SYNTHESIS OF NOVEL PEPTIDOMIMETICS, CYCLIC HEXAMERS OF UNNATURAL AMINO ACIDS, 2,5-DISUBSTITUTED 3-AMINOBENZOIC ACIDS[1]

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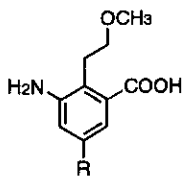
Abstract - Coupling of 3-aminobenzoic acids and cyclization of their peptides have been accomplished, for the first time, using methanesulfonyl chloride. Cylindrical conformations for the 30-membered cyclic hexapeptides, with *trans* configuration at the amide bonds, are suggested by ROESY study as well as MM calculations.

Biochemical activity of peptides is due primarily to the spacial disposition of certain amino acid residues, while the peptide backbone is, in many cases, merely for holding such structural requirement.[2]
This report describes a novel design and synthesis of such cyclic peptides, as those having various functional groups on a rigid peptide framework, from appropriately substituted 3-aminobenzoic acids.



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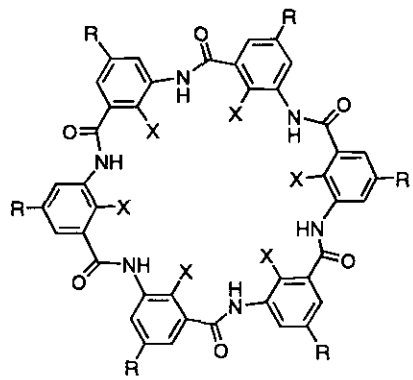

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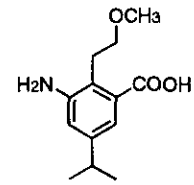
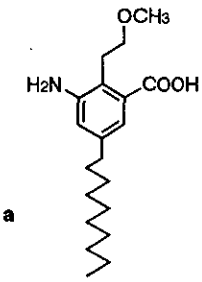


