 1636 and 1533; ^{1}H-NMR ($CDCl_3$): δ 0.70-1.01 (t, 6H, CH_3 × 2), 1.01-1.80 (m, 56H, $CH_3(CH_2)_{14}$ × 2), 1.80-2.20 (t, 2H, $*CHCH_2$), 2.20-2.54 (t, 2H, $C(=O)CH_2$), 2.89 (br, 2H, NH_2), 3.02-3.36 (m, 4H, CH_2NH × 2), 3.68-4.70 (m, 1H, *CH), 6.82 (br, 1H, NH), 7.41 (br, 1H, NH): **6**, yield 0.96 g (94 %); m.p. 123-135 ˚C; FT-IR (KBr): /cm^{-1} 3298, 2958, 2920, 2854, 1719, 1640, 1555, 1470 and 719; ^{1}H-NMR ($CDCl_3$): δ 0.79-0.97 (m, 6H, CH_3 × 2), 0.99-1.42 (m, 52H, $CH_3(CH_2)_{13}$ × 2), 1.42-1.62 (m, 56H, $CH_3(CH_2)_{13}CH_2$ × 2), 1.84-2.04 (m, 2H, $*CHCH_2$), 2.04-2.19 (m, 2H, $CH_2CH_2C(=O)O$), 2.19-2.49 (m, 6H, $C(=O)CH_2$ × 3), 3.10-3.31 (m, 4H, CH_2NH × 2), 4.31-4.47 (m, 1H, *CH), 6.41-6.56 (m, 1H, NH), 6.99-7.14 (m, 1H, NH),

7.31-7.45 (m, 1H, NH); (Found: C, 69.75; H, 11.56; N, 5.93. Calc. for $C_{42}H_{81}N_3O_5 \cdot 0.8H_2O$: C, 69.75; H, 11.52; N, 5.81 %).

***N',N"*-Didodecyl-N^{α}-[(4-carboxy-3-methyl)butanoyl]-L-glutamide** (**7**). **7** was prepared by coupling of *N',N"*-didodecyl-L-glutamide[5] and 3-methylglutaric anhydride as described above: yield 0.750 g (69.7 %); m.p. 115-121 ˚C; FT-IR (KBr): /cm^{-1} 3296, 2960, 2922, 2854, 1719, 1638, 1557, 1468, 1379 and 721; ^{1}H-NMR ($CDCl_3$): δ 0.82-0.94 (t, 6H, $CH_3 \times 2$), 0.98-1.05 (d, 3H, CH_3CH), 1.15-1.39 (m, 36H, $CH_3(CH_2)_9 \times 2$), 1.39-1.59 (m, 4H, $CH_3(CH_2)_9CH_2 \times 2$), 1.59-1.74 (m, 1H, CH), 1.94-2.17 (m, 2H, *$CHCH_2$), 2.17-2.32 (m, 4H, $NHC(=O)CH_2 \times 2$), 2.32-2.46 (m, 2H, $CH_2C(=O)O$), 3.07-3.31 (m, 4H, $CH_2NH \times 2$), 3.85-3.95 (m, 1H, *CH), 7.57-7.95 (m, 2H, $NH \times 2$), 8.03-8.16 (m, 1H, NH); (Found: C, 67.88; H, 11.92; N, 6.80. Calc. For $C_{35}H_{67}N_3O_5 \cdot 0.5H_2O$: C, 67.88; H, 11.07; N, 6.79 %).

***N',N"*-Bis(octylaminocarbonylethyl)-N^{α}-[(4-carboxy)butanoyl]-L-glutamide** (**8**). 1-Aminooctane (2.50 g, 19.3 mmol), β-Ala-Z (4.75 g, 21.3 mmol), and triethylamine (4.32 g, 42.7 mmol) were dissolved in 100 cm^3 of THF and stirred with cooling to 0 ˚C. To the solution was added DEPC (4.11 g, 25.2 mmol) and stirred in an ice bath for 30 min. After being stirred for 1 day at room temperature, the solution was concentrated *in vacuo*. The residue was dissolved in 200 cm^3 of chloroform and was washed with 5 wt% aqueous $NaHCO_3$ (200 cm^3, in twice), deionized water (20 cm^3, once), 0.3 N HCl (200 cm^3, in twice), and deionized water (20 cm^3, once). The solution was dried over Na_2SO_4. After filtration, the filtrate was concentrated *in vacuo* and recrystallized from methanol to give white powder *N*-octyl-3-(*N'*-benzyloxycarbonyl)aminopropanamide (**31**): yield 5.64 g (87.2 %); m.p. 115-119 ˚C; FT-IR (KBr): /cm^{-1} 3344, 3308, 2960, 2928, 2874, 2854, 1686, 1638, 1537, 1464 and 698; ^{1}H-NMR ($CDCl_3$): δ 0.84-0.91 (t, 3H, CH_3), 1.20-1.36 (m, 10H, $CH_3(CH_2)_5$), 1.41-1.51 (m, 2H, $CH_3(CH_2)_5CH_2$), 2.34-2.43 (t, 2H, $C(=O)CH_2$), 3.16-3.24 (q, 2H, $CH_3(CH_2)_6CH_2$), 3.43-3.51 (q, 2H, $C(=O)CH_2CH_2$), 5.04-5.13 (s, 2H, $CH_2C_6H_5$), 5.43-5.53 (s, 1H, NH), 5.62-5.72 (s, 1H, NH), 7.27-7.38 (m, 5H, C_6H_5). **31** (5.50 g, 16.4 mmol) was dissolved in 200 cm^3 of ethanol with heating and Pd black (1 g) was added to

the solution. H_2 gas was bubbled slowly into the solution for 5 hours. After confirming the removal of the Z-group by FTIR measurement, Pd black was removed by filtration. The filtration was concentrated and dried *in vacuo* to give yellowish oil *N*-octyl-3-aminopropanamide (**32**): yield 3.29 g (100 %); FT-IR (KBr): /cm^{-1} 3298, 2960, 2922, 2854, 1649, 1553, 1450 and 721; ^{1}H-NMR ($CDCl_3$): δ 0.83-0.93 (t, 3H, $C\underline{H}_3$), 1.18-1.37 (m, 10H, $CH_3(C\underline{H}_2)_5$), 1.43-1.55 (m, 2H, $CH_3(CH_2)_5C\underline{H}_2$), 2.31-2.37 (t, 2H, $C(=O)C\underline{H}_2$), 2.43-2.52 (s, 2H, $N\underline{H}_2$), 2.98-3.05 (t, 2H, $C\underline{H}_2NH_2$), 3.17-3.28 (q, 2H, $NHC\underline{H}_2$), 6.96-7.07 (s, 1H, N$\underline{H}$). **32** (3.13 g, 15.6 mmol), L-Glu-Z (2.00 g, 7.11 mmol), and triethylamine (3.38 g, 33.4 mmol) were dissolved in 150 cm^3 of THF and stirred with cooling to 0 ˚C. DEPC (2.92 g, 17.9 mmol) was added to the mixture and stirred for 30 min in an ice bath. After being stirred for 1 day at room temperature, the solution was concentrated *in vacuo* and the residue was recrystallized from methanol to give white solid *N',N''*-bis(octylaminocarbonylethyl)-N^{α}-benzyloxycarbonyl-L-glutamide **33**: yield 2.87 g (62.5 %); m.p. 221-224 ˚C; FT-IR (KBr): /cm^{-1} 3300, 2960, 2928, 2858, 1692, 1644, 1547, 1456, 725 and 696; ^{1}H-NMR ($CDCl_3$): δ 0.82-0.92 (m, 6H, $C\underline{H}_3 \times 2$), 1.16-1.24 (m, 20H, $CH_3(C\underline{H}_2)_5 \times 2$), 1.24-1.52 (m, 4H, $CH_3(CH_2)_5C\underline{H}_2 \times 2$), 1.93-2.06 (m, 2H, $*CHC\underline{H}_2$), 2.18-2.29 (m, 2H, $*CHCH_2C\underline{H}_2$), 2.34-2.45 (m, 2H, $C(=O)C\underline{H}_2CH_2NH$), 3.13-3.27 (m, 4H, $CH_3(CH_2)_6C\underline{H}_2 \times 2$), 3.40-3.66 (m, 4H, $C(=O)CH_2C\underline{H}_2NH \times 2$), 4.16-4.23 (m, 1H, $*C\underline{H}$), 5.05-5.12 (m, 2H, $C\underline{H}_2C_6H_5$), 5.66-5.72 (m, 1H, N$\underline{H}$), 5.89-6.06 (m, 2H, $N\underline{H} \times 2$), 6.78-6.88 (m, 1H, N$\underline{H}$), 7.30-7.47 (m, 6H, $C_6\underline{H}_5$, N$\underline{H}$). **33** (2.70 g, 4.18 mmol) was dissolved in 200 cm^3 of DMF with heating and Pd black (1 g) was added to the solution. H_2 gas was bubbled slowly into the solution for 6 hours. After confirming the removal of Z-group by FTIR measurement, Pd black was removed by filtration. The filtrate was concentrated and dried *in vacuo* to give white solid *N',N''*-bis(octylaminocarbonylethyl)-L-glutamide (**34**): yield 2.14 g (100 %); m.p. 181-185 ˚C; FT-IR (KBr): /cm^{-1} 3298, 2960, 2924, 2854, 1638, 1549, 1468, 1377 and 723; ^{1}H-NMR ($CDCl_3$): δ 0.81-0.95 (t, 6H, $C\underline{H}_3 \times 2$), 1.15-1.40 (m, 20H, $CH_3(C\underline{H}_2)_5 \times 2$), 1.40-1.56 (m, 4H, $CH_3(CH_2)_5C\underline{H}_2 \times 2$), 1.87-2.53 (m, 10H, $*CH(C\underline{H}_2)_2$,

