Electronic Supplementary Information for

Crystallographic characterization of the 9/11-helix: a left-handed helix for 1:1 α/β-peptides containing L-α-amino acid residues

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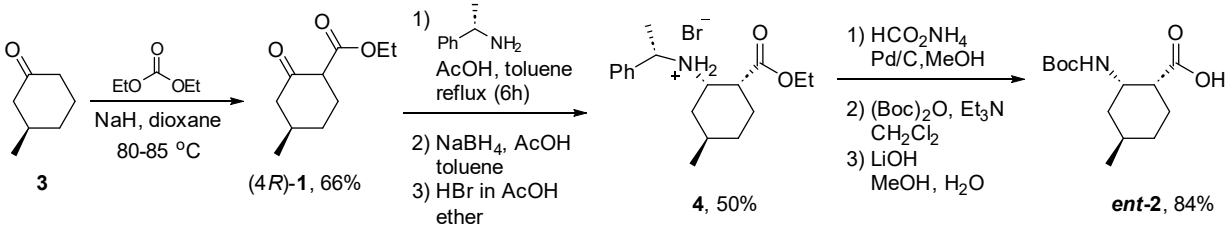
Experimental details and characterization data

General. 1-Ethyl-3-(3-dimethylaminopropyl)-carbodiimide (EDCI) were purchased from Chem-Impex International. Other reagents were purchased from Sigma-Aldrich, Alfa Aesar, Samchun Chemical, and TCI. Analytical thin-layer chromatography (TLC) was carried out on Pre-coated silica gel glass plate (Merck silica gel 60, F254, 0.25 mm). Silica gel 60 (230~240 mesh, Merck) was used for flash column chromatography. FT-IR spectra were recorded on Bruker Vertex 70 FT-IR spectrometer at 4000 cm^{-1} ~ 400 cm^{-1} of wave numbers. Mass spectra (MS) were acquired using an LTQ Orbitrap Spectrometer (ThermoFisher scientific Inc.). H-NMR and ^{13}C-NMR spectra were recorded on a 400 MHz FT-NMR Spectrometer (Bruker Biospin Avance Ⅱ or Bruker Biospin Avance Ⅲ HD 400).

Synthesis of *cis*,*trans*-mACHC monomer from a chiral precursor



Ethyl 4-(*R*)-methyl-2-cyclohexanonecarboxylate ((4*R*)-1). Diethyl carbonate (39.6 mL, 326.6 mmol, 8 eq.) and sodium hydride (~1.9 g, ~80 mmol, ~2 eq.) were added to dry dioxane (300 mL) in a 500 mL three-necked, round-bottom flask. (*R*)-(+)-3-methylcyclohexanone (**1**; 5 mL, 40.8 mmol, 1 eq.) was added dropwise over 3 h under nitrogen gas stream with stirring at 80-85 °C.[S1] The mixture was then stirred for additional 2h and cooled in an ice bath. As the reaction proceeded, hydrogen gas evolved and the reaction mixture became red. The solution was diluted with ether and washed with aqueous 1M HCl and brine. The organic layer was dried over magnesium sulfate, filtered and concentrated in vacuo to give a crude product, which was purified by vacuum distillation to yield (4*R*)-**1** as a yellowish liquid (TLC R_f = 0.6, 10 % ethyl acetate in hexane; 4.9 g, 26.9 mmol, 66%). The HPLC trace of (4*R*)-**1** was very similar to that of commercially available ethyl 4-methyl-2-cyclohexanonecarboxylate (Figure S1).