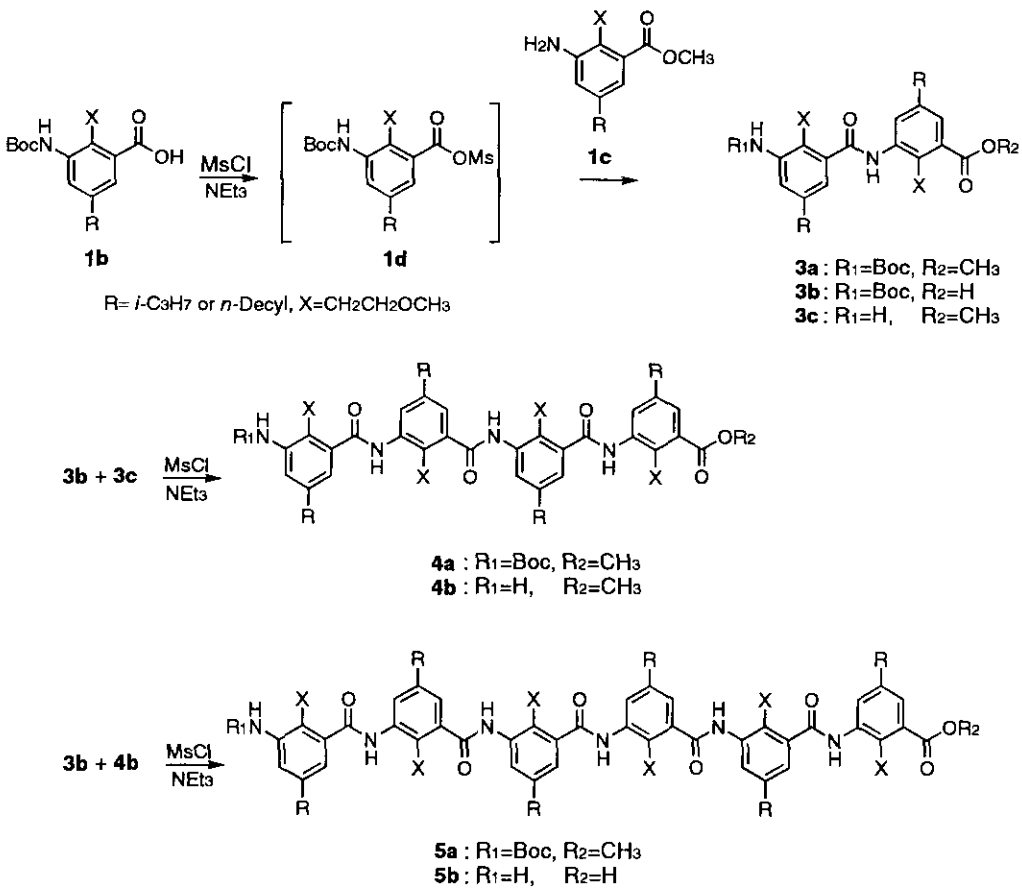


1a

The building blocks, 5-alkyl-3-amino-2-methoxyethylbenzoic acids (**1a**), were selected for this purpose, and were synthesized from 4-isopropylbenzaldehyde or cinnamic acid.[3]
The substituent at 2-position could be modified to such functional groups as those of natural amino acid residues.[4] The other substituent at 5-position endows the amino acids and the peptides with lipophilic or hydrophilic characters, as well as to restrict conformational mobility.

Coupling reaction of aminobenzoic acid has not been reported so far, since both amino and carboxyl groups are in conjugation with a respective phenyl ring, so that reactivity to amide formation with usual coupling reagents, for natural amino acids, did not give satisfactory results. Specifically, treatment of appropriately protected 3-aminobenzoic acids (**1b** and **1c**) with DCC [5] or CDI [6] afforded no coupling product within 3 days. It is thought that a mixed anhydride of the carboxyl group and a very hard acid might be a better acylating agent, and thus, methanesulfonyl chloride was tested for this reaction, resulting clean couplings to take place, and afforded the dipeptides (**3a**) in almost quantitative yields.[7]

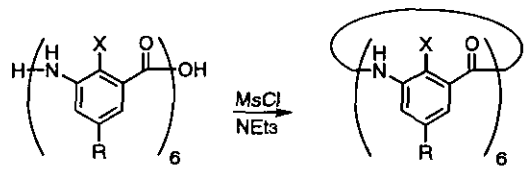
Elongation of the peptide chain was also carried out by this method, with excellent isolated yields in each steps, and linear tetra- and hexapeptides (**4a**) and (**5a**) were prepared accordingly (Scheme 1).



Scheme 1

Further, unprotected hexamers (**5b**) were subjected to cyclization, with the same procedure, to furnish the cyclic hexamers (**2**), 30-membered rings, in varying yields up to 80% (not optimized).[8] The results indicated methanesulfonyl chloride to react with highly basic carboxylic oxygens selectively, without touching weakly basic amino nitrogen atoms.[7]

The structures of the cyclization products (**2**) were supported by observing molecular ions, at *m/z* 1315 for R=*i*-C_3H_7 and 1903 for R=*n*-Decyl, in Fab-MS, as well as upfield shifts of most of the signals, except the isopropyl or decyl groups, owing to the diamagnetic anisotropic effect of the phenyl rings in the ^{1}H NMR *spectra* (*Figure* 1).



5b **2**

R= *i*-C3H7 or *n*-Decyl, X=CH2CH2OCH3

Table 1. Cyclization Reactions of Linear Hexamers (**5b**)

5b	Solvent	Concentration	Time (temp)	2
R= *i*-C_3H_7	CH_2Cl_2	0.3 mmol/L	12h (rt)	66 %
R=*n*-Decyl	CH_2Cl_2	0.3 mmol/L	12h (rt)	45 %

Further, NOE measurements indicated the configuration of the cyclic hexamers (**2**) to have *trans* (*anti*) at the amide bonds, as were the same in the linear counterparts (**3**~**5**). MM Calculations for **2** (R=*i*-C_3H_7), using the CVFF forcefield (Discover 95.0), also suggested a stable cylindrical conformation with the isopropyl groups oriented outwards and the methoxyethyl groups inwards alternatingly.

Extended research on syntheses of analogues, and modifications of substituents are in progress.