C(=O)C$\underline{H}_2$CH$_2$NH × 2, N$\underline{H}_2$), 3.11-3.28 (q, 4H, CH$_3$(CH$_2$)$_6$C$\underline{H}_2$ × 2), 3.41-3.57 (m, 4H, C(=O)CH$_2$C$\underline{H}_2$NH × 2), 4.01-4.17 (m, 1H, *C$\underline{H}$), 6.34-6.52 (m, 2H, N$\underline{H}$ × 2), 7.05-7.17 (m, 1H, N$\underline{H}$), 7.93-8.02 (m, 1H, N$\underline{H}$). **34** (1.40 g, 2.74 mmol) and triethylamine (0.293 g, 2.90 mmol) were dissolved in 100 cm^3 of DMF. Glutaric anhydride (0.468 g, 4.10 mmol) was added in the solution and stirred in an ice bath. After being stirred for 1 day at room temperature, the solution was concentrated *in vacuo*. The residue was recrystallized from methanol and dried *in vacuo* to give a white solid (**8**): yield 1.34 g (78.4 %); m.p. 207-209 ˚C; FT-IR (KBr) /cm^{-1} 3300, 3290, 2960, 2928, 2858, 1709, 1638, 1553, 1456, 1438 and 723; ^{1}H-NMR (CDCl$_3$): δ 0.76-0.95 (m, 6H, C$\underline{H}_3$ × 2), 1.10-1.42 (m, 20H, CH$_3$(C$\underline{H}_2$)$_5$ × 2), 1.42-2.79 (m, 18H, CH$_3$(CH$_2$)$_5$C$\underline{H}_2$ × 2, *CH(C$\underline{H}_2$)$_2$, (C$\underline{H}_2$)$_3$C(=O)O, C(=O)C$\underline{H}_2$CH$_2$NH × 2), 3.13-3.30 (m, 4H, CH$_3$(CH$_2$)$_6$C$\underline{H}_2$ × 2), 3.39-3.61 (m, 4H, C(=O)CH$_2$C$\underline{H}_2$NH × 2), 3.96-4.18 (m, 1H, *C$\underline{H}$). (Found: C, 60.87; H, 9.46; N, 11.24. Calc. for C$_{32}$H$_{59}$N$_5$O$_7$·0.3H$_2$O: C, 60.87; H, 9.52; N, 11.09 %).

***N'*,*N"*-Bis(octylaminocarbonylethyl)-*N*$^{\alpha}$-[(3-carboxy)propanoyl]-L-glutamide** (**9**). The related compound **9** was prepared as described above using succinic anhydride instead of glutaric anhydride: yield 0.453 g (75.8%); m.p. 191-193 ˚C; FT-IR (KBr): /cm^{-1} 3298, 2960, 2928, 2858, 1719, 1644, 1551 and 723; ^{1}H-NMR (CDCl$_3$): δ 0.78-0.90 (m, 6H, C$\underline{H}_3$ × 2), 1.17-1.36 (m, 20H, CH$_3$(C$\underline{H}_2$)$_5$ × 2), 1.36-1.92 (m, 6H, CH$_3$(CH$_2$)$_5$C$\underline{H}_2$ × 2, *CHC$\underline{H}_2$), 1.92-2.73 (m, 10H, C(=O)C$\underline{H}_2$CH$_2$NH × 2, *CHCH$_2$C$\underline{H}_2$, (C$\underline{H}_2$)$_2$C(=O)O), 3.13-3.29 (m, 4H, CH$_3$(CH$_2$)$_6$C$\underline{H}_2$ × 2), 3.37-3.70 (m, 4H, C(=O)CH$_2$C$\underline{H}_2$NH × 2), 4.00-4.15 (m, 1H, *C$\underline{H}$); (Found: C, 60.49; H, 9.33; N, 11.38. Calc. for C$_{31}$H$_{57}$N$_5$O$_7$·0.2H$_2$O: C, 60.49; H, 9.40; N, 11.38 %).

Anionic amphiphiles derived from basic α-amino acid (L-Lys)

***N*$^{\alpha}$,*N*$^{\varepsilon}$-Bis(hexadecanoyl)-*N*-[(3-carboxy)propyl]-L-lysinamide** (**10**) GABA (5.00 g, 48.5 mmol), benzyl alcohol (10.49 g, 97.0 mmol), and *p*-toluenesulfonic acid monohydrate (10.15 g, 53.4 mmol) were suspended in 300 cm^3 of toluene and refluxed for 5 hours,

