Electronic Supplementary Informations

Formation of specific dipolar microenvironments complementary to dipolar betaine dye by nonionic peptide lipids in nonpolar medium

Preparation of peptide lipids

***N',N"*-Didodecyl-N^{α}-[(*N'''*-benzyloxycarbonyl)glycynoyl]-L-glutamide (1).** *N',N"*-Didodecyl-L-glutamide[1] (1.64 g, 3.40 mmol), Gly-Z (0.853 g, 4.08 mmol), and triethylamine (0.827 g, 8.17 mmol) were dissolved in 100 cm^3 of tetrahydrofuran (THF) and stirred with cooling to 0 ˚C. To the solution was added diethylphosphoryl cyanidate (DEPC) (0.605 g, 5.10 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 0.3 N HCl (200 cm^3, in twice), deionized water (20 cm^3, once), 5 wt% aqueous $NaHCO_3$ (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 (**1**): yield 1.59 g (67.7 %); m.p. 147 ˚C; FT-IR (KBr): /cm^{-1} 3291, 2921, 2851, 1697, 1643 and 1556; ^{1}H-NMR ($CDCl_3$): δ 0.85-0.90 (t, 6H, CH_3 × 2), 1.14-1.37 (m, 36H, $CH_3(CH_2)_9$ × 2), 1.38-1.48 (m, 4H, $CH_3(CH_2)_9CH_2$ × 2), 1.92-2.12 (m, 2H, *$CHCH_2$), 2.29-2.32 (m, 2H, *$CHCH_2CH_2$), 3.15-3.20 (m, 4H, $CH_3(CH_2)_{10}CH_2$ × 2), 3.85-3.93 (m, 2H, $C(=O)CH_2NH$), 4.36-4.42 (m, 1H, *CH), 5.18-5.14 (s, 2H, $CH_2C_6H_5$), 5.79-5.89 (t, 1H, NH), 6.25-6.34 (t, 1H, NH), 6.73-7.14 (t, 1H, NH), 7.29-7.34 (s, 5H, C_6H_5), 7.74-7.82 (d, 1H, NH); (Found: C, 67.80; H, 10.08; N, 7.93. Calc. for $C_{39}H_{68}N_4O_5 \cdot 1.0H_2O$: C, 67.80; H, 10.21; N, 8.11 %). The related compounds were synthesized as described above using L-Ala-Z for **2**, L-Val-Z for **3**, L-Leu-Z for **4**, L-Ile-Z for **5**, L-Phe-Z for **6**, and Sar-Z for **7** instead of Gly-Z, respectively: *N',N"*-Didodecyl-N^{α}-[(*N'''*-benzyloxycarbonyl)-L-alanoyl]-L-glutamide (**2**), yield 0.687 g (61.0 %); m.p. 164-168 ˚C; FT-IR (KBr): /cm^{-1} 3287, 2917, 2850, 1699, 1639

and 1534; ^{1}H-NMR ($CDCl_3$): δ 0.77-0.96 (t, 6H, C<u>H</u>$_3$ × 2), 1.11-1.36 (m, 36H, $CH_3(C\underline{H}_2)_9$ × 2), 1.36-1.41 (d, 3H, *CHC<u>H</u>$_3$), 1.46-1.58 (m, 4H, $CH_3(CH_2)_9C\underline{H}_2$ × 2), 1.93-2.16 (m, 2H, *CHC<u>H</u>$_2$), 2.18-2.40 (m, 2H, *$CHCH_2C\underline{H}_2$), 3.04-3.30 (m, 4H, C<u>H</u>$_2$NH × 2), 4.14-4.27 (m, 1H, *C<u>H</u>), 4.32-4.43 (m, 1H, *C<u>H</u>), 5.02-5.19 (m, 2H, C<u>H</u>$_2$C$_6$H$_5$), 5.58-5.66 (d, 1H, N<u>H</u>), 6.13-6.27 (t, 1H, N<u>H</u>), 6.94-7.07 (t, 1H, N<u>H</u>), 7.28-7.39 (s, 5H, C$_6$<u>H</u>$_5$), 7.82-7.94 (d, 1H, N<u>H</u>); (Found: C, 