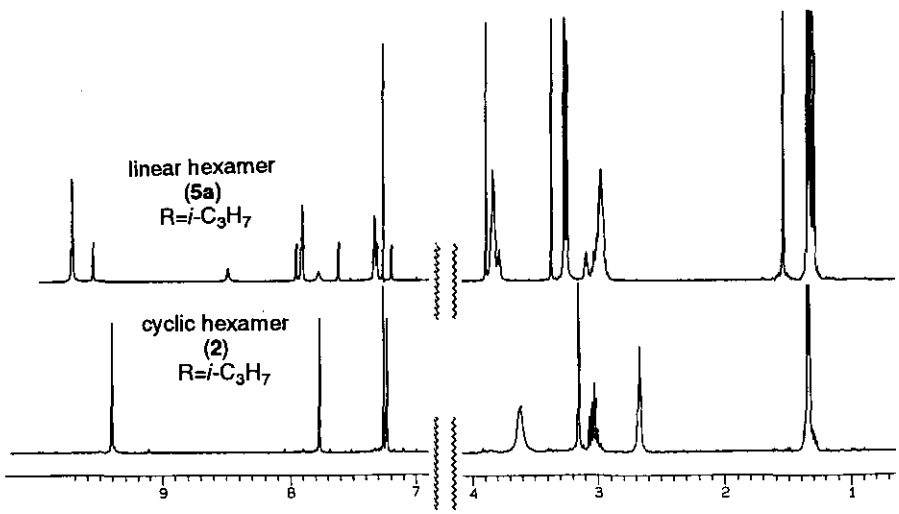
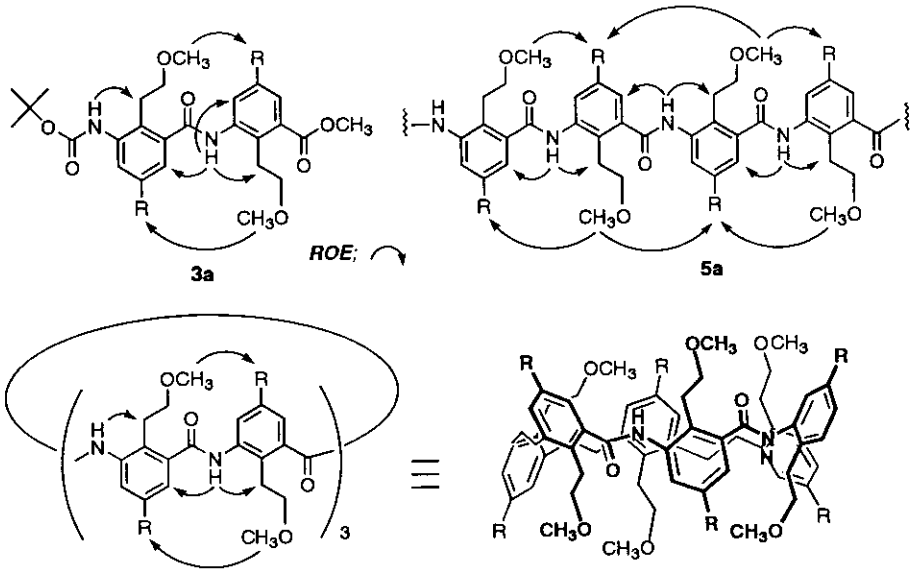


Figure 1 ^{1}H-NMR Spectra of Linear Hexamer (**5a**) and Cyclic Hexamer (**2**) (CDCl3)



2 : R= *i*-C3H7 or *n*-Decyl

Scheme 2

EXPERIMENTAL

General Melting points were uncorrected. IR Spectra were recorded on a JASCO FT/IR-5000 spectrophotometer. UV spectra were obtained with a Beckman DU-7500 spectrophotometer. ^{1}H and ^{13}C-NMR spectra were recorded on a JEOL GSX-400 (400MHZ) spectrometer with TMS as an internal standard. High-MS (EI) and Fab-MS spectral data were obtained with a JEOL JMS DX-303 GC mass spectrometer.

The synthesis of the unnatural benzoic amino acids were reported previously.[3]

Standard procedure for coupling To a CH_2Cl_2 solution (5 mL) of an *N*-protected amino acid (1 mmol), Et_3N (152 mg, 1.5 mmol) in CH_2Cl_2 (5 mL) and MsCl (137 mg, 1.2 mmol) in CH_2Cl_2 (2 mL) was added successively at 0 °C. After 10 min, an *O*-protected amino acid (1 mmol) in CH_2Cl_2 (3 mL) was added to the solution. The reaction mixture was stirred for 1 h at 0 °C, and washed with satd. aq. $NaHCO_3$, water, brine, and dried on Na_2SO_4, filtered and concentrated. The residue was subjected to column chromatography on silica gel using hexane-AcOEt (4:1). Cyclizations were similarly carried out with deprotected peptides at rt with concentrations of 0.1~0.3 mmol/L and longer reaction times (12 h).

Deprotection of Boc-amino groups To a CH_2Cl_2 solution (3 mL) of a Boc-amino acid (1 mmol), TFA (2 mL) was added at 0 °C. The reaction mixture was stirred at 0 °C for 1 h, and was neutralized with satd. aq. $NaHCO_3$, and then extracted with AcOEt followed by washing with water, brine, dried on Na_2SO_4, filtered and concentrated. The residue was subjected to a column chromatography on silica gel using hexane-AcOEt (2:1) or CH_2Cl_2-MeOH (30:1).