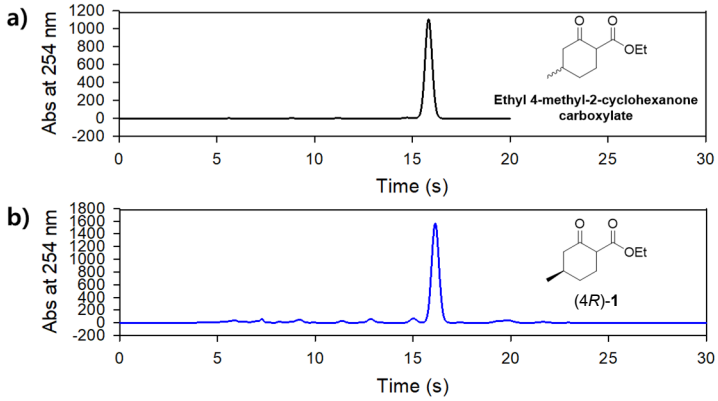


Figure S1. HPLC traces of 4-methyl-2-cyclohexanonecarboxylate: (a) racemate and (b) (4*R*)-**1** eluted by 70% acetonitrile in water.

Ethyl (1*R*,2*S*,4*R*)-4-methyl-2-(((*S*)-1-phenylethyl)amino)cyclohexane-1-carboxylate hydrobromide (4). To a three-necked, round-bottomed flask charged with toluene (35 mL) and equipped with a magnetic stirrer, a Dean-Stark trap fitted with a reflux condenser and a nitrogen gas inlet, (4*R*)-**1** (920 mg, 5 mmol, 1 eq.), (*S*)-1-phenylethylamine (0.7 mL, 5.5 mmol, 1.1 eq.) and glacial AcOH (0.31 mL, 5.5 mmol, 1.1 eq.) were added. The reaction mixture was stirred for 10 min at rt and then heated to reflux in a silicon oil bath (about 130 °C) for 6 h with azeotropic removal of water. The mixture was allowed to cool to rt, diluted with glacial acetic acid (20 mL) and cooled to 0 °C in an ice bath. $NaBH_4$ (473 mg, 12.5 mmol, 2.5 eq.) was slowly added to the cold mixture with vigorous stirring, maintaining the internal temperature below 50 °C. After the ice bath was removed, the viscous mixture was stirred for 2 h at rt. The reaction progress was monitored by TLC analysis on silica gel with 10% ethyl acetate in hexane as an eluent and visualization with 20% phosphomolybdenic acid in ethanol. The diluted reaction mixture was transferred to an Erlenmeyer flask equipped with a magnetic stirrer. The pH of the mixture was adjusted to 9 by the addition of aqueous 10 M NaOH solution, maintaining the internal temperature below 30 °C in an ice bath. The resulting mixture was then extracted with ether. Combined organic layers were dried over $MgSO_4$, filtered and concentrated by a rotary evaporator to provide a crude product, which was purified by flash column chromatography. The isolate major product (R_f = 0.4, 10% ethyl acetate in hexane; 720 mg, 2.5 mmol, 50%) was dissolved in ether (3.5 mL) and was added with 33% (w/w) HBr in acetic acid (0.53 mL, 3 mmol, 1.2 eq.). The mixture was

concentrated in vacuo to give the desired product **4** (930 mg, 2.5 mmol, 50% over the three steps). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.09 (s, 1H), 8.96 (s, 1H), 7.84 (d, *J* = 7.0 Hz, 2H), 7.44 (m, 3H), 4.56 (s, 1H), 4.27 (m, 2H), 3.55 (s, 1H), 3.00 (s, 1H), 2.30 (m, 2H), 2.03 (d, *J* = 7.0 Hz, 3H), 1.83 (m, 1H), 1.63 (m, 2H), 1.48 (s, 1H), 1.32 (t, *J* = 7.5 Hz, 3H), 1.14 (s, 1H), 0.84 (q, *J* = 6.0 Hz, 3H) ; ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.4, 136.2, 129.8, 129.7, 129.3, 128.3, 62.4, 62.1, 42.4, 26.3, 26.1, 20.5, 14.5, 14.1, 13.7 ; HRMS *m/z* Calcd for $C_{18}H_{27}NO_2$·HBr $[M+H-Br]^+$ 290.2115, found 290.2114.