69.16; H, 10.44; N, 8.03. Calc. for $C_{40}H_{70}N_4O_5\cdot0.4H_2O$: C, 69.16; H, 10.28; N, 8.07 %). *N',N''*-Didodecyl-N^{α}-[(*N'''*-benzyloxycarbonyl)-L-valinoyl]-L-glutamide (**3**), yield 0.720 g (61.7 %); m.p. 201-203 ˚C; FT-IR (KBr): /cm^{-1} 3290, 2922, 2852, 1692, 1638 and 1543; ^{1}H-NMR ($CDCl_3$): δ 0.75-1.02 (m, 12H, C<u>H</u>$_3$ × 4), 1.02-1.39 (m, 36H, $CH_3(C\underline{H}_2)_9$ × 2), 1.39-1.59 (m, 4H, $CH_3(CH_2)_9C\underline{H}_2$ × 2), 1.60-1.84 (m, 1H, *CHC<u>H</u>), 1.93-2.16 (m, 2H, *CHC<u>H</u>$_2$), 2.23-2.40 (m, 2H, *$CHCH_2C\underline{H}_2$), 3.04-3.30 (m, 4H, C<u>H</u>$_2$NH × 2), 3.82-4.00 (t, 1H, *C<u>H</u>), 4.32-4.43 (m, 1H, *C<u>H</u>), 5.02-5.19 (s, 2H, C<u>H</u>$_2$C$_6$H$_5$), 5.58-5.66 (d, 1H, N<u>H</u>), 6.13-6.27 (t, 1H, N<u>H</u>), 6.94-7.07 (t, 1H, N<u>H</u>), 7.28-7.39 (s, 5H, C$_6$<u>H</u>$_5$), 7.82-7.93 (d, 1H, N<u>H</u>); (Found: C, 70.16; H, 10.66; N, 7.85. Calc. for $C_{42}H_{74}N_4O_5\cdot0.2H_2O$: C, 70.16; H, 10.44; N, 7.79 %). *N',N''*-Didodecyl-N^{α}-[(*N'''*-benzyloxycarbonyl)-L-leucinoyl]-L-glutamide (**4**), yield 0.452 g (90.4 %); m.p. 202-205 ˚C; FT-IR (KBr): /cm^{-1} 3293, 2923, 2852, 1693, 1638 and 1542; ^{1}H-NMR ($CDCl_3$): δ 0.76-1.01 (t, 6H, C<u>H</u>$_3$ × 4), 1.07-1.38 (m, 37H, $CH_3(C\underline{H}_2)_9$ × 2, C<u>H</u>$(CH_3)_2$), 1.39-1.57 (m, 4H, $CH_3(CH_2)_9C\underline{H}_2$ × 2), 1.58-1.81 (m, 2H, C<u>H</u>$_2$CH), 1.91-2.17 (m, 2H, *$CHC\underline{H}_2CH_2$), 2.17-2.40 (m, 2H, *$CHCH_2C\underline{H}_2$), 2.99-3.30 (m, 4H, C<u>H</u>$_2$NH × 2), 4.09-4.22 (m, 1H, *C<u>H</u>), 4.29-4.42 (m, 1H, *C<u>H</u>), 5.01-5.18 (s, 2H, C<u>H</u>$_2$C$_6$H$_5$), 5.41-5.54 (d, 1H, N<u>H</u>), 6.10-6.24 (t, 1H, N<u>H</u>), 6.90-7.07 (t, 1H, N<u>H</u>), 7.28-7.42 (s, 5H, C$_6$<u>H</u>$_5$), 7.68-7.87 (d, 1H, N<u>H</u>); (Found: C, 69.29; H, 10.70; N, 7.79. Calc. for $C_{43}H_{76}N_4O_5\cdot3.8H_2O$: C, 64.72; H, 10.57; N, 7.02 %). *N',N''*-Didodecyl-N^{α}-[(*N'''*-benzyloxycarbonyl)-L-isoleucinoyl]-L-glutamide (**5**), yield 0.33 g (66 %); m.p. 202-205 ˚C; FT-IR (KBr): /cm^{-1} 3327, 2921, 2850, 1692, 1637 and 1533; ^{1}H-NMR ($CDCl_3$): δ 0.77-0.99 (t, 12H, C<u>H</u>$_3$ × 4), 1.10-1.40 (m, 38H, $CH_3(C\underline{H}_2)_9$ × 2, CHC<u>H</u>$_2$), 1.40-1.61 (m, 4H, $CH_3(CH_2)_9C\underline{H}_2$ × 2), 1.64-1.79 (m, 1H, *CHC<u>H</u>), 1.91-2.11