removing water azeotropically. The reaction mixture was concentrated *in vacuo* and an excess amount of diethyl ether was added. The precipitates formed were collected and reprecipitated from methanol-diethyl ether. The solid was dried *in vacuo* to give white powder γ-aminobutyric acid benzyl ester *p*-toluenesulfonate (**35**): yield 17.20 g (97.1 %); m.p. 103-105 ˚C; FT-IR (KBr): /cm^{-1} 2928, 1736, 1638, 1499, 1193 and 1038; ^{1}H-NMR ($CDCl_3$): δ 1.80-1.91 (m, 2H, $C\underline{H}_2CH_2C(=O)$), 2.26-2.34 (t, 5H, $C\underline{H}_3$, $C\underline{H}_2C(=O)$), 2.82-2.92 (t, 2H, $^+NH_3C\underline{H}_2$), 4.98-5.03 (s, 2H, $C\underline{H}_2C_6H_5$), 7.04-7.10 (d, 2H, $CH_3C_6\underline{H}_4$), 7.23-7.36 (m, 5H, $C_6\underline{H}_5$), 7.66-7.80 (d, 5H, $C_6\underline{H}_4SO_3^-\cdot{}^+N\underline{H}_3$). δ-Aminovaleric acid benzyl ester *p*-toluenesulfonate (**36**) and ε-aminocaproic acid benzyl ester *p*-toluenesulfonate (**37**) were prepared similarly: **36**, yield 6.18 g (95.3 %); m.p. 74-76 ˚C; FT-IR (KBr): /cm^{-1} 3074, 1744, 1632, 1489, 1170 and 1033; ^{1}H-NMR ($CDCl_3$): δ 1.45-1.57 (m, 4H, $(C\underline{H}_2)_2CH_2C(=O)$), 2.12-2.21 (t, 2H, $C\underline{H}_2C(=O)$), 2.27-2.33 (s, 3H, $C\underline{H}_3$), 2.71-2.79 (t, 2H, $^+NH_3C\underline{H}_2$), 5.01-5.06 (s, 2H, $C\underline{H}_2C_6H_5$), 7.09-7.17 (d, 2H, $CH_3C_6\underline{H}_4$), 7.26-7.37 (m, 5H, $C_6\underline{H}_5$), 7.56-7.76 (m, 5H, $C_6\underline{H}_4SO_3^-\cdot{}^+N\underline{H}_3$). **37**, yield 13.92 g (92.9 %); m.p. 103-106 ˚C; FT-IR (KBr): /cm^{-1} 3048, 1729, 1628, 1483, 1178 and 1040; ^{1}H-NMR ($CDCl_3$): δ 1.13-1.24 (m, 2H, $C\underline{H}_2(CH_2)_2C(=O)$), 1.42-1.54 (m, 4H, $C\underline{H}_2CH_2C\underline{H}_2CH_2C(=O)$), 2.16-2.24 (t, 2H, $C\underline{H}_2C(=O)$), 2.28-2.36 (s, 3H, $C\underline{H}_3$), 2.69-2.79 (m, 2H, $^+NH_3C\underline{H}_2$), 5.04-5.10 (s, 2H, $C\underline{H}_2C_6H_5$), 7.11-7.19 (d, 2H, $CH_3C_6\underline{H}_4$), 7.27-7.38 (m, 5H, $C_6\underline{H}_5$), 7.57-7.79 (m, 5H, $C_6\underline{H}_4SO_3^-\cdot{}^+N\underline{H}_3$). $N^{\alpha},N^{\varepsilon}$-Dihexadecanoyl-L-lysine[3a] (1.50 g, 2.41 mmol), **35** (1.32 g, 3.61 mmol), and triethylamine (0.614 g, 6.07 mmol) were dissolved in 100 cm^3 of THF and stirred with cooling to 0 ˚C. DEPC (0.560 g, 3.43 mmol) was added to the mixture and stirred for 30 min in an ice bath. After being stirred for 1 day at room temperature, the solution was concentrated *in vacuo* and the residue was dissolved in 250 cm^3 of chloroform. The solution was washed with 5 wt% aqueous $NaHCO_3$ (200 cm^3, in twice), deionized water (20 cm^3, once), 0.3 N HCl (200 cm^3, in twice), and deionized water (20 cm^3, once). The solution was dried over Na_2SO_4. After filtration, the filtrate was concentrated *in vacuo* and recrystallized from methanol to give white solid $N^{\alpha},N^{\varepsilon}$-

dihexadecanoyl-*N*-[3-(benzyloxycarbonyl)propyl]-L-lysinamide **38**: yield 1.76 g (91.7 %); m.p. 110-115 ˚C; FT-IR (KBr): /cm^{-1} 3314, 2954, 2920, 2854, 1738, 1640, 1557, 1470, 719 and 700; ^{1}H-NMR ($CDCl_3$): δ 0.69-0.93 (t, 6H, C$\underline{H}_3$ × 2), 0.93-1.37 (m, 50H, $CH_3(C\underline{H}_2)_{12}$ × 2, *$CHCH_2C\underline{H}_2$), 1.37-1.94 (m, 10H, $CH_3(CH_2)_{12}C\underline{H}_2$ × 2, *$CHC\underline{H}_2CH_2C\underline{H}_2$, $C\underline{H}_2CH_2C(=O)O$), 2.02-2.26 (m, 4H, $CH_3(CH_2)_{13}C\underline{H}_2$ × 2), 2.26-2.53 (m, 2H, $C\underline{H}_2C(=O)O$), 3.11-3.35 (m, 2H, $NHC\underline{H}_2$), 3.35-3.52 (m, 2H, $NHC\underline{H}_2$), 4.21-4.51 (m, 1H, *C$\underline{H}$), 5.04-5.16 (s, 2H, $C\underline{H}_2C_6H_5$), 5.68-6.03 (m, 1H, N$\underline{H}$), 6.42-6.67 (m, 1H, N$\underline{H}$), 6.70-7.01 (m, 1H, N$\underline{H}$), 7.27-7.46 (m, 5H, $C_6\underline{H}_5$). **38** (1.50 g, 1.88 mmol) was dissolved in 200 cm^3 of THF with heating and Pd black (1 g) was added to the solution. H_2 gas was bubbled slowly into the solution for 6 hours. After confirming the removal of benzyl group by FTIR measurement, Pd black was removed by filtration. The filtrate was concentrated *in vacuo* and the residue was recrystallized from methanol to give white solid (**10**): yield 1.24 g (93.2 %); m.p. 115-119 ˚C; FT-IR (KBr): /cm^{-1} 3316, 2958, 2920, 2854, 1719, 1638, 1562, 1462 and 719; ^{1}H-NMR ($CDCl_3$): δ 0.75-0.95 (m, 6H, C$\underline{H}_3$ × 2), 1.06-1.43 (m, 50H, $CH_3(C\underline{H}_2)_{12}$ × 2, *$CHCH_2C\underline{H}_2$), 1.47-1.93 (m, 10H, $C\underline{H}_2CH_2C(=O)$ × 3, *$CHC\underline{H}_2CH_2C\underline{H}_2$), 2.07-2.29 (m, 4H, $CH_3(CH_2)_{13}C\underline{H}_2$ × 2), 2.35-2.44 (m, 2H, $C\underline{H}_2C(=O)O$), 3.12-3.44 (m, 2H, $NHC\underline{H}_2$), 3.66-3.80 (m, 2H, $NHC\underline{H}_2$), 4.51-4.64 (m, 1H, *C$\underline{H}$), 5.60-5.69 (m, 2H, N$\underline{H}$ × 2), 6.11-6.22 (m, 1H, N$\underline{H}$); (Found: C, 67.86; H, 11.15; N, 6.16. Calc. for $C_{42}H_{81}N_3O_5 \cdot 2.0H_2O$: C, 67.86; H, 11.51; N, 5.65 %).

***N*$^{\alpha}$,*N*$^{\varepsilon}$-dihexadecanoyl-*N*-[(4-carboxy)butyl]-L-lysinamide** (**11**). The related compound **11** was prepared similarly using **36** instead of **35**, via *N*$^{\alpha}$,*N*$^{\varepsilon}$-bis(hexadecanoyl)-*N*-[4-(benzyloxycarbonyl)butyl]-L-lysinamide (**39**). **39**, yield 0.77 g (81 %); m.p. 98-102 ˚C; FT-IR (KBr): /cm^{-1} 3316, 2958, 2920, 2852, 1738, 1638, 1562, 1466, 719 and 698; ^{1}H-NMR ($CDCl_3$): δ 0.87-1.00 (t, 6H, C$\underline{H}_3$ × 2), 1.03-1.40 (m, 50H, $CH_3(C\underline{H}_2)_{12}$ × 2, *$CHCH_2C\underline{H}_2$), 1.40-2.01 (m, 12H, $CH_3(CH_2)_{12}C\underline{H}_2$ × 2, *$CHC\underline{H}_2CH_2C\underline{H}_2$, $(C\underline{H}_2)_2CH_2C(=O)O$), 2.01-2.50 (m, 6H, $C\underline{H}_2C(=O)$ × 3), 2.85-3.09 (m, 2H, $NHC\underline{H}_2$), 3.09-3.37 (m, 2H, $NHC\underline{H}_2$), 4.22-4.55 (m, 1H, *C$\underline{H}$), 5.06-5.22 (s, 2H, $C\underline{H}_2C_6H_5$), 5.67-6.11 (m,

1H, NH), 6.43-6.86 (m, 2H, NH × 2), 7.30-7.67 (m, 5H, C_6H_5). **11**, yield 0.53 g (92 %); m.p. 104-109 ˚C; FT-IR (KBr): /cm^{-1} 3316, 2958, 2920, 2854, 1719, 1638, 1562, 1462 and 719; ^{1}H-NMR ($CDCl_3$): δ 0.75-0.99 (m, 6H, CH_3 × 2), 0.99-1.41 (m, 50H, $CH_3(CH_2)_{12}$ × 2, *$CHCH_2CH_2$), 1.41-1.83 (m, 12H, $CH_3(CH_2)_{12}CH_2$ × 2, *$CHCH_2CH_2CH_2$, $(CH_2)_2CH_2C(=O)O$), 2.03-2.43 (m, 6H, $CH_2C(=O)$ × 3), 3.12-3.47 (m, 4H, $NHCH_2$ × 2), 4.18-4.54 (m, 1H, *CH); (Found: C, 68.18; H, 11.24; N, 6.02. Calc. for $C_{43}H_{83}N_3O_5 \cdot 2.0H_2O$: C, 68.18; H, 11.57; N, 5.55 %).