(1*R*,2*S*,4*R*)-2-((tert-butoxycarbonyl)amino)-4-Methylcyclohexane-1-carboxylic acid (*ent*-2). To a three-necked round-bottomed flask with reflux condenser equipped with a magnetic stirrer and a nitrogen gas inlet, 10% Pd/C (900 mg) and methanol (30 mL) were successively added slowly under nitrogen gas stream. After the addition of **4** (930 mg, 2.5 mmol, 1 eq.) and ammonium formate (681.1 mg, 10.8 mmol, 5 eq.), the reaction mixture was stirred for 8 hr at 100 °C. After the reaction was complete, the mixture was filtered through celite pad. The filtrate was concentrated in vacuo to give the corresponding debenzylated amine salt (680 mg, quantitative), which was used for the next step without purification. To a solution of the amine salt (145 mg, 0.54 mmol, 1 eq.) in dichloromethane (10 mL), trimethylamine (0.66 mg, 0.65 mmol, 1.2 eq.) and $(Boc)_2O$ (178 mg, 0.81 mmol, 1.5 mmol) were added. The reaction mixture was stirred overnight at rt, diluted with ethyl acetate, washed with brine, dried over $MgSO_4$, filtered and concentrated in vacuo to give a crude product, which was purified by column chromatography to give a mixture of the corresponding N-Boc protected methyl and ethyl esters. The mixture was subsequently dissolved in methanol (3 mL) and THF (9 mL) and then was slowly added with LiOH (97 mg, 2.3 mmol, ~5 eq.) in H_2O (3 mL). The reaction mixture was stirred overnight, acidifed to pH 1 with aqueous 1 M HCl and extracted with ethyl acetate several times. The combined organic layer was washed with brine, dried over $MgSO_4$, filtered and concentrated in vacuo to give desired product ***ent*-2** (129 mg, 84% over three steps) ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.00 (s, 2H), 6.41 (s, 1H), 5.03 (s, 1H), 4.24 (s, 2H), 2.54 (s, 1H), 2.44 (s, 1H), 1.95-1.53 (m, 12H), 1.43 (s, 21H), 1.30-0.80 (m, 14H) ; ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.5, 177.3, 158.1, 155.5, 81.0, 79.7, 77.4, 49.3, 47.3, 45.3, 44.8, 39.9, 38.8, 33.4, 32.3, 29.8, 28.4, 26.6, 26.1, 22.9, 22.4, 22.1, 21.6 ; HRMS *m/z* Calcd for $C_{13}H_{23}NO_4$ $[M+Na]^+$, 280.1519, found 280.1534; calcd for $[2M+Na]^+$ 537.3146, found 537.3165; $[\alpha]_D^{20} = 410$, *c* 1.0 $CHCl_3$.