Hydrolysis of methyl esters To an EtOH solution (5 mL) of a methyl ester (1 mmol), 10% aq.

NaOH (0.6 mL) was adedd. The reaction mixture was stirred at 60 °C for 3 h, and was neutralized with 10% aq. citric acid and extracted with AcOEt (50 mL), followed by washing with water, brine, dried on Na_2SO_4 filtered and concentrated. The residue was subjected to column chromatography on silica gel using AcOEt, or CH_2Cl_2-MeOH (10:1).

*Dimer (**3a**), R=i-C_3H_7 (Methyl 3-[3-t-butoxycarbonylamino-5-isopropyl-2-(2-methoxyethyl)benzoyl]-amino-5-isopropyl-2-(2-methoxyethyl)benzoate) from **1b**+**1c*** (92%) - mp 89~92 °C (hexane-AcOEt). IR (nujol) cm^{-1}: 3350, 1727, 1680. ^{1}H-NMR ($CDCl_3$) δ: 1.29 (6H, d, *J* 6.9 Hz), 1.30 (6H, d, *J* 6.9 Hz), 1.54 (9H, s), 2.92 (1H, septet, *J* 6.9 Hz), 2.93 (1H, septet, *J* 6.9 Hz), 2.97 (2H, t, *J* 5.0 Hz), 3.08 (2H, t, *J* 5.0 Hz), 3.23 (3H, s), 3.36 (3H, s), 3.76 (2H, t, *J* 5.0 Hz), 3.82 (2H, t, *J* 5.0 Hz), 3.88 (3H, s), 7.17 (1H, d, *J* 2.0 Hz), 7.60 (1H, d, *J* 1.7 Hz), 7.77 (1H, br), 7.96 (1H, d, *J* 2.0 Hz), 8.48 (1H, br), 9.55 (1H, br). High-MS *m/z*: Calcd $C_{32}H_{46}N_2O_7$: 570.3302; found 570.3312.

*Dimer (**3a**), R=n-Decyl (Methyl 3-[3-t-butoxycarbonylamino-5-decyl-2-(2-methoxyethyl)benzoyl]amino-5-decyl-2-(2-methoxyethyl)benzoate) from **1b**+**1c*** (83%) - mp 96~99 °C (hexane-AcOEt). IR (nujol) cm^{-1}: 3344, 1731, 1671. ^{1}H-NMR ($CDCl_3$) δ: 0.88 (6H, brt, *J* 6.6 Hz), 1.20~1.40 (28H, br), 1.53 (9H, s), 1.58~1.71 (4H, br), 2.62 (2H, t, *J* 8.0 Hz), 2.64 (2H, t, *J* 8.0 Hz), 2.97 (2H, t, *J* 5.0 Hz), 3.07 (2H, t, *J* 5.0 Hz), 3.23 (3H, s), 3.35 (3H, s), 3.77 (2H, t, *J* 5.0 Hz), 3.83 (2H, t, *J* 5.0 Hz), 3.87 (3H, s), 7.12 (1H, s), 7.54 (1H, d, *J* 1.8 Hz), 7.72 (1H, br), 7.94 (1H, d, *J* 1.8 Hz), 8.46 (1H, br), 9.60 (1H, br). High-MS *m/z*: Calcd $C_{46}H_{74}N_2O_7$: 766.5496; found 766.5565.

*Dimer (**3b**), R=i-C_3H_7 (3-[3-t-Butoxycarbonylamino-5-isopropyl-2-(2-methoxyethyl)benzoyl]amino-5-isopropyl-2-(2-methoxyethyl)benzoic acid) from **3a*** (95%) - mp 93~94 °C (hexane-AcOEt). IR (nujol) cm^{-1}: 3400~3000, 1720, 1685. ^{1}H-NMR ($CDCl_3$) δ: 1.29 (6H, d, *J* 6.9 Hz), 1.31 (6H, d, *J* 6.9 Hz), 1.54 (9H, s), 2.96 (1H, septet, *J* 6.9 Hz), 2.97 (1H, septet, *J* 6.9 Hz), 2.97 (2H, t, *J* 5.0 Hz), 3.17 (2H, t, *J* 5.0 Hz), 3.24 (3H, s), 3.36 (3H, s), 3.76 (2H, t, *J* 5.0 Hz), 3.82 (2H, t, *J* 5.0 Hz), 7.18 (1H, d, *J* 1.7 Hz), 7.77 (2H, br), 8.01 (1H, d, *J* 2.0 Hz), 8.48 (1H, br), 9.55 (1H, br). Fab-MS *m/z*: 557 $(M+1)^+$.