***N*$^{\alpha}$,*N*$^{\varepsilon}$-dihexadecanoyl-*N*-[(5-carboxy)pentyl]-L-lysinamide** (**12**). The related compound **12** was prepared similarly using **37** instead of **35**, via *N*$^{\alpha}$,*N*$^{\varepsilon}$-bis(hexadecanoyl)-*N*-[5-(benzyloxycarbonyl)pentyl]-L-lysinamide (**40**). **40**, yield 0.89 g (92 %); m.p. 106-109 ˚C; FT-IR (KBr): /cm^{-1} 3316, 2958, 2920, 2854, 1738, 1638, 1562, 1466, 719 and 698; ^{1}H-NMR ($CDCl_3$): δ 0.73-1.00 (t, 6H, CH_3 × 2), 1.03-1.36 (m, 52H, $CH_3(CH_2)_{12}$ × 2, *$CHCH_2CH_2$, $CH_2(CH_2)_2C(=O)O$), 1.36-1.90 (m, 12H, $CH_3(CH_2)_{12}CH_2$ × 2, *$CHCH_2CH_2CH_2$, $CH_2CH_2CH_2CH_2C(=O)O$), 2.00-2.50 (m, 6H, $CH_2C(=O)$ × 3), 2.86-3.10 (m, 2H, $NHCH_2$), 3.16-3.39 (m, 2H, $NHCH_2$), 4.19-4.49 (m, 1H, *CH), 5.03-5.17 (s, 2H, $CH_2C_6H_5$), 5.67-5.96 (m, 1H, NH), 6.44-6.80 (m, 2H, NH × 2), 7.31-7.58 (m, 5H, C_6H_5). **12**, yield 0.61 g (91 %); m.p. 108-111 ˚C; FT-IR (KBr): /cm^{-1} 3318, 2958, 2920, 2854, 1717, 1638, 1560, 1468 and 719; ^{1}H-NMR ($CDCl_3$): δ 0.76-1.00 (t, 6H, CH_3 × 2), 1.06-1.37 (m, 52H, $CH_3(CH_2)_{12}$ × 2, *$CHCH_2CH_2$, $CH_2(CH_2)_2C(=O)O$), 1.37-1.89 (m, 12H, $CH_3(CH_2)_{12}CH_2$ × 2, *$CHCH_2$, *$CH(CH_2)_2CH_2$, $CH_2CH_2CH_2CH_2C(=O)O$), 2.07-2.47 (m, 6H, $CH_2C(=O)$ × 3), 3.16-3.45 (m, 4H, $NHCH_2$ × 2), 6.43-6.59 (m, 2H, NH × 2), 6.90-7.08 (m, 1H, NH); (Found: C, 71.13; H, 11.49; N, 5.87. Calc. for $C_{44}H_{85}N_3O_5 \cdot 0.4H_2O$: C, 71.13; H, 11.63; N, 5.66 %).

***N*$^{\alpha}$,*N*$^{\varepsilon}$-Bis[3-(*N*-dodecanoyl)aminopropanoyl]-*N'*-[(2-carboxy)ethyl]-L-lysinamide** (**13**). β-Alanine benzyl ester *p*-toluenesulfonate[2a] (7.12 g, 20.2 mmol), dodecanoic acid (3.44 g, 17.0 mmol), and triethylamine (6.84 g, 67.6 mmol) were dissolved in 100 cm^3 of THF and stirred with cooling to 0˚C. DEPC (4.72 g, 26.0 mmol) was added to the solution

and stirred for 30 min in an ice bath. After being stirred for 1 day at room temperature, the solution was concentrated *in vacuo* and the residue was dissolved in 250 cm^3 of chloroform. The solution was washed with 5 wt% aqueous $NaHCO_3$ (200 cm^3, in twice), deionized water (20 cm^3, once), 0.3 N HCl (200 cm^3, in twice), and deionized water (20 cm^3, once). The solution was dried over Na_2SO_4. After filtration, the filtrate was concentrated *in vacuo* and recrystallized from methanol to give white solid *N*-dodecanoyl-β-alanine benzyl ester (**41**): yield 5.65 g (91.6 %); m.p. 76-77 ˚C; FT-IR (KBr): /cm^{-1} 3312, 2958, 2920, 2854, 1738, 1723, 1640, 1551, 1460, 1446 and 1373; ^{1}H-NMR ($CDCl_3$): δ 0.85-0.92 (t, 3H, C<u>H</u>$_3$), 1.20-1.34 (m, 16H, CH_3(C<u>H</u>$_2$)$_8$), 1.53-1.62 (m, 2H, $CH_3(CH_2)_8$C<u>H</u>$_2$), 2.09-2.14 (t, 2H, $CH_3(CH_2)_9$C<u>H</u>$_2$), 2.56-2.62 (t, 2H, C<u>H</u>$_2$C(=O)O), 3.50-3.56 (q, 2H, NHC<u>H</u>$_2$), 5.10-5.16 (s, 2H, C<u>H</u>$_2$$C_6H_5$), 5.98-6.06 (m, 1H, N<u>H</u>), 7.30-7.39 (m, 5H, C_6<u>H</u>$_5$). **41** (5.21 g, 14.4 mmol) was dissolved in 200 cm^3 of THF with heating and Pd black (1 g) was added to the solution. H_2 gas was bubbled slowly into the solution for 6 hours. After confirming the removal of benzyl group by FTIR measurement, Pd black was removed by filtration. The filtrate was concentrated and dried *in vacuo* to give white powder *N*-dodecanoyl-β-alanine (**42**): yield 3.61 g (100 %); m.p. 114-117 ˚C; FT-IR (KBr): /cm^{-1} 3304, 2958, 2920, 2854, 1696, 1638, 1551, 1448 and 717; ^{1}H-NMR ($CDCl_3$): δ 0.85-0.91 (t, 3H, C<u>H</u>$_3$), 1.20-1.35 (m, 16H, CH_3(C<u>H</u>$_2$)$_8$), 1.56-1.66 (m, 2H, $CH_3(CH_2)_8$C<u>H</u>$_2$), 2.14-2.20 (t, 2H, $CH_3(CH_2)_9$C<u>H</u>$_2$), 2.58-2.63 (t, 2H, C<u>H</u>$_2$C(=O)O), 3.50-3.56 (q, 2H, NHC<u>H</u>$_2$), 5.38 (br, 1H, O<u>H</u>), 6.07-6.15 (m, 1H, N<u>H</u>). L-Lysine benzyl ester bis(*p*-toluenesulfonate)[2a] (2.01 g, 3.64 mmol), **42** (2.18 g, 8.00 mmol), and triethylamine (1.39 g, 13.7 mmol) were dissolved in 100 cm^3 of THF and stirred with cooling to 0 ˚C. DEPC (1.61 g, 8.87 mmol) was added to the solution and stirred for 30 min in an ice bath. After being stirred for 1 day at room temperature, the solution was concentrated *in vacuo* and recrystallized from methanol to give white solid N^{α},N^{ε}-bis[3-(*N*-dodecanoyl)aminopropanoyl]-L-lysine benzyl ester (**43**): yield 2.27 g (88.3 %); m.p. 167-170 ˚C; FT-IR (KBr): /cm^{-1} 3304, 2922, 1742, 1640 and 1551; ^{1}H-NMR ($CDCl_3$): δ 0.83-0.94 (t, 6H, C<u>H</u>$_3$ × 2), 1.17-1.43 (m, 34H,