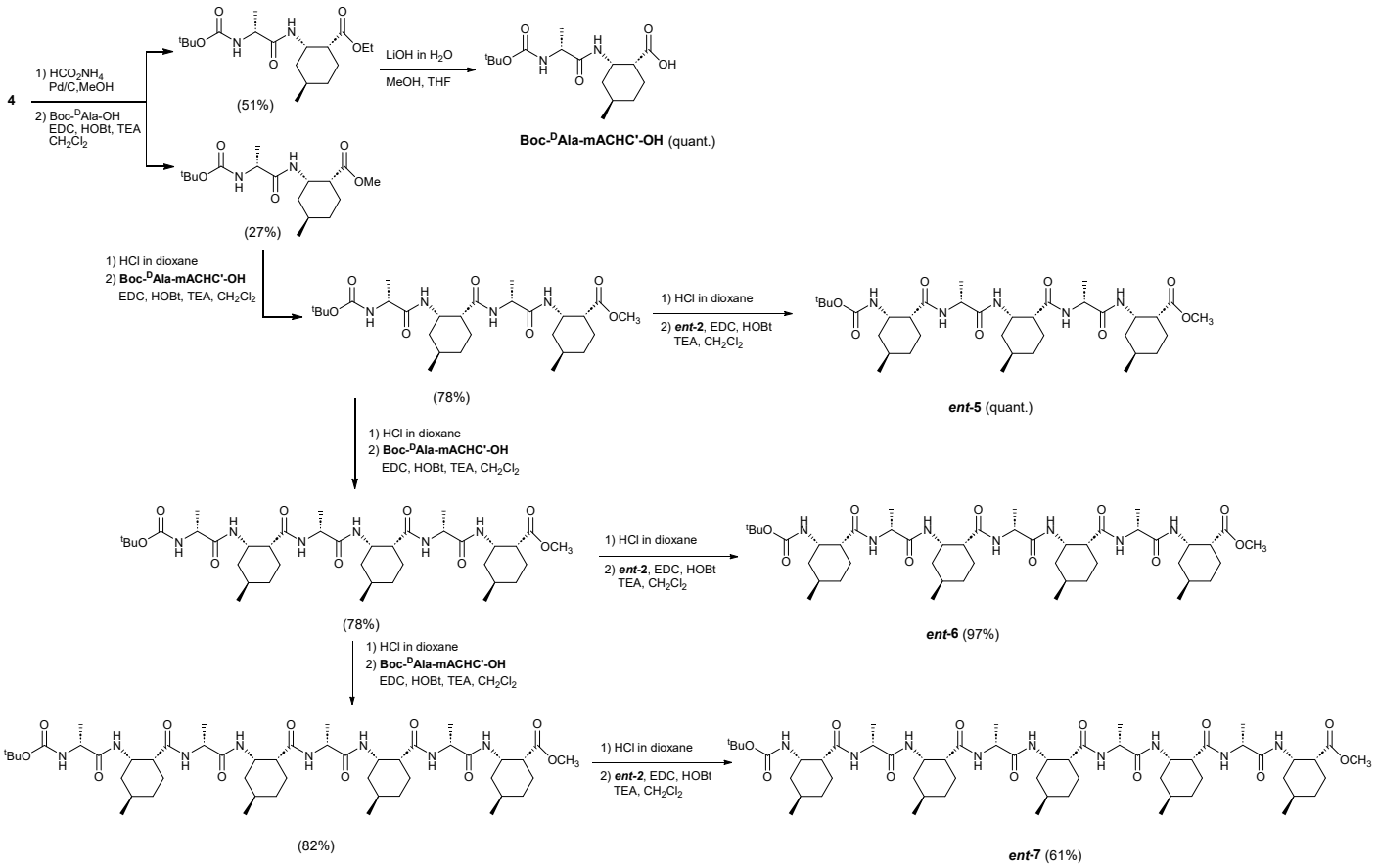
Synthesis of 1:1 α/β-peptide oligomers containing *cis*,*trans*-mACHC

1:1 α/β-Peptide oligomers **5**, ***ent*-5**, **6**, ***ent*-6**, **7** and ***ent*-7** were synthesized by a conventional fragment coupling strategy employing the genenral procedures analogous to the methods reported previously.[S2] The opposite enantiomers containing

General procedure for peptide coupling. A *N*-Boc protected peptide (1 eq.), EDC (1.5 eq.), HOBt (1.3 eq.) and triethylamine (1.1 eq.) are dissolved in dichloromethane (~0.1 M), and then an aminoester (1 eq) is added. The reaction mixture is stirred at rt for 24~48 h. The reaction mixture is diluted with ethyl acetate and successively washed with 10 % citric acid (x2), brine (x2), Na_2CO_3 (x2) and brine (x2). The organic layer is then dried over $MgSO_4$, filtered and concentrated to give a crude product, which is purified by column chromatography.

General procedure for deprotection of Boc group with HCl in dioxane. A *N*-Boc protected peptide (1 eq.) is treated with 4.0 M HCl in dioxane (*ca*. 10 eq.) for 1 h with stirring, and the mixture was concentrated under a nitrogen gas stream to give the corresponding HCl salt form of the amine segment.