*Dimer (**3b**), R=n-Decyl (3-[3-t-Butoxycarbonylamino-5-decyl-2-(2-methoxyethyl)benzoyl]amino-5-decyl-2-(2-methoxyethyl)benzoic acid) from **3a*** (96%) - mp 117~120 °C (hexane-AcOEt). IR (nujol) cm^{-1}: 3400~3000, 1713, 1686. ^{1}H-NMR ($CDCl_3$) δ: 0.88 (6H, brt, *J* 6.6 Hz), 1.20~1.40 (28H, br), 1.54 (9 H, s), 1.60~1.71 (4H, br), 2.62 (2H, t, *J* 7.7 Hz), 2.66 (2H, t, *J* 7.7 Hz), 2.98 (2H, t, *J* 5.0 Hz), 3.15 (2H, t, *J* 5.0 Hz), 3.25 (3H, s), 3.36 (3H, s), 3.77 (2H, t, *J* 5.0 Hz), 3.83 (2H, t, *J* 5.0 Hz), 7.13 (1H, s), 7.70 (1H, s), 7.72 (1H, br), 7.99 (1H, s), 8.47 (1H, br), 9.62 (1H, br). High-MS *m/z*: Calcd $C_{45}H_{72}N_2O_7$: 752.5340; found 752.5272.

*Dimer (**3c**), R=i-C_3H_7 (Methyl 3-[3-amino-5-isopropyl-2-(2-methoxyethyl)benzoyl]amino-5-isopropyl-2-(2-methoxyethyl)benzoate) from **3a*** (98%) - Oil. IR (film) cm^{-1}: 3420, 3370, 1725, 1670. ^{1}H-NMR ($CDCl_3$) δ: 1.24 (6H, d, *J* 6.9 Hz), 1.30 (6H, d, *J* 6.9 Hz), 2.82 (1H, septet, *J* 6.9 Hz), 2.97 (2H, t, *J* 5.0 Hz), 2.98 (1H, septet, *J* 6.9 Hz), 3.09 (2H, t, *J* 5.0 Hz), 3.23 (3H, s), 3.32 (3H, s), 3.76 (2H, t, *J* 5.0 Hz), 3.78 (2H, t, *J* 5.0 Hz), 3.88 (3H, s), 6.67 (1H, d, *J* 1.7 Hz), 6.86 (1H, d, *J* 2.0 Hz), 7.59 (1H, d, *J* 2.0 Hz), 7.99 (1H, d, *J* 1.7 Hz), 9.48 (1H, br). High-MS *m/z*: Calcd $C_{27}H_{38}N_2O_5$: 470.2779; found

470.2758.

*Dimer (**3c**), R=n-Decyl (Methyl 3-[3-amino-5-decyl-2-(2-methoxyethyl)benzoyl]amino-5-decyl-2-(2-methoxyethyl)benzoate) from **3a*** (97%) - mp 77~79 °C (hexane-AcOEt). IR (nujol) cm^{-1}: 3410, 3348, 1723, 1678. ^{1}H-NMR ($CDCl_3$) δ: 0.88 (6H, brt, *J* 6.6 Hz), 1.20~1.40 (28H, br), 1.53~1.71 (4H, br), 2.52 (2H, t, *J* 8.0 Hz), 2.64 (2H, t, *J* 8.0 Hz), 2.96 (2H, t, *J* 5.5 Hz), 3.09 (2H, t, *J* 5.5 Hz), 3.24 (3H, s), 3.32 (3H, s), 3.76 (2H, t, *J* 5.5 Hz), 3.78 (2H, t, *J* 5.5 Hz), 3.87 (3H, s), 6.63 (1H, s), 6.81 (1H, s), 7.53 (1H, d, *J* 1.7 Hz), 7.96 (1H, d, *J* 1.7 Hz), 9.53 (1H, br). High-MS *m/z*: Calcd $C_{41}H_{66}N_2O_5$: 666.4973; found 666.4927.