$CH_3(C\underline{H}_2)_8 \times 2$, *$CHCH_2C\underline{H}_2$), 1.43-1.88 (m, 8H, $CH_3(CH_2)_8C\underline{H}_2 \times 2$, *$CHC\underline{H}_2CH_2C\underline{H}_2$), 2.11-2.21 (m, 4H, $CH_3(CH_2)_9C\underline{H}_2 \times 2$), 2.33-2.54 (m, 4H, $NHCH_2C\underline{H}_2C(=O) \times 2$), 3.07-3.16 (m, 2H, *$CH(CH_2)_3C\underline{H}_2$), 3.40-3.60 (m, 4H, $NHC\underline{H}_2CH_2C(=O) \times 2$), 4.48-4.55 (m, 1H, *C<u>H</u>), 5.10-5.23 (q, 2H, $C\underline{H}_2C_6H_5$), 6.37-6.44 (t, 1H, N<u>H</u>), 6.69-6.76 (t, 1H, N<u>H</u>), 6.81-6.88 (t, 1H, N<u>H</u>), 6.88-6.94 (d, 1H, N<u>H</u>), 7.31-7.41 (m, 5H, $C_6\underline{H}_5$). **43** (2.05 g, 2.76 mmol) was dissolved in 200 cm^3 of THF with heating and Pd black (1 g) was added to the solution. H_2 gas was bubbled slowly into the solution for 6 hours. After confirming the removal of benzyl group by FTIR measurement, Pd black was removed by filtration. The filtrate was concentrated and dried *in vacuo* to give white solid N^{α},N^{ε}-bis[3-(*N*-dodecanoyl)aminopropanoyl]-L-lysine (**44**): yield 1.80 g (100 %); m.p. 186-188 ˚C; FT-IR (KBr): /cm^{-1} 3306, 2920, 1717, 1642 and 1555; ^{1}H-NMR ($CDCl_3$): δ 0.83-0.94 (t, 6H, $C\underline{H}_3 \times 2$), 1.19-1.40 (m, 34H, $CH_3(C\underline{H}_2)_8 \times 2$, *$CHCH_2C\underline{H}_2$), 1.46-1.95 (m, 8H, $CH_3(CH_2)_8C\underline{H}_2 \times 2$, *$CHC\underline{H}_2CH_2C\underline{H}_2$), 2.12-2.24 (m, 4H, $CH_3(CH_2)_9C\underline{H}_2 \times 2$), 2.40-2.54 (m, 4H, $NHCH_2C\underline{H}_2C(=O) \times 2$), 3.10-3.21 (m, 2H, *$CH(CH_2)_3C\underline{H}_2$), 3.34-3.64 (m, 4H, $NHC\underline{H}_2CH_2C(=O) \times 2$), 4.47-4.56 (m, 1H, *C<u>H</u>), 6.10-6.18 (m, 1H, N<u>H</u>), 6.27-6.33 (m, 1H, N<u>H</u>), 6.69-6.79 (m, 2H, N<u>H</u> × 2). **44** (0.801 g 1.23 mmol), β-alanine benzyl ester *p*-toluenesulfonate[2a] (0.649 g, 1.84 mmol), and triethylamine (0.395 g, 3.69 mmol) was dissolved in 100 cm^3 of THF and stirred with cooling to 0 ˚C. DEPC (0.490 g, 2.46 mmol) was added to the mixture and stirred for 30 min in an ice bath. After being stirred for 1 day at room temperature, the solution was concentrated *in vacuo* and the residue was recrystallized from methanol to give white solid N^{α},N^{ε}-bis[3-(*N*-dodecanoyl)aminopropanoyl]-*N'*-[3-(benzyloxycarbonyl)ethyl]-L-lysinamide (**45**): yield 0.756 g (76 %); m.p. 176-185 ˚C; FT-IR (KBr): /cm^{-1} 3306, 2920, 1740, 1640 and 1557; ^{1}H-NMR ($CDCl_3$): δ 0.83-0.92 (t, 6H, $C\underline{H}_3 \times 2$), 1.19-1.42 (m, 34H, $CH_3(C\underline{H}_2)_8 \times 2$, *$CHCH_2C\underline{H}_2$), 1.42-1.84 (m, 8H, $CH_3(CH_2)_8C\underline{H}_2 \times 2$, *$CHC\underline{H}_2CH_2C\underline{H}_2$), 2.12-2.21 (t, 4H, $CH_3(CH_2)_9C\underline{H}_2 \times 2$), 2.38-2.65 (m, 6H, $NHCH_2C\underline{H}_2C(=O) \times 3$), 3.07-3.22 (m, 2H, *$CH(CH_2)_3C\underline{H}_2$), 3.43-3.61 (m, 6H, $NHC\underline{H}_2CH_2C(=O) \times 3$), 4.20-4.29 (m, 1H, *C<u>H</u>), 5.10-

5.16 (s, 2H, C$\underline{H}_2$C$_6$H$_5$), 6.45-6.50 (m, 1H, N$\underline{H}$), 6.67-6.73 (m, 1H, N$\underline{H}$), 6.79-6.89 (m, 2H, N$\underline{H}$ × 2), 6.97-7.03 (m, 1H, N$\underline{H}$), 7.28-7.42 (m, 5H, C$_6\underline{H}_5$). **45** (0.446 g, 0.548 mmol) was dissolved in 200 cm^3 of THF with heating and Pd black (1 g) was added to the solution. H_2 gas was bubbled slowly into the solution for 6 hours. After confirming the removal of benzyl group by FTIR measurement, Pd black was removed by filtration. The filtrate was concentrated *in vacuo* and the residue was recrystallized from methanol to give white solid N^{α},N^{ε}-bis[3-(*N*-dodecanoyl)aminopropanoyl]-*N'*-[(2-carboxy)ethyl]-L-lysinamide (**13**): yield 0.361 g (81 %); m.p. 182-186 ˚C; FT-IR (KBr): /cm^{-1} 3304, 2958, 1719, 1640 and 1555; ^{1}H-NMR (CDCl$_3$): δ 0.79-0.93 (t, 6H, C$\underline{H}_3$ × 2), 1.16-1.41 (m, 34H, CH$_3$(C$\underline{H}_2$)$_8$ × 2, *CHCH$_2$C$\underline{H}_2$), 1.46-1.66 (m, 8H, CH$_3$(CH$_2$)$_8$C$\underline{H}_2$ × 2, *CHC$\underline{H}_2$CH$_2$C$\underline{H}_2$), 2.08-2.30 (m, 4H, CH$_3$(CH$_2$)$_9$C$\underline{H}_2$ × 2), 2.39-2.70 (m, 6H, NHCH$_2$C$\underline{H}_2$C(=O) × 3), 3.23-3.30 (q, 2H, *CH(CH$_2$)$_3$C$\underline{H}_2$), 3.35-3.62 (m, 6H, NHC$\underline{H}_2$CH$_2$C(=O) × 3), 4.46-4.56 (m, 1H, *C$\underline{H}$), 6.16-6.26 (m, 1H, N$\underline{H}$), 6.45-6.59 (m, 1H, N$\underline{H}$), 6.64-6.73 (m, 1H, N$\underline{H}$), 6.73-6.83 (m, 1H, N$\underline{H}$), 6.83-6.91 (m, 1H, N$\underline{H}$); (Found: C, 64.60; H, 10.12; N, 9.21. Calc. for $C_{39}H_{73}N_5O_7$: C, 64.60; H, 10.16; N, 9.66 %).