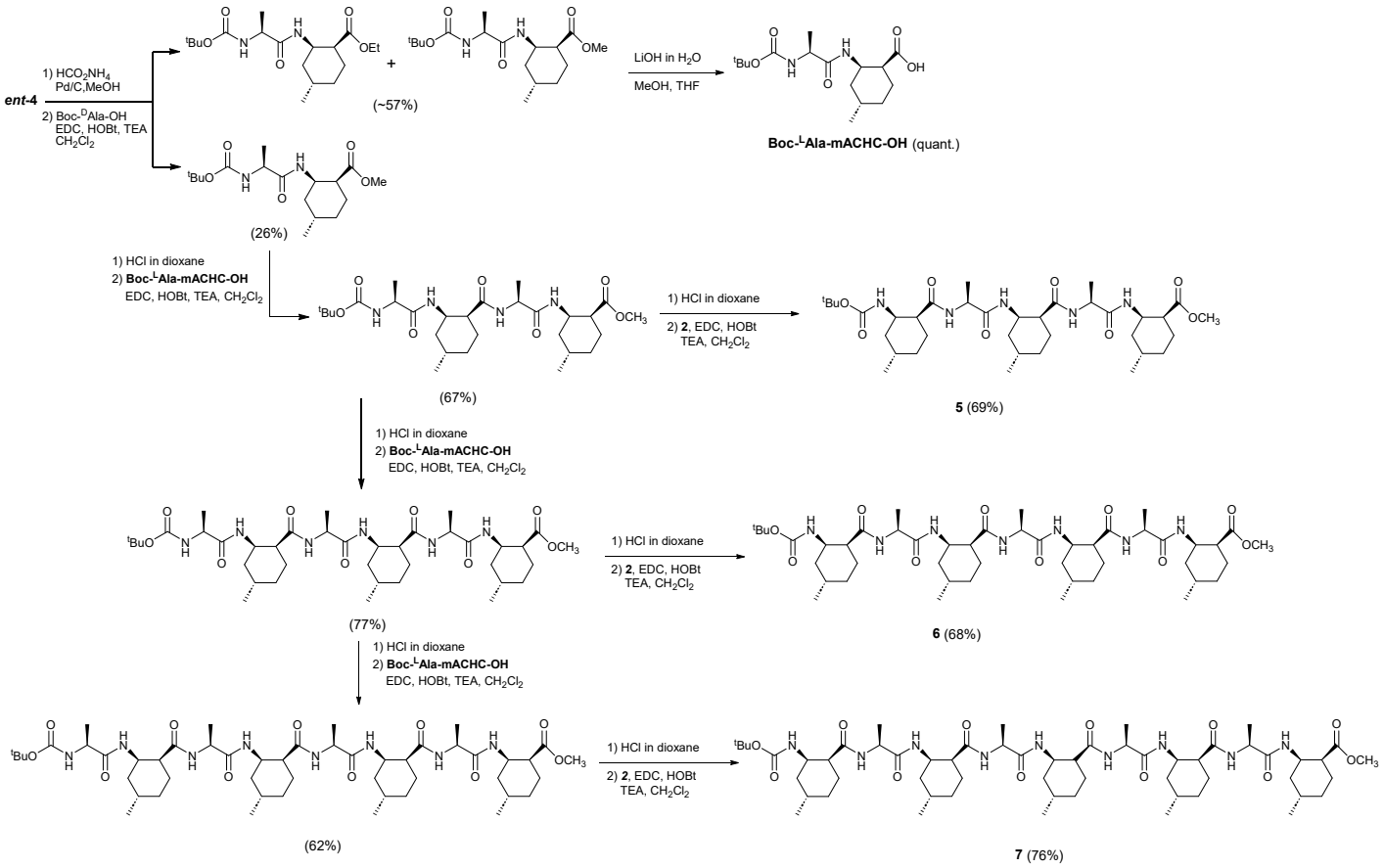
General procedure for saponification of the C-terminal ethyl ester group. To a 0.1 M solution of an ethyl ester (1 eq.) in methanol, H_2O and THF, LiOH (5 eq.) is added at 0 ℃. The mixture is stirred for 12 h at 0 ℃. After the reaction is over, aqueous 1 M HCl is added until pH 1. The mixture is extracted with EtOAc. The organic layer is washed with brine, dried over $MgSO_4$, filtered and concentrated in vacuo to give the carboxylic acid form, which is used without purification.