*Tetramer (**4a**), R=i-C_3H_7 (Methyl 3-[3-[3-[3-t-butoxycarbonylamino-5-isopropyl-2-(2-methoxyethyl)benzoyl]amino-5-isopropyl-2-(2-methoxyethyl)benzoyl]amino-5-isopropyl-2-(2-methoxyethyl)benzoyl]amino-5-isopropyl-2-(2-methoxyethyl)benzoate) from **3b+3c*** (83%) - mp 114~116 °C (hexane-AcOEt). ^{1}H-NMR ($CDCl_3$) δ: 1.29 (6H, d, *J* 6.9 Hz), 1.31 (6H, d, *J* 6.9 Hz), 1.33~1.34 (12H, m), 1.54 (9H, s), 2.95~3.04 (10H, m), 3.09 (2H, t, *J* 5.1 Hz), 3.24 (3H, s), 3.25 (3H, s), 3.26 (3H, s), 3.27 (3H, s), 3.77 (2H, t, *J* 5.1 Hz), 3.81~3.85 (6H, m), 3.89 (3H, s), 7.19 (1H, d, *J* 1.8 Hz), 7.31 (1H, d, *J* 1.8 Hz), 7.32 (1 H, d, *J* 1.5 Hz), 7.62 (1H, d, *J* 1.8 Hz), 7.77 (1H, br), 7.89 (1H, d, *J* 1.5 Hz), 7.91 (1H, d, *J* 1.8 Hz), 7.95 (1H, d, *J* 1.8 Hz), 8.49 (1H, br), 9.55 (1H, br), 9.71 (1H, s), 9.72 (1H, s). Fab-MS *m/z*: 1010 $(M+1)^+$.

*Tetramer (**4a**), R=n-Decyl (Methyl 3-[3-[3-[3-t-butoxycarbonylamino-5-decyl-2-(2-methoxyethyl)benzoyl]amino-5-decyl-2-(2-methoxyethyl)benzoyl]amino-5-decyl-2-(2-methoxyethyl)benzoyl]amino-5-decyl-2-(2-methoxyethyl)benzoate) from **3b+3c*** (78%) - mp 186~189 °C (CH_2Cl_2-MeOH). ^{1}H-NMR ($CDCl_3$) δ: 0.85~0.90 (12H, br), 1.20~1.40 (56H, br), 1.54 (9H, s), 1.60~1.73 (8H, br), 2.66 (8H, brt, *J* 8.0 Hz), 2.90~3.01 (6H, br), 3.07 (2H, brt, *J* 5.0 Hz), 3.25 (3H, s), 3.26 (3H, s), 3.27 (3H, s), 3.36 (3H, s), 3.78 (2H, brt, *J* 5.0 Hz), 3.80~3.87 (6H, br), 3.88 (3H, s), 7.15 (1H, s), 7.24 (1H, s), 7.26 (1H, s), 7.55 (1H, s), 7.72 (1H, br), 7.88 (1H, s), 7.89 (1H, s), 7.94 (1H, s), 8.46 (1H, br), 9.64 (1H, s), 9.76 (1H, s), 9.80 (1H, s). Fab-MS *m/z*: 1401 $(M+1)^+$.

*Tetramer (**4b**), R=i-C_3H_7 (Methyl 3-[3-[3-[3-amino-5-isopropyl-2-(2-methoxyethyl)benzoyl]amino-5-isopropyl-2-(2-methoxyethyl)benzoyl]amino-5-isopropyl-2-(2-methoxyethyl)benzoyl]amino-5-isopropyl-2-(2-methoxyethyl)benzoate) from **4a*** (95%) - mp 144~147 °C (hexane-AcOEt). ^{1}H-NMR ($CDCl_3$) δ: 1.26 (6 H, d, *J* 6.9 Hz), 1.27 (6H, d, *J* 6.9 Hz), 1.30 (6H, d, *J* 6.9 Hz), 1.33 (6H, d, *J* 6.9 Hz), 2.89~3.09 (12 H, m), 3.23 (3H, s), 3.24 (3H, s), 3.26 (3H, s), 3.35 (3H, s), 3.78~3.86 (8H, br), 3.88 (3H, s), 7.24 (1H, br), 7.31~7.33 (3H, br), 7.61 (1H, d, *J* 2.0 Hz), 7.90 (1H, d, *J* 1.3 Hz), 7.92 (1H, d, *J* 1.7Hz), 7.95 (1H, d, *J* 2.0 Hz), 9.56 (1H, br), 9.75 (1H, br), 9.84 (1H, br). Fab-MS *m/z*: 910 $(M+1)^+$.