(m, 2H, *CHC$\underline{H}_2$), 2.14-2.41 (m, 2H, *CHCH$_2$C$\underline{H}_2$), 2.94-3.30 (m, 4H, C$\underline{H}_2$NH × 2), 3.93-4.07 (m, 1H, *C$\underline{H}$), 4.26-4.48 (m, 1H, *C$\underline{H}$), 4.98-5.14 (s, 2H, C$\underline{H}_2$C$_6$H$_5$), 5.33-5.48 (m, 1H, N$\underline{H}$), 5.90-6.04 (m, 1H, N$\underline{H}$), 6.68-6.78 (m, 1H, N$\underline{H}$), 7.27-7.39 (m, 5H, C$_6\underline{H}_5$), 7.72-7.87 (m, 1H, N$\underline{H}$); (Found: C, 69.71; H, 10.79; N, 7.59. Calc. for $C_{43}H_{76}N_4O_5 \cdot 0.7H_2O$: C, 69.71; H, 10.52; N, 7.56 %). *N',N''*-Didodecyl-*N*$^{\alpha}$-[(*N'''*-benzyloxycarbonyl)-L-phenylalanoyl]-L-glutamide (**6**), yield 0.177 g (88.5 %); m.p. 168-172 ˚C; FT-IR (KBr): /cm^{-1} 3292, 2921, 2851, 1694, 1639 and 1539; ^{1}H-NMR ($CDCl_3$): δ 0.81-0.96 (t, 6H, C$\underline{H}_3$ × 2), 1.10-1.38 (m, 36H, CH$_3$(C$\underline{H}_2$)$_9$ × 2), 1.39-1.59 (m, 4H, CH$_3$(CH$_2$)$_9$C$\underline{H}_2$ × 2), 1.91-2.11 (m, 2H, *CHC$\underline{H}_2$CH$_2$), 2.12-2.40 (m, 2H, *CHCH$_2$C$\underline{H}_2$), 2.94-3.08 (m, 2H, *CHC$\underline{H}_2$C$_6$H$_5$), 3.08-3.28 (m, 4H, C$\underline{H}_2$NH × 2), 4.26-4.37 (m, 1H, *C$\underline{H}$CH$_2$CH$_2$), 4.37-4.48 (m, 1H, *C$\underline{H}$CH$_2$C$_6$H$_5$), 5.00-5.12 (s, 2H, C(=O)OC$\underline{H}_2$C$_6$H$_5$), 5.34-5.44 (d, 1H, N$\underline{H}$), 5.89-6.02 (t, 1H, N$\underline{H}$), 6.65-6.80 (t, 1H, N$\underline{H}$), 7.01-7.42 (m, 10H, C$_6\underline{H}_5$ × 2), 7.59-7.72 (d, 1H, N$\underline{H}$); (Found: C, 71.28; H, 9.72; N, 7.17. Calc. for $C_{46}H_{74}N_4O_5 \cdot 0.7H_2O$: C, 71.28; H, 9.80; N, 7.23 %). *N',N''*-Didodecyl-*N*$^{\alpha}$-[*N'''*-benzyloxycarbonyl-*N'''*-methylglycinoyl]-L-glutamide (**7**), yield 0.476 g (95.2 %); m.p. 153-160 ˚C; FT-IR (KBr): /cm^{-1} 3292, 2922, 2851, 1683, 1642 and 1543; ^{1}H-NMR ($CDCl_3$): δ 0.78-0.96 (t, 6H, C$\underline{H}_3$ × 2), 1.16-1.41 (m, 36H, CH$_3$(C$\underline{H}_2$)$_9$ × 2), 1.43-1.58 (m, 4H, CH$_3$(CH$_2$)$_9$C$\underline{H}_2$ × 2), 1.93-2.12 (m, 2H, *CHC$\underline{H}_2$), 2.24-2.42 (m, 2H, *CHCH$_2$C$\underline{H}_2$), 2.99-3.11 (s, 3H, C$\underline{H}_3$N), 3.13-3.31 (m, 4H, C$\underline{H}_2$NH × 2), 3.68-4.00 (m, 2H, C(=O)C$\underline{H}_2$N), 4.30-4.46 (m, 1H, *C$\underline{H}$), 5.09-5.20 (s, 2H, C$\underline{H}_2$C$_6$H$_5$), 6.01-6.17 (t, 1H, N$\underline{H}$), 6.93-7.12 (t, 1H, N$\underline{H}$), 7.27-7.44 (m, 5H, C$_6\underline{H}_5$), 7.72-7.83 (d, 1H, N$\underline{H}$); (Found: C, 69.41; H, 8.07; N, 7.17. Calc. for $C_{43}H_{76}N_4O_5 \cdot 0.3H_2O$: C, 69.41; H, 10.28; N, 8.09 %).