Boc-(1*R*,2*S*,4*R*)mACHC –(D-Ala-(1*R*,2*S*,4*R*)mACHC)$_2$-OMe (*ent*-5). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, *J* = 10.3 Hz, 1H), 7.64 (d, *J* = 8.6 Hz, 1H), 7.35 (d, *J* = 6.0 Hz, 1H), 6.76 (d, *J* = 6.7 Hz, 1H), 5.12 (d, *J* = 10.1 Hz, 1H), 4.76 (m, 1H), 4.58 (q, *J* = 4.8 Hz, 1H), 4.32 (d, *J* = 6.3 Hz, 2H), 4.19 (quintet, *J* = 6.7 Hz, 1H), 3.65 (s, 3H), 2.54 (m, 1H), 2.49-2.29 (m, 4H), 2.05-1.62 (m, 17H), 1.48 (m, 2H), 1.41 (s, 11H), 1.33 (m, 3H), 1.27 (m, 6H), 1.20 (d, *J* = 6.4 Hz, 5H), 0.95 (m, 3H), 0.92-0.81 (m, 13H) ; ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.9, 174.3, 173.3, 173.1, 171.9, 155.8, 79.7, 52.2, 49.5, 48.8, 48.7, 47.8, 47.0, 46.5, 46.2, 45.9, 39.7, 39.2, 39.0, 33.5, 33.4, 33.1, 29.9, 28.4, 27.0, 25.8, 23.0; HRMS *m/z* calculated for $C_{36}H_{61}N_5O_8$ 691.4520, found 714.4413 $[M+Na]^+$; $[\alpha]_D^{20} = 64$, *c* 0.1 $CHCl_3$.

Boc-(1*R*,2*S*,4*R*)mACHC –[D-Ala-(1*R*,2*S*,4*R*)mACHC]$_3$-OMe (*ent*-6). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (d, *J* = 9.2 Hz, 1H), 7.93 (d, *J* = 9.2 Hz, 1H), 7.52 (d, *J* = 6.9 Hz, 3H), 7.06 (s, 1H), 5.09 (d, *J* = 9.2 Hz, 1H), 4.76 (d, *J* = 4.6 Hz, 1H), 4.67 (s, 1H), 4.56 (d, *J* = 4.6 Hz, 1H), 4.33 (d, *J* = 6.9 Hz, 2H), 4.18 (t, *J* = 6.9 Hz, 2H), 3.66 (s, 3H), 2.54 (d, *J* = 11.6 Hz, 1H), 2.40 (m, 4H), 2.00-1.61 (m, 19H), 1.41 (s, 10H), 1.35-1.17 (m, 15H), 1.02-0.87 (m, 14H), 0.84 (d, *J* = 6.2 Hz, 3H) ; ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.5, 174.3, 173.5, 172.7, 172.3, 155.8, 79.6, 52.3, 49.6, 48.7, 469, 46.2, 45.6, 39.8, 39.0, 33.4, 33.0, 28.4, 27.0, 26.1, 25.8, 23.0, 22.9, 22.6, 22.4, 22.1, 17.2, 16.9; HRMS *m/z* calculated for $C_{47}H_{79}N_7O_{10}$ 901.5888, found 902.5962 $[M+H]^+$; $[\alpha]_D^{20} = 39$, *c* 0.1 $CHCl_3$.