*Tetramer (**4b**), R=n-Decyl (Methyl 3-[3-[3-[3-amino-5-decyl-2-(2-methoxyethyl)benzoyl]amino-5-decyl-2-(2-methoxyethyl)benzoyl]amino-5-decyl-2-(2-methoxyethyl)benzoyl]amino-5-decyl-2-(2-methoxyethyl)benzoate) from **4a*** (96%) - mp 185~188 °C (CH_2Cl_2-MeOH). ^{1}H-NMR ($CDCl_3$) δ: 0.88 (12H, brt, *J* 6.6 Hz), 1.20~1.40 (56H, br), 1.51~1.78 (8H, br), 2.53 (2H, t, *J* 7.7 Hz), 2.67 (6H, brt, *J* 8.0 Hz), 3.00 (8H, brt, *J* 5.0 Hz), 3.26 (6H, s), 3.27 (3H, s), 3.33 (3H, s), 3.75~3.85 (8H, br), 3.88 (3H, s),

6.65 (1H, s), 6.84 (1H, s), 7.24 (2H, brs), 7.55 (1H, d, *J* 1.7 Hz), 7.89 (1H, s), 7.91 (1H, s), 7.94 (1H, d, *J* 1.7 Hz), 9.64 (1H, br), 9.69 (1H, br), 9.80 (1H, br). Fab-MS *m/z*: 1301 $(M+1)^+$.

*Hexamer (**5a**), R=i-C_3H_7 (Methyl 3-[3-[3-[3-[3-[3-t-butoxycarbonylamino-5-isopropyl-2-(2-methoxyethyl)-benzoyl]amino-5-isopropyl-2-(2-methoxyethyl)benzoyl]amino-5-isopropyl-2-(2-methoxyethyl)benzoylamino-5-isopropyl-2-(2-methoxyethyl)benzoyl]amino-5-isopropyl-2-(2-methoxyethyl)benzoyl]amino-5-isopropyl-2-(2-methoxyethyl)benzoate) from **3b** + **4b*** (76%) - mp 295~296 °C (hexane-AcOEt). ^{1}H-NMR ($CDCl_3$) δ: 1.29 (6H, d, *J* 6.9 Hz), 1.31 (6H, d, *J* 6.9 Hz), 1.33~1.35 (24H, m), 1.54 (9H, s), 2.93~3.04 (16H, br), 3.09 (2H, t, *J* 5.1 Hz), 3.24 (3H, s), 3.25 (3H, s), 3.26 (3H, s), 3.27 (6H, s), 3.36 (3H, s), 3.77 (2H, t, *J* 5.1 Hz), 3.82~3.85 (6H, br), 3.89 (3H, s), 7.19 (1H, d, *J* 1.8 Hz), 7.31 (1H, d, *J* 1.8 Hz), 7.32 (1H, d, *J* 1.8 Hz), 7.33 (1H, d, *J* 1.8 Hz), 7.62 (1H, d, *J* 1.8 Hz), 7.77 (1H, brs), 7.89~7.91 (4H, br), 7.95 (1H, d, *J* 1.8 Hz), 8.49 (1H, brs), 9.55 (1H, brs), 9.71~ 9.72 (4H, br). Fab-MS *m/z*: 1448 $(M+1)^+$.

*Hexamer (**5a**), R =n-Decyl (Methyl 3-[3-[3-[3-[3-[3-t-butoxycarbonylamino-5-decyl-2-(2-methoxyethyl) benzoyl] amino-5-decyl-2-(2-methoxyethyl) benzoyl] amino-5-decyl-2- (2-methoxyethyl) benzoyl] amino-5-decyl-2-(2-methoxyethyl)benzoyl]amino-5-decyl-2-(2-methoxyethyl)benzoyl]amino-5-decyl-2- (2-methoxyethyl)benzoate) from **3b** + **4b*** (80%) - mp above 300 °C (CH_2Cl_2-MeOH). ^{1}H-NMR ($CDCl_3$) δ: 0.88 (18 H, br), 1.20~1.40 (84H, br), 1.53 (9H, s), 1.60~1.75 (12H, br), 2.66 (12H, brt, *J* 8.0 Hz), 2.90~3.00 (10H, br), 3.08 (2H, brt, *J* 5.0 Hz), 3.25 (3H, s), 3.26 (3H, s), 3.27 (9H, s), 3.35 (3H, s), 3.83 (12H, brt, *J* 5.0Hz), 3.88 (3H, s), 7.14 (1H, s), 7.25 (4H, brs), 7.55 (1H, s), 7.72 (1H, brs), 7.89 (4H, brs), 7.93 (1H, s), 8.46 (1H, br), 9.64 (1H, br), 9.76 (1H, br), 9.80 (3H, br).