***N',N''*-Didodecyl-*N*$^{\alpha}$-[*N'''*-[(*N''''*-benzyloxycarbonyl)glycynoyl]-3-aminopropanoyl]-L-glutamide (8).** *N',N''*-Didodecyl-*N*$^{\alpha}$-(3-aminopropanoyl)-L-glutamide[1a] (0.878 g, 1.59 mmol), Gly-Z (0.413 g, 1.91 mmol), and triethylamine (0.483 g, 4.76 mmol) were dissolved in 100 cm^3 of THF and stirred with cooling to 0 ˚C. To the solution was added DEPC (0.419 g, 2.54 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 0.3 N HCl (200 cm^3, in twice), deionized water (20 cm^3, once), 5 wt% aqueous $NaHCO_3$ (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 yellow solid (**8**): yield 0.838 g (71 %); m.p. 99-100 ˚C; FT-IR (KBr): /cm^{-1} 3296, 2922, 2854, 1717, 1636 and 1560; ^{1}H-NMR ($CDCl_3$): δ 0.79-0.98 (t, 6H, CH_3 × 2), 0.98-1.39 (m, 36H, $CH_3(CH_2)_9$ × 2), 1.39-1.59 (m, 4H, $CH_3(CH_2)_9CH_2$ × 2), 1.83-2.16 (m, 2H, *$CHCH_2$), 2.16-2.55 (m, 2H, C(=O)CH_2 × 2), 3.09-3.39 (m, 4H, $CH_3(CH_2)_{10}CH_2$ × 2), 3.39-3.78 (m, 2H, C(=O)CH_2CH_2NH), 3.93-4.22 (m, 2H, C(=O)CH_2NH), 4.22-4.43 (m, 1H, *CH), 5.04-5.17 (s, 2H, $CH_2C_6H_5$), 5.77-5.92 (d, 1H, NH), 6.17-6.49 (m, 1H, NH), 6.88-7.14 (m, 1H, NH), 7.29-7.50 (m, 5H, C_6H_5); (Found: C, 66.75; H, 9.89; N, 8.14. Calc. for $C_{42}H_{73}N_5O_6$·0.6H_2O: C, 66.75; H, 9.91; N, 9.27 %). The related compound *N',N''*-didodecyl-N^{α}-[*N'''*-[(*N''''*-benzyloxycarbonyl-*N''''*-methylglycinoyl)-3-aminopropanoyl]-L-glutamide (**9**) was synthesized as described above using Sar-Z instead of Gly-Z to give yellow solid: yield 0.48 g (39 %); m.p. 99-105 ˚C; FT-IR (KBr): /cm^{-1} 3298, 2922, 2854, 1711, 1660, 1638 and 1555; ^{1}H-NMR ($CDCl_3$): δ 0.77-0.98 (t, 6H, CH_3 × 2), 0.98-1.39 (m, 36H, $CH_3(CH_2)_9$ × 2), 1.39-1.60 (m, 4H, $CH_3(CH_2)_9CH_2$ × 2), 1.76-2.00 (m, 2H, *$CHCH_2$), 2.00-2.15 (m, 2H, *$CHCH_2CH_2$), 2.22-2.57 (m, 2H, C(=O)CH_2CH_2NH), 2.95-3.09 (s, 3H, NCH_3), 3.09-3.29 (m, 4H, $CH_3(CH_2)_{10}CH_2$ × 2), 3.45-3.80 (m, 2H, C(=O)CH_2CH_2NH), 3.94-4.26 (m, 2H, C(=O)CH_2N), 4.26-4.42 (m, 1H, *CH), 5.05-5.20 (m, 2H, $CH_2C_6H_5$), 6.04-6.16 (s, 1H, NH), 6.20-6.34 (s, 1H, NH), 6.42-6.95 (m, 1H, NH), 7.06-7.21 (m, 1H, NH), 7.28-7.43 (m, 5H, C_6H_5); (Found: C, 67.96; H, 10.17; N, 8.33. Calc. for $C_{43}H_{75}N_5O_6$·0.5H_2O: C, 67.96; H, 9.98; N, 9.22 %).