Boc-(1*R*,2*S*,4*R*)mACHC –[L-Ala-(1*R*,2*S*,4*R*)mACHC]$_4$-OMe (*ent*-7) ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.20(d, J = 8.5 Hz, 1H), 7.95(m, 2H), 7.72(d, J = 8.17 Hz, 1H), 7.58(m, 3H), 7.07(s, 1H), 5.08(d, J = 9.7 Hz, 1H), 4.71(s, 2H), 4.59(s, 2H), 4.33(m, 2H), 4.21(m, 3H), 3.65(s, 3H), 2.54(dt, J_a = 12.3 Hz, J_b = 7.5 Hz, 1H), 2.42(m, 4H), 2.03-1.61(m, 22H), 1.41(s, 9H), 1.32-1.18(m, 20H), 0.98-0.80(m, 20H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 175.7, 174.2, 173.3, 173.2, 172.9, 155.8, 79.6, 52.3, 49.6, 48.7, 47.0, 46.1, 45.7, 39.8, 39.1, 33.7, 33.4, 33.1, 29.9, 28.4, 27.0, 26.1, 25.8, 23.0, 22.8, 22.6, 22.5, 22.3, 22.1, 16.9, 16.8, 14.3; MALDI-TOF MS m/z calculated for $C_{58}H_{97}N_9O_{12}$ $[M(Boc\ deprotecting)+H]^+$ 1012.68, found 1012.67, for $C_{58}H_{97}N_9O_{12}$ $[M+Na]^+$ 1134.71, found 1134.72, for $C_{58}H_{97}N_9O_{12}$ $[M+K]^+$ 1150.69, found 1150.64.



Boc-(1*S*,2*R*,4*S*)mACHC –(L-Ala-(1*S*,2*R*,4*S*)mACHC)$_2$-OMe (5). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, *J* = 10.3 Hz, 1H), 7.64 (d, *J* = 8.6 Hz, 1H), 7.35 (d, *J* = 6.0 Hz, 1H), 6.76 (d, *J* = 6.7 Hz, 1H), 5.12 (d, *J* = 10.1 Hz, 1H), 4.76 (m, 1H), 4.58 (q, *J* = 4.8 Hz, 1H), 4.32 (d, *J* = 6.3 Hz, 2H), 4.19 (quintet, *J* = 6.7 Hz, 1H), 3.65 (s, 3H), 2.54 (m, 1H), 2.49-2.29 (m, 4H), 2.05-1.62 (m, 17H), 1.48 (m, 2H), 1.41 (s, 11H), 1.33 (m, 3H), 1.27 (m, 6H), 1.20 (d, *J* = 6.4 Hz, 5H), 0.95 (m, 3H), 0.92-0.81 (m, 13H) ; ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.9, 174.3, 173.3, 173.1, 171.9, 155.8, 79.7, 52.2, 49.5, 48.8, 48.7, 47.8, 47.0, 46.5, 46.2, 45.9, 39.7, 39.2, 39.0, 33.5, 33.4, 33.1, 29.9, 28.4, 27.0, 25.8, 23.0

Boc-(1*S*,2*R*,4*S*)mACHC –[L-Ala-(1*S*,2*R*,4*S*)mACHC]$_3$-OMe (6). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (d, *J* = 9.2 Hz, 1H), 7.93 (d, *J* = 9.2 Hz, 1H), 7.52 (d, *J* = 6.9 Hz, 3H), 7.06 (s, 1H), 5.09 (d, *J* = 9.2 Hz, 1H), 4.76 (d, *J* = 4.6 Hz, 1H), 4.67 (s, 1H), 4.56 (d, *J* = 4.6 Hz, 1H), 4.33 (d, *J* = 6.9 Hz, 2H), 4.18 (t, *J* = 6.9 Hz, 2H), 3.66 (s, 3H), 2.54 (d, *J* = 11.6 Hz, 1H), 2.40 (m, 4H), 2.00-1.61 (m, 19H), 1.41 (s, 10H), 1.35-1.17 (m, 15H), 1.02-0.87 (m, 14H), 0.84 (d, *J* = 6.2 Hz, 3H) ; ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.5, 174.3, 173.5, 172.7, 172.3, 155.8, 79.6, 52.3, 49.6, 48.7, 469, 46.2, 45.6, 39.8, 39.0, 33.4, 33.0, 28.4, 27.0, 26.1, 25.8, 23.0, 22.9, 22.6, 22.4, 22.1, 17.2, 16.9