N^{α},N^{ε}-bis[3-(*N*-decanoyl)aminopropanoyl]-*N'*-[(2-carboxy)ethyl]-L-lysinamide (**14**). The compound **14** related to **13** was prepared as described above using decanoic acid instead of dodecanioc acid. *N*-Decanoyl-β-alanine benzyl ester (**46**): yield 2.45 g (79.2 %); m.p. 65-66 ˚C; FT-IR (KBr): /cm^{-1} 3310, 2920, 2854, 1738, 1723, 1640 and 1551; ^{1}H-NMR (CDCl$_3$): δ 0.84-0.92 (t, 3H, C$\underline{H}_3$), 1.18-1.35 (m, 12H, CH$_3$(C$\underline{H}_2$)$_6$), 1.49-1.63 (m, 2H, CH$_3$(CH$_2$)$_6$C$\underline{H}_2$), 2.07-2.16 (t, 2H, CH$_3$(CH$_2$)$_7$C$\underline{H}_2$), 2.55-2.63 (t, 2H, C$\underline{H}_2$C(=O)O), 3.47-3.56 (q, 2H, NHC$\underline{H}_2$), 5.09-5.19 (s, 2H, C$\underline{H}_2$C$_6$H$_5$), 5.97-6.07 (s, 1H, N$\underline{H}$), 7.28-7.42 (m, 5H, C$_6\underline{H}_5$). *N*-decanoyl-β-alanine (**47**): yield 1.46 g (99.0 %); m.p. 105-108 ˚C; FT-IR (KBr): /cm^{-1} 3302, 3066, 2958, 2920, 2854, 1694, 1638 and 1547; ^{1}H-NMR (CDCl$_3$): δ 0.83-0.94 (t, 3H, C$\underline{H}_3$), 1.18-1.33 (m, 12H, CH$_3$(C$\underline{H}_2$)$_6$), 1.56-1.68 (m, 2H, CH$_3$(CH$_2$)$_6$C$\underline{H}_2$), 2.14-2.23 (t, 2H, CH$_3$(CH$_2$)$_7$C$\underline{H}_2$), 2.54-2.64 (t, 2H, C$\underline{H}_2$C(=O)O), 3.49-3.58 (q, 2H, NHC$\underline{H}_2$), 6.24-6.33 (s, 1H, N$\underline{H}$), 8.00 (br, 1H, O$\underline{H}$). N^{α},N^{ε}-bis[3-(*N*-

decanoyl)aminopropanoyl]-L-lysine benzyl ester (**48**): yield 0.716 g (46.3 %); m.p. 158-159 ˚C; FT-IR (KBr): /cm^{-1} 3304, 3082, 2958, 2924, 2854, 1744, 1640 and 1553; ^{1}H-NMR ($CDCl_3$): δ 0.83-0.93 (t, 6H, $CH_3 \times 2$), 1.19-1.39 (m, 26H, $CH_3(CH_2)_6 \times 2$, *$CHCH_2CH_2$), 1.39-1.88 (m, 8H, $CH_3(CH_2)_6CH_2 \times 2$, *$CHCH_2CH_2CH_2$), 2.10-2.22 (m, 4H, $CH_3(CH_2)_7CH_2 \times 2$), 2.39-2.54 (m, 4H, $NHCH_2CH_2C(=O) \times 2$), 3.07-3.39 (m, 2H, *$CH(CH_2)_3CH_2$), 3.39-3.60 (m, 4H, $NHCH_2CH_2C(=O) \times 2$), 4.48-4.56 (m, 1H, *CH), 5.09-5.22 (q, 2H, $CH_2C_6H_5$), 6.49-6.55 (t, 1H, NH), 6.75-6.83 (t, 1H, NH), 6.91-6.95 (t, 1H, NH), 6.95-7.01 (d, 1H, NH), 7.30-7.40 (m, 5H, C_6H_5). $N^{\alpha},N^{\varepsilon}$-bis[3-(*N*-decanoyl)aminopropanoyl]-L-lysine (**49**): yield 0.538 g (100 %); m.p. 176-178 ˚C; FT-IR (KBr): /cm^{-1} 3302, 3084, 2958, 2924, 2856, 1731, 1642 and 1551. $N^{\alpha},N^{\varepsilon}$-Bis[3-(*N*-decanoyl)aminopropanoyl]-*N'*-[2-(benzyloxycarbonyl)ethyl]-L-lysinamide (**50**): yield 0.420 g (57.1 %); m.p. 148-152 ˚C; FT-IR (KBr): /cm^{-1} 3308, 3298, 3082, 2958, 2924, 2856, 1738, 1642 and 1553; ^{1}H-NMR ($CDCl_3$): δ 0.81-0.90 (t, 6H, $CH_3 \times 2$), 1.16-1.38 (m, 26H, $CH_3(CH_2)_6 \times 2$, *$CHCH_2CH_2$), 1.46-1.65 (m, 8H, $CH_3(CH_2)_6CH_2 \times 2$, *$CHCH_2CH_2CH_2$), 2.13-2.22 (t, 4H, $CH_3(CH_2)_7CH_2 \times 2$), 2.40-2.55 (m, 4H, $NHCH_2CH_2C(=O) \times 2$), 2.59-2.79 (m, 2H, $NHCH_2CH_2C(=O)$), 3.05-3.13 (q, 2H, *$CH(CH_2)_3CH_2$), 3.40-3.58 (m, 6H, $NHCH_2CH_2C(=O) \times 3$), 5.10-5.16 (s, 2H, $CH_2C_6H_5$), 7.28-7.39 (m, 5H, C_6H_5). **14**, yield 0.175 g (53.7 %); m.p. 160-162 ˚C; FT-IR (KBr): /cm^{-1} 3304, 3086, 2958, 2924, 2856, 1719, 1640 and 1557; ^{1}H-NMR ($CDCl_3$): δ 0.80-0.93 (t, 6H, $CH_3 \times 2$), 1.15-1.69 (m, 34H, $CH_3(CH_2)_7 \times 2$, *$CH(CH_2)_3$), 2.11-2.24 (m, 4H, $CH_3(CH_2)_7CH_2 \times 2$), 2.36-2.62 (m, 6H, $NHCH_2CH_2C(=O) \times 3$), 3.04-3.12 (q, 2H, *$CH(CH_2)_3CH_2$), 3.41-3.63 (m, 6H, $NHCH_2CH_2C(=O) \times 3$), 4.45-4.53 (m, 1H, *CH), 6.24-6.34 (m, 1H, NH), 6.49-6.67 (m, 1H, NH), 6.71-6.92 (m, 1H, NH), 6.92-7.09 (m, 1H, NH), 7.13-7.24 (m, 1H, NH); (Found: C, 62.50; H, 9.87; N, 9.50. Calc. for $C_{35}H_{65}N_5O_7 \cdot 0.3H_2O$: C, 62.50; H, 9.82; N, 10.41 %).

***N*$^{\alpha}$,*N*$^{\varepsilon}$-bis[3-(*N*-octanoyl)aminopropanoyl]-*N'*-[(2-carboxy)ethyl]-L-lysinamide** (**15**). The compound **15** related to **13** was prepared as described above using octanoic acid