***N',N''*-Didodecyl-N^{α}-[3-(benzyloxycarbonyl)propanoyl]-L-glutamide (10).** *N',N''*-Didodecyl-N^{α}-[(3-carboxy)propanoyl]-L-glutamide[1c] (0.601 g, 1.03 mmol), benzyl alcohol (0.168 g, 1.55 mmol), and triethylamine (0.209 g, 2.07 mmol) were dissolved in 100 cm^3 of

chloroform and stirred with cooling to 0 ˚C. To the solution was added DEPC (0.236 g, 1.45 mmol) and stirred in an ice bath for 30 min. After being stirred for 1 day at room temperature, the solution was washed with 0.3 N HCl (200 cm^3, in twice), deionized water (20 cm^3, once), 5 wt% aqueous $NaHCO_3$ (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 (**10**): yield 0.368 g (53.0 %); m.p. 72-78 ˚C; FT-IR (KBr): /cm^{-1} 3298, 2928, 2854, 1713, 1642 and 1543; ^{1}H-NMR ($CDCl_3$): δ 0.70-1.05 (t, 6H, C<u>H</u>$_3$ × 2), 1.05-1.81 (m, 40H, CH_3(C<u>H</u>$_2$)$_{10}$ × 2), 1.87-2.62 (m, 8H, *CH(C<u>H</u>$_2$)$_2$, C(=O)(C<u>H</u>$_2$)$_2$C(=O)), 2.92-3.50 (m, 4H, C<u>H</u>$_2$NH × 2), 4.47-4.79 (m, 1H, *C<u>H</u>), 4.96-5.24 (s, 2H, C<u>H</u>$_2$$C_6H_5$), 5.84 (m, 1H, N<u>H</u>), 6.71-7.63 (m, 7H, C_6<u>H</u>$_5$, N<u>H</u> × 2); (Found: C, 68.76; H, 10.61; N, 6.79. Calc. for $C_{40}H_{69}N_3O_5$·1.5H_2O: C, 68.76; H, 10.38; N, 6.01 %).