Boc-(1*S*,2*R*,4*S*)mACHC –[L-Ala-(1*S*,2*R*,4*S*)mACHC]$_4$-OMe (7)**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21(s, 1H), 7.97(m, 2H), 7,62(s, 3H), 7.13(s, 1H), 5.13(d, J = 9.6 Hz, 1H), 4.72(s, 2H), 4.60(s, 2H), 4.34(m, 2H), 4.22(m, 3H), 4.13(q, J = 7.3 Hz, 1H), 3.66(s, 3H), 2.55(dt, J_a = 12.4 Hz, J_b = 3.7 Hz, 1H), 2.44(m, 4H), 2.03-1.62(m, 22H), 1.42(s, 9H), 1.32-1.18(m, 16H), 1.01-0.87(m, 15H), 1.03-0.80(m, 19H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 175.4, 174.0, 173.3, 173.0, 172.7, 172.1, 155.7, 79.4, 52.1, 52.0, 49.4, 48.6, 46.8, 46.0, 45.5, 39.6, 39.0, 33.2, 32.9, 29.7, 29.3, 28.3, 26.8, 26.0, 25.7, 22.8, 22.7, 22.5, 22.3, 22.2, 22.0, 21.3, 21.0, 20.9, 16.7, 16.6, 14.2, 14.1; HRMS *m/z* calculated for $C_{58}H_{97}N_9O_{12}$ $[M+Na]^+$ 1134.7149, found 1134.7153.

Circular Dichroism Experiment

Circular Dichroism spectra were measured by using JASCO-815 spectrometer at 298K. The spectra were acquired using 1-mm path length cell, wavelength range of 190 to 260 nm with 0.1 nm data interval, 1.0 nm bandwidth, and 100 nm/min scanning speed. CD data were acquired by the background from the sample spectrum and smoothened over 25 data points. The final spectra were normalized for path length and concentration. The sample concentrations were 0.3 mM in methanol or acetonitrile.

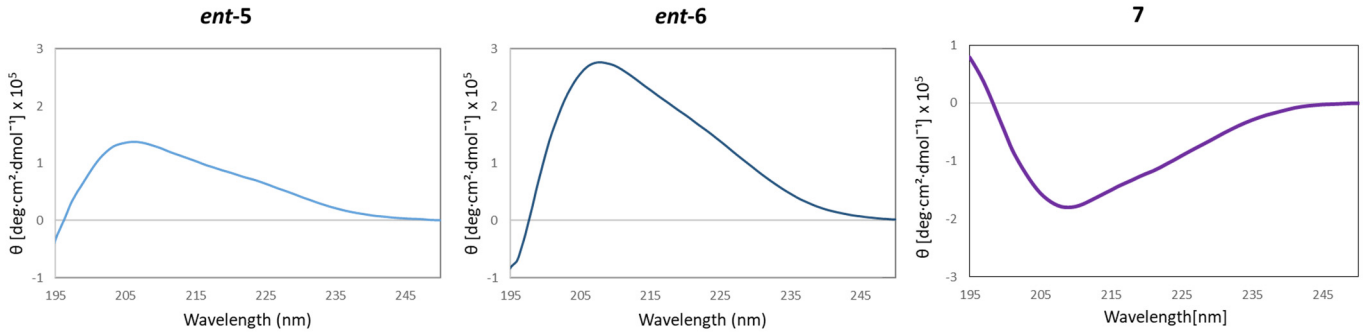


Figure S2. CD spectra of pentamer ***ent*-5**, heptamer ***ent*-6** and nonamer **7** in methanol.

Two-dimensional NMR Experiments

Two-dimensional NMR data were acquired at Korea Basic Science Institute (KBSI, Western Seoul branch). ROESY and TOCSY spectra of ***ent*-5**, ***ent*-6** and **7** in CD_3CN (10 mM) were recorded on Varian UNITY INIVA 500 NMR spectrometer at 293 K. All resonance for each of peptides was assigned based on TOCSY data and sequential NOEs from ROESY data.