instead of dodecanioc acid. *N*-octanoyl-β-alanine benzyl ester (**51**): yield 18.36 g (86.7 %); m.p. 56-57 ˚C; FT-IR (KBr): /cm^{-1} 3310, 2958, 2932, 2920, 2874, 2856, 1738, 1723, 1640, 1551, 1195, 737 and 698; ^{1}H-NMR ($CDCl_3$): δ 0.78-0.99 (t, 3H, $C\underline{H}_3$), 1.14-1.41 (m, 8H, $CH_3(C\underline{H}_2)_4$), 1.49-1.69 (m, 2H, $CH_3(CH_2)_4C\underline{H}_2$), 2.04-2.19 (t, 2H, $CH_3(CH_2)_4C\underline{H}_2$), 2.52-2.66 (t, 2H, $C\underline{H}_2C(=O)O$), 3.44-3.60 (m, 2H, $NHC\underline{H}_2$), 5.06-5.22 (s, 2H, $C\underline{H}_2C_6H_5$), 5.92-6.16 (s, 1H, N$\underline{H}$), 7.27-7.47 (m, 5H, $C_6\underline{H}_5$). *N*-octanoyl-β-alanine (**52**): yield 9.27 g (91.4 %); m.p. 102-103 ˚C; FT-IR (KBr): /cm^{-1} 3302, 2958, 2924, 2874, 2856, 1696, 1640, 1547, 1466, 1441, 928 and 723; ^{1}H-NMR ($CDCl_3$): δ 0.78-0.98 (t, 3H, $C\underline{H}_3$), 1.15-1.42 (m, 8H, $CH_3(C\underline{H}_2)_4$), 1.51-1.72 (m, 2H, $CH_3(CH_2)_4C\underline{H}_2$), 2.10-2.26 (t, 2H, $CH_3(CH_2)_4C\underline{H}_2$), 2.50-2.68 (t, 2H, $C\underline{H}_2C(=O)O$), 3.44-3.61 (m, 2H, $NHC\underline{H}_2$), 6.34-6.54 (m, 1H, N$\underline{H}$), 9.94 (br, 1H, O$\underline{H}$). $N^{\alpha},N^{\varepsilon}$-bis[3-(*N*-octanoyl)aminopropanoyl]-L-lysine benzyl ester (**53**): yield 6.10 g (80.3 %); m.p. 157-159 ˚C; FT-IR (KBr): /cm^{-1} 3302, 2958, 2926, 2856, 1742, 1640, 1549, 1460 and 698; ^{1}H-NMR ($CDCl_3$): δ 0.74-0.99 (m, 6H, $C\underline{H}_3 \times 2$), 1.13-1.42 (m, 18H, $CH_3(C\underline{H}_2)_4 \times 2$, $*CHCH_2C\underline{H}_2$), 1.42-1.52 (m, 2H, $*CH(CH_2)_2C\underline{H}_2$), 1.52-1.68 (m, 4H, $CH_3(CH_2)_4C\underline{H}_2 \times 2$), 1.68-1.92 (m, 2H, $*CHC\underline{H}_2$), 2.07-2.31 (m, 4H, $CH_3(CH_2)_5C\underline{H}_2 \times 2$), 2.35-2.61 (m, 4H, $NHCH_2C\underline{H}_2C(=O) \times 2$), 3.03-3.18 (m, 2H, $*CH(CH_2)_3C\underline{H}_2$), 3.40-3.63 (m, 4H, $NHC\underline{H}_2CH_2C(=O) \times 2$), 4.43-4.59 (m, 1H, $*C\underline{H}$), 5.07-5.27 (m, 2H, $C\underline{H}_2C_6H_5$), 6.56-6.69 (t, 1H, N$\underline{H}$), 6.78-6.89 (t, 1H, N$\underline{H}$), 6.89-7.00 (t, 1H, N$\underline{H}$), 7.00-7.12 (d, 1H, N$\underline{H}$), 7.28-7.46 (m, 5H, $C_6\underline{H}_5$). $N^{\alpha},N^{\varepsilon}$-bis[3-(*N*-octanoyl)aminopropanoyl]-L-lysine (**54**): yield 4.35 g (89.7 %); m.p. 167-169 ˚C; FT-IR (KBr): /cm^{-1} 3306, 2958, 2928, 2856, 1717, 1642, 1557, 1458, 1379 and 721; ^{1}H-NMR ($CDCl_3$): δ 0.81-0.97 (t, 6H, $C\underline{H}_3 \times 2$), 1.18-1.39 (m, 18H, $CH_3(C\underline{H}_2)_4 \times 2$, $*CHCH_2C\underline{H}_2$), 1.39-1.90 (m, 8H, $*CHC\underline{H}_2CH_2C\underline{H}_2$, $CH_3(CH_2)_4C\underline{H}_2 \times 2$), 2.07-2.24 (m, 4H, $CH_3(CH_2)_5C\underline{H}_2 \times 2$), 2.37-2.56 (m, 4H, $NHCH_2C\underline{H}_2C(=O) \times 2$), 2.86-2.98 (m, 2H, $*CH(CH_2)_3C\underline{H}_2$), 3.40-3.61 (m, 4H, $NHC\underline{H}_2CH_2C(=O) \times 2$), 4.09-4.23 (m, 1H, $*C\underline{H}$), 5.95-6.17 (m, 1H, N$\underline{H}$), 6.56-6.69 (m, 1H, N$\underline{H}$), 6.69-6.90 (m, 1H, N$\underline{H}$), 6.90-7.03 (m, 1H, N$\underline{H}$). $N^{\alpha},N^{\varepsilon}$-bis[3-(*N*-octanoyl)aminopropanoyl]-*N'*-[2-(benzyloxycarbonyl)ethyl]-L-lysinamide (**55**): yield 2.37 g (79.3 %); m.p. 176-180 ˚C; FT-

IR (KBr): /cm^{-1} 3302, 2958, 2926, 2856, 1740, 1638, 1555, 1458, 1381 and 698; ^{1}H-NMR ($CDCl_3$) δ 0.77-0.96 (t, 6H, C<u>H</u>$_3$ × 2), 1.15-1.41 (m, 18H, $CH_3(C\underline{H}_2)_4$ × 2, *$CHCH_2C\underline{H}_2$), 1.41-1.53 (m, 2H, *$CH(CH_2)_2C\underline{H}_2$), 1.53-1.71 (m, 4H, $CH_3(CH_2)_4C\underline{H}_2$ × 2), 1.71-1.88 (m, 2H, *$CHC\underline{H}_2$), 2.09-2.28 (t, 4H, $CH_3(CH_2)_5C\underline{H}_2$ × 2), 2.37-2.53 (m, 4H, $NHCH_2C\underline{H}_2C(=O)NH$ × 2), 2.53-2.66 (t, 2H, $C\underline{H}_2C(=O)O$), 3.10-3.23 (m, 2H, *$CH(CH_2)_3C\underline{H}_2$), 3.39-3.67 (m, 6H, $NHC\underline{H}_2CH_2C(=O)$ × 3), 4.20-4.30 (m, 1H, *C<u>H</u>), 5.11-5.20 (s, 2H, $C\underline{H}_2C_6H_5$), 6.34-6.47 (m, 1H, N<u>H</u>), 6.61-6.72 (m, 1H, N<u>H</u>), 6.72-6.87 (m, 2H, N<u>H</u> × 2), 6.87-7.00 (m, 1H, N<u>H</u>), 7.29-7.46 (m, 5H, $C_6\underline{H}_5$). **15**, yield 1.28 g (67.4 %); m.p. 171-173 ˚C; FT-IR (KBr): /cm^{-1} 3306, 2958, 2928, 2856, 1716, 1638, 1557, 1468, 1456, 1381 and 719; ^{1}H-NMR ($CDCl_3$): δ 0.76-0.98 (m, 6H, C<u>H</u>$_3$ × 2), 1.06-1.47 (m, 20H, $CH_3(C\underline{H}_2)_4$ × 2, *$CHCH_2(C\underline{H}_2)_2$), 1.49-1.70 (m, 4H, $CH_3(CH_2)_4C\underline{H}_2$ × 2), 1.70-1.93 (m, 2H, *$CHC\underline{H}_2$), 2.07-2.30 (m, 4H, $CH_3(CH_2)_5C\underline{H}_2$ × 2), 2.34-2.57 (m, 4H, $NHCH_2C\underline{H}_2C(=O)NH$ × 2), 2.57-2.76 (m, 2H, $C\underline{H}_2C(=O)O$), 2.76-2.91 (m, 2H, *$CH(CH_2)_3C\underline{H}_2$), 3.42-3.69 (m, 6H, $NHC\underline{H}_2CH_2C(=O)$ × 3), 4.19-4.32 (m, 1H, *C<u>H</u>), 6.67-6.88 (m, 2H, N<u>H</u> × 2), 6.88-7.00 (m, 1H, N<u>H</u>), 7.69-8.12 (m, 1H, N<u>H</u>), 8.12-8.27 (m, 1H, N<u>H</u>); (Found: C, 57.37; H, 9.47; N, 11.13. Calc. for $C_{31}H_{57}N_5O_7 \cdot 2.1H_2O$: C, 57.37; H, 9.49; N, 10.79 %).