*Hexamer (**5b**), R=i-C_3H_7 (3-[3-[3-[3-[3-[3-Amino-5-isopropyl-2-(2-methoxyethyl)benzoyl]amino-5-isopropyl-2-(2-methoxyethyl)benzoyl]amino-5-isopropyl-2-(2-methoxyethyl)benzoyl]amino-5-isopropyl-2-(2-methoxyethyl) benzoyl] amino-5-isopropyl-2-(2-methoxyethyl)benzoyl] amino-5-isopropyl-2-(2-methoxyethyl)-benzoic acid) from **5a*** (92%) - mp above 300 °C (hexane-AcOEt). ^{1}H-NMR ($CDCl_3$) δ: 1.24 (6H, d, *J* 6.9 Hz), 1.29~1.34 (30H, br), 2.82 (1H, septet, *J* 6.9 Hz), 2.85~3.10 (15H, br), 3.14 (2H, br), 3.23 (3H, s), 3.24 (3H, s), 3.25 (3H, s), 3.26 (6H, br), 3.33 (3H, s), 3.67 (2H, br), 3.77~3.81 (10H, br), 6.67 (1H, br), 6.88 (1H, br), 7.27~7.32 (4H, br), 7.66 (1H, br), 7.80~7.90 (4H, br), 7.94 (1H, d *J* 1.3 Hz), 9.39 (1H, br), 9.66 (1H, br), 9.72 (3H, br). Fab-MS *m/z*: 1334 $(M+1)^+$.

*Hexamer (**5b**), R=n-Decyl (3-[3-[3-[3-[3-[3-Amino-5-decyl-2-(2-methoxyethyl)benzoyl]amino-5-decyl-2-(2-methoxyethyl)benzoyl]amino-5-decyl-2-(2-methoxyethyl)benzoyl]amino-5-decyl-2-(2-methoxyethyl)-benzoyl]amino-5-decyl-2-(2-methoxyethyl)benzoyl]amino-5-decyl-2-(2-methoxyethyl)benzoic acid) from **5a*** (72%) - mp above 300 °C (CH_2Cl_2-MeOH). ^{1}H-NMR ($CDCl_3$) δ: 0.85~0.90 (18H, br), 1.20~1.40 (84H, br), 1.50~1.78 (12H, br), 2.53 (2H, t, *J* 7.7 Hz), 2.60~2.75 (10H, br), 2.95 (10H, br), 3.15 (2 H, t, *J* 5.0 Hz), 3.25 (3H, s), 3.26 (3H, s), 3.27 (9H, s), 3.32 (3H, s), 3.75~3.85 (12H, br), 3.88 (3H, s), 6.64 (1H, s), 6.84 (1H, s), 7.24 (3H, brs), 7.55 (1H, s), 7.89 (4H, brs), 7.91 (1H, s), 7.97 (1H, s), 9.64 (1H, br), 9.69 (1H, br), 9.80 (3H, br).

*Hexamer (**2**), R=i-C_3H_7 (Cyclo[3-amino-5-isopropyl-2-(2-methoxyethyl)benzoyl]6) from **5b*** (66%) -

mp above 300 °C (CH_2Cl_2-MeOH). IR (film) cm^{-1}: 3292, 1671, 1524. ^{1}H-NMR ($CDCl_3$) δ: 1.33 (36H, d, *J* 6.9 Hz), 2.66 (12H, br), 3.05 (6H, septet, *J* 6.9 Hz), 3.14 (18H, s), 3.60 (12H, br), 7.23 (6H, d, *J* 1.7 Hz), 7.77 (6H, d, *J* 1.7 Hz), 9.41 (6H, s). ^{13}C-NMR ($CDCl_3$) δ: 24.50, 29.93, 33.83, 58.81, 74.99, 120.02, 124.67, 127.57, 137.20, 139.06, 148.14, 168.95. Fab-MS *m/z*: 1315 $(M+1)^+$.

Hexamer (2), R=n-Decyl (Cyclo[3-amino-5-decyl-2-(2-methoxyethyl)benzoyl]6) from ***5b*** (45%) - mp above 300 °C (CH_2Cl_2-MeOH). IR (film) cm^{-1}: 3306, 1667, 1520. ^{1}H-NMR ($CDCl_3$) δ: 0.88 (18H, d, *J* 6.8 Hz), 1.20~1.50 (84H, br), 1.69 (12H, brt, *J* 7.1 Hz), 2.64 (12H, br), 2.68 (12H, br), 3.15 (18H, s), 3.59 (12H, br), 7.17 (6H, d, *J* 1.6 Hz), 7.72 (6H, d, *J* 1.6 Hz), 9.43 (6H, s). ^{13}C-NMR ($CDCl_3$) δ: 14.12, 22.70, 29.35, 29.52, 29.55, 29.59, 29.65, 29.71, 31.23, 31.92, 35.85, 58.86, 74.97, 122.17, 125.96, 127.46, 137.23, 139.03, 142.46, 168.87. Fab-MS *m/z*: 1903 $(M+1)^+$.

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