***N'*,*N"*-Didodecyl-*N*$^{\alpha}$-[3-(*N'''*-benzyloxycarbonyl)aminopropanoyl]-L-glutamide** (**11**). L-**11** was prepared as reported previously[1a] to give white solid: yield 3.83 g (88 %); m.p. 167-170 ˚C; FT-IR (KBr): /cm^{-1} 3300, 2922, 2854, 1696, 1638 and 1555; ^{1}H-NMR ($CDCl_3$): δ 0.70-1.08 (t, 6H, C<u>H</u>$_3$ × 2), 1.08-1.80 (m, 40H, CH_3(C<u>H</u>$_2$)$_{10}$ × 2), 1.80-2.19 (m, 2H, *CHC<u>H</u>$_2$), 2.19-2.70 (m, 4H, C(=O)C<u>H</u>$_2$ × 2), 3.01-3.39 (m, 4H, $CH_3(CH_2)_{10}$C<u>H</u>$_2$ × 2), 3.39-3.69 (m, 2H, C<u>H</u>$_2$NHC(=O)O), 4.00-4.50 (m, 1H, *C<u>H</u>), 4.96-5.22 (s, 2H, C<u>H</u>$_2$$C_6H_5$), 5.47 (br t, 1H, N<u>H</u>), 5.99 (br t, 1H, N<u>H</u>), 6.88 (br t, 1H, N<u>H</u>), 7.32 (m, 5H, C_6<u>H</u>$_5$); (Found: C, 68.00; H, 10.08; N, 7.93. Calc. for $C_{40}H_{70}N_4O_5$: C, 68.00; H, 10.30; N, 7.93 %). The corresponding racemate (DL-**11**) was similarly prepared to give white solid: yield 3.00 g (72 %); m.p. 87-107 ˚C; FT-IR (KBr): /cm^{-1} 3300, 2924, 2856, 1698, 1638 and 1560; ^{1}H-NMR ($CDCl_3$): δ 0.69-1.03 (t, 6H, C<u>H</u>$_3$ × 2), 1.03-1.70 (m, 40H, CH_3(C<u>H</u>$_2$)$_{10}$ × 2), 1.70-2.71 (m, 6H, *CH(C<u>H</u>$_2$)$_2$, C(=O)C<u>H</u>$_2$C<u>H</u>$_2$NH), 2.71-3.70 (m, 6H, C<u>H</u>$_2$NH × 3), 4.21-4.62 (m, 1H, *C<u>H</u>), 4.62-5.40 (s, 2H, C<u>H</u>$_2$$C_6H_5$), 5.36-5.83 (m, 1H, N<u>H</u>), 5.78 (br s, 1H, N<u>H</u>), 6.64 (br s, 1H, N<u>H</u>), 7.33 (s, 5H, C_6<u>H</u>$_5$), 8.22 (br s, 1H, N<u>H</u>); (Found: C, 69.78; H, 10.35; N, 8.20. Calc. for $C_{40}H_{70}N_4O_5$: C, 69.93; H, 10.27; N, 8.16 %).

***N',N"*-Didodecyl-N^{α}-[4-(*N'''*-benzyloxycarbonyl)aminobutanoyl]-L-glutamide (12).** γ-Aminobutanoic acid (GABA) (5.00 g, 48.5 mmol) and sodium hydroxide (5.82 g, 145 mmol) were dissolved in 80 cm^3 of deionized water with cooling in an ice bath. Benzyl chloroformate (Z-Cl) (12.42 g, 72.8 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 was filtered and collected to obtain white powder, γ-(*N*-benzyloxycarbonyl)aminobutanoic acid (GABA-Z) (**17**): 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',N"*-Didodecyl-L-glutamide[4] (2.83 g, 5.88 mmol), **17** (2.09 g, 8.82 mmol), and triethylamine (1.66 g, 16.4 mmol) were dissolved in 100 cm^3 of THF and stirred with cooling to 0 ˚C. To the solution was added DEPC (1.82 g, 11.2 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 0.3 N HCl (200 cm^3, in twice), deionized water (20 cm^3, once), 5 wt% aqueous $NaHCO_3$ (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 (**12**): yield 2.68 g (65.0 %); m.p. 166-169 ˚C; FT-IR (KBr): /cm^{-1} 3300, 2922, 1690, 1638 and 1547; ^{1}H-NMR ($CDCl_3$): δ 0.70-1.00 (t, 6H, $C\underline{H}_3 \times 2$), 1.00-1.71 (m, 40H, $CH_3(C\underline{H}_2)_{10} \times 2$), 1.71-2.70 (m, 8H, *$CH(C\underline{H}_2)_2$, $C(=O)(C\underline{H}_2)_2CH_2NH$), 2.80-3.60 (m, 6H, $C\underline{H}_2NH \times 3$), 3.88-4.61 (m, 1H, *C$\underline{H}$), 5.09 (s, 2H, $C\underline{H}_2C_6H_5$), 5.20 (br t, 1H, N$\underline{H}$), 6.19 (br t, 1H, N$\underline{H}$), 6.95 (br t, 2H, N$\underline{H} \times 2$), 7.34 (s, 5H, $C_6\underline{H}_5$); (Found: C, 69.68; H, 10.09; N, 7.60. Calc. for $C_{41}H_{72}N_4O_5 \cdot 0.5H_2O$: C, 69.39; H, 10.16; N, 7.90 %). The related compound *N',N"*-didodecyl-N^{α}-[6-(*N'''*-benzyloxycarbonyl)aminohexanoyl]-L-glutamide (**13**) was

prepared similarly using ε-(*N*-benzyloxycarbonyl)aminohexanoic acid (**18**) instead of **17** to give white powder (**13**): yield 1.84 g (59 %); m.p. 140-149 ˚C; FT-IR (KBr): /cm^{-1} 3300, 2922, 1690, 1636 and 1545; ^{1}H-NMR ($CDCl_3$): δ 0.64-1.03 (t, 6H, C$\underline{H}_3$ × 2), 1.03-2.67 (m, 52H, $CH_3(C\underline{H}_2)_{10}$ × 2, *CH($C\underline{H}_2$)$_2$, C(=O)($C\underline{H}_2$)$_4$NH), 2.67-3.55 (m, 6H, $C\underline{H}_2$NH × 3), 4.12-4.60 (m, 1H, *C$\underline{H}$), 5.00 (br t, 1H, N$\underline{H}$), 5.09 (s, 2H, $C\underline{H}_2C_6H_5$), 6.37 (br s, 1H, N$\underline{H}$), 6.95-7.23 (m, 2H, N$\underline{H}$ × 2), 7.34 (s, 5H, $C_6\underline{H}_5$); (Found: C, 70.47; H, 10.36; N, 7.42. Calc. for $C_{43}H_{76}N_4O_5{\cdot}0.2H_2O$: C, 70.47; H, 10.51; N, 7.65 %). ε-(*N*-Benzyloxycarbonyl)aminohexanoic acid (**18**): yield 19.08 g (93 %); m.p. 49-50 ˚C; FT-IR (KBr): /cm^{-1} 3336, 2948, 1723, 1692 and 1535; ^{1}H-NMR ($CDCl_3$): δ 0.85-1.99 (m, 6H, C(=O)$CH_2(C\underline{H}_2)_3$), 2.10-2.60 (t, 2H, C(=O)$C\underline{H}_2$), 2.72-3.54 (q, 2H, $C\underline{H}_2$NH), 4.90 (br s, 1H, N$\underline{H}$), 5.09 (s, 2H, $C\underline{H}_2C_6H_5$), 6.89-7.70 (s, 5H, $C_6\underline{H}_5$), 9.77 (br s, 1H, O$\underline{H}$).

***N',N"*-Didodecyl-N^{α}-[3-(*N'''*-benzyloxycarbonyl)aminopropanoyl]-L-aspartamide (14). 14** was prepared by the coupling of *N',N"*-didodecyl-L-aspartamide[1b] and Ala-Z using DEPC and triethylamine as described above to give white solid: yield 2.31 g (80 %); m.p. 188-190 ˚C; FT-IR (KBr): /cm^{-1} 3288, 2922, 2854, 1688, 1644 and 1541; ^{1}H-NMR ($CDCl_3$): δ 0.71-1.01 (t, 6H, C$\underline{H}_3$ × 2), 1.01-1.75 (m, 40H, $CH_3(C\underline{H}_2)_{10}$ × 2), 2.30-2.62 (t, 4H, C(=O)$C\underline{H}_2$), 3.00-3.34 (m, 4H, $CH_3(CH_2)_{10}C\underline{H}_2$ × 2), 3.34-3.70 (m, 2H, $C\underline{H}_2$NHC(=O)O), 4.46-4.84 (m, 1H, *C$\underline{H}$), 5.10 (s, 2H, $C\underline{H}_2C_6H_5$), 5.48 (br t, 1H, N$\underline{H}$), 6.17 (br t, 2H, N$\underline{H}$ × 2), 7.09-7.70 (m, 