***N*$^{\alpha}$,*N*$^{\varepsilon}$-Didodecanoyl-*N*-(2-carboxy)ethyl-L-lysinamide** (**16**). L-Lysine benzyl ester bis(*p*-toluenesulfonate)[2a] (3.00 g, 5.17 mmol) and triethylamine (2.99 g, 15.6 mmol) was dissolved in 100 cm^3 of THF and stirred with cooling to 0 ˚C. A 20 cm^3 portion of THF containing dodecanoyl chloride (2.49 g, 11.4 mmol) was added dropwise to the solution and stirred in an ice bath for 30 min. After being stirred for 1 day at room temperature, the solution was concentrated *in vacuo* and the residue was dissolved in 250 cm^3 of chloroform. The solution was washed with 5 wt% aqueous $NaHCO_3$ (200 cm^3, in twice), deionized water (20 cm^3, once), 0.3 N HCl (200 cm^3, in twice), and deionized water (20 cm^3, once). The solution was dried over Na_2SO_4. After filtration, the filtrate was concentrated *in vacuo* and recrystallized from methanol to give white solid *N*$^{\alpha}$,*N*$^{\varepsilon}$-didodecanoyl-L-lysine benzyl ester (**56**): yield 2.50 g (80.6 %); m.p. 101-105 ˚C; FT-IR

(KBr): /cm^{-1} 3322, 2958, 2924, 2854, 1723, 1642, 1545 and 1468; ^{1}H-NMR ($CDCl_3$): δ 0.80-1.00 (t, 6H, C$\underline{H}_3$ × 2), 1.17-1.43 (m, 34H, $CH_3(C\underline{H}_2)_8$ × 2, *$CHCH_2C\underline{H}_2$), 1.43-1.55 (m, 2H, *$CH(CH_2)_2C\underline{H}_2$), 1.55-1.78 (m, 4H, $CH_3(CH_2)_8C\underline{H}_2$ × 2), 1.78-1.92 (m, 2H, *$CHC\underline{H}_2$), 2.09-2.32 (m, 4H, $C\underline{H}_2C(=O)$ × 2), 3.12-3.28 (m, 2H, $NHC\underline{H}_2$), 4.56-4.71 (m, 1H, *C$\underline{H}$), 5.09-5.26 (m, 2H, $C\underline{H}_2C_6H_5$), 5.62-5.76 (m, 1H, N$\underline{H}$), 6.17-6.30 (d, 1H, N$\underline{H}$), 7.28-7.47 (m, 5H, $C_6\underline{H}_5$). **56** (2.29 g, 3.81 mmol) was dissolved in 200 cm^3 of THF with heating and Pd black (1 g) was added to the solution. H_2 gas was bubbled slowly into the solution for 7 hours. After confirming the removal of benzyl group by FTIR measurement, Pd black was removed by filtration. The filtrate was concentrated *in vacuo* and the residue was recrystallized from methanol to give white solid $N^{\alpha},N^{\varepsilon}$-didodecanoyl-L-lysine (**57**): yield 1.75 g (89.7 %); m.p. 118-122 ˚C; FT-IR (KBr): /cm^{-1} 3310, 2958, 2920, 2854, 1715, 1647, 1557, 1470 and 719; ^{1}H-NMR ($CDCl_3$) δ 0.79-0.95 (t, 6H, C$\underline{H}_3$ × 2), 1.16-1.44 (m, 34H, $CH_3(C\underline{H}_2)_8$ × 2, *$CHCH_2C\underline{H}_2$), 1.47-1.69 (m, 6H, $CH_3(CH_2)_8C\underline{H}_2$ × 2, *$CH(CH_2)_2C\underline{H}_2$), 1.72-1.97 (m, 2H, *$CHC\underline{H}_2$), 2.13-2.31 (m, 4H, $C\underline{H}_2C(=O)$ × 2), 3.11-3.42 (m, 2H, $NHC\underline{H}_2$), 4.50-4.60 (m, 1H, *C$\underline{H}$), 6.04-6.16 (t, 1H, N$\underline{H}$), 6.76-6.85 (d, 1H, N$\underline{H}$), 7.95 (br, 1H, O$\underline{H}$). **57** (1.00 g, 1.96 mmol), β-alanine benzyl ester *p*-toluenesulfonate[2a] (1.03 g, 2.94 mmol), and triethylamine (0.816 g, 8.06 mmol) was dissolved in 100 cm^3 of THF and stirred with cooling to 0 ˚C. DEPC (0.546 g, 3.35 mmol) was added to the mixture and stirred in an ice bath for 30 min. After being stirred for 1 day at room temperature, the solution was concentrated *in vacuo* and the residue was dissolved in 250 cm^3 of chloroform. The solution was washed with 5 wt% aqueous $NaHCO_3$ (200 cm^3, in twice), deionized water (20 cm^3, once), 0.3 N HCl (200 cm^3, in twice), and deionized water (20 cm^3, once). The solution was dried over Na_2SO_4. After filtration, the filtrate was concentrated *in vacuo* and recrystallized from methanol to give white solid $N^{\alpha},N^{\varepsilon}$-didodecanoyl-*N*-[2-(benzyloxycarbonyl)ethyl]-L-lysinamide (**58**): yield 1.18 g (89.4 %); m.p. 119-127 ˚C; FT-IR (KBr): /cm^{-1} 3318, 2958, 2920, 2852, 1740, 1642, 1557, 1470, 1458, 1390, 719 and 698; ^{1}H-NMR ($CDCl_3$): δ 0.82-0.96 (t, 6H, C$\underline{H}_3$ × 2), 1.12-1.40

(m, 34H, $CH_3(C\underline{H}_2)_8 \times 2$, *$CHCH_2C\underline{H}_2$), 1.43-1.53 (m, 2H, *$CH(CH_2)_2C\underline{H}_2$), 1.53-1.70 (m, 4H, $CH_3(CH_2)_8C\underline{H}_2 \times 2$), 1.74-1.87 (m, 2H, *$CHC\underline{H}_2$), 2.10-2.39 (m, 4H, $CH_3(CH_2)_9C\underline{H}_2 \times 2$), 2.52-2.66 (t, 2H, $C\underline{H}_2C(=O)O$), 3.11-3.31 (m, 2H, *$CH(CH_2)_3C\underline{H}_2$), 3.42-3.63 (m, 2H, $C\underline{H}_2CH_2C(=O)O$), 4.29-4.40 (m 1H *C<u>H</u>), 5.08-5.23 (s, 2H, $C\underline{H}_2C_6H_5$), 5.83-5.97 (t, 1H, N<u>H</u>), 6.43-6.55 (d, 1H, N<u>H</u>), 6.88-7.00 (t, 1H, N<u>H</u>), 7.29-7.49 (m, 5H, $C_6\underline{H}_5$). **58** (1.06 g, 1.58 mmol) was dissolved in 200 cm^3 of THF with heating and Pd black (1 g) was added to the solution. H_2 gas was bubbled slowly into the solution for 6 hours. After confirming the removal of benzyl group by FTIR measurement, Pd black was removed by filtration. The filtrate was concentrated *in vacuo* and the residue was recrystallized from methanol to give white solid (**16**): yield 0.740 g (80.6 %); m.p. 131-134 ˚C; FT-IR (KBr): /cm^{-1} 3316, 2958, 2820, 2854, 1717, 1644, 1560, 1470 and 719; ^{1}H-NMR ($CDCl_3$): δ 0.76-0.97 (t, 6H, $C\underline{H}_3 \times 2$), 1.07-1.41 (m, 34H, $CH_3(C\underline{H}_2)_8 \times 2$, *$CHCH_2C\underline{H}_2$), 1.46-1.53 (m, 2H, *$CH(CH_2)_2C\underline{H}_2$), 1.53-1.69 (m, 4H, $CH_3(CH_2)_8C\underline{H}_2 \times 2$), 1.69-1.88 (m, 2H, *$CHC\underline{H}_2$), 2.09-2.30 (m, 4H, $CH_3(CH_2)_9C\underline{H}_2 \times 2$), 2.47-2.69 (m, 2H, $C\underline{H}_2C(=O)O$), 3.01-3.33 (m, 2H, *$CH(CH_2)_3C\underline{H}_2$), 3.37-3.71 (m, 2H, $C\underline{H}_2CH_2C(=O)O$), 4.45-4.62 (m, 1H, *C<u>H</u>), 6.01-6.32 (m, 1H, N<u>H</u>), 6.70-6.94 (m, 1H, N<u>H</u>), 7.31-7.55 (m, 1H, N<u>H</u>); (Found: C, 65.45; H, 10.43; N, 7.06. Calc. for $C_{33}H_{63}N_3O_5 \cdot 1.3H_2O$: C, 65.45; H, 10.92; N, 6.94 %).

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