6H, $C_6\underline{H}_5$, N$\underline{H}$); (Found: C, 69.59; H, 10.25; N, 8.31. Calc. for $C_{39}H_{68}N_4O_5$: C, 69.60; H, 10.19; N, 7.33 %). The related compound *N',N"*-didodecyl-L-2-N^{α}-[3-(*N'''*-benzyloxycarbonyl)aminopropanoyl]-aminoadipamide (**15**) was prepared as described above using *N',N"*-didodecyl-L-2-aminoadipamide[2] instead of *N',N"*-didodecyl-L-aspartamide[1b] to give white solid: yield 2.69 g (73.7 %); m.p. 210-213 ˚C; FT-IR (KBr): /cm^{-1} 3297, 2815, 1697, 1632 and 1594; ^{1}H-NMR ($CDCl_3$): δ 0.79-0.94 (t, 6H, C$\underline{H}_3$ × 2), 1.16-1.38 (m, 36H, $CH_3(C\underline{H}_2)_9$ × 2), 1.38-1.88 (m, 8H, $CH_3(CH_2)_9C\underline{H}_2$ × 2, *CH($C\underline{H}_2$)$_2$), 1.96-2.35 (m, 2H, *CH$(CH_2)_2C\underline{H}_2$), 2.35-2.51 (m, 2H, C(=O)$C\underline{H}_2CH_2$NH), 3.12-3.29 (m, 4H, $CH_3(CH_2)_{10}C\underline{H}_2$ × 2), 3.41-3.53 (q, 4H, $C\underline{H}_2$NHC(=O)O), 4.25-4.36 (m,

1H, *CH), 5.03-5.15 (s, 2H, $CH_2C_6H_5$), 5.55-5.65 (m, 1H, NH), 5.72-5.81 (m, 1H, NH), 6.75-6.83 (d, 1H, NH), 6.83-6.92 (m, 1H, NH), 7.29-7.41 (s, 5H, C_6H_5); (Found: C, 69.84; H, 10.11; N, 7.93. Calc. for $C_{41}H_{72}N_4O_5 \cdot 0.2H_2O$: C, 69.84; H, 10.36; N, 7.95 %). The related compound *N',N''*-dihexadecyl-N^{α}-[3-(*N'''*-benzyloxycarbonyl)aminopropanoyl]-L-glutamide (**16**) was prepared as described above using *N',N''*-dihexadecyl-L-glutamide **(20)** derived from *N',N''*-dihexadecyl-N^{α}-benzyloxycarbonyl-L-glutamide **(19)** instead of *N',N''*-didodecyl-L-glutamide.[1] **19**: white solid, yield 3.6g (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, $CH_3 \times 2$), 1.03-1.72 (m, 56H, $CH_3(CH_2)_{14} \times 2$), 1.72-2.63 (m, 4H, *$CH(CH_2)_2$), 2.63-3.42 (m, 4H, $CH_2NH \times 2$), 4.03-4.40 (m, 1H, *CH), 4.98-5.20 (s, 2H, $CH_2C_6H_5$), 7.23-7.50 (s, 5H, C_6H_5). **20**: 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, $CH_3 \times 2$), 1.01-1.80 (m, 56H, $CH_3(CH_2)_{14} \times 2$), 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, $CH_2NH \times 2$), 3.68-4.70 (m, 1H, *CH), 6.82 (br, 1H, NH), 7.41 (br, 1H, NH). **16**: yield 2.74g (68 %); m.p. 143 ˚C; FT-IR (KBr): /cm^{-1} 3298, 2922, 2854,1698, 1638 and 1543; ^{1}H-NMR ($CDCl_3$): δ 0.68-1.03 (t, 6H, $CH_3 \times 2$), 1.03-1.80 (m, 56H, $CH_3(CH_2)_{14} \times 2$), 1.80-2.17 (m, 2H, *$CHCH_2$), 2.17-2.74 (m, 4H, $C(=O)CH_2 \times 2$), 2.97-3.36 (m, 4H, $CH_3(CH_2)_{14}CH_2 \times 2$), 3.36-3.78 (m, 2H, $CH_2NHC(=O)O$), 4.20-4.59 (m, 1H, *CH), 4.90-5.30 (s, 2H, $CH_2C_6H_5$), 7.18-7.59 (s, 5H, C_6H_5). (Found: C, 71.37; H, 10.87; N, 6.54. Calc. for $C_{48}H_{86}N_4O_5 \cdot 0.5H_2O$: C, 71.37; H, 10.85; N, 6.94 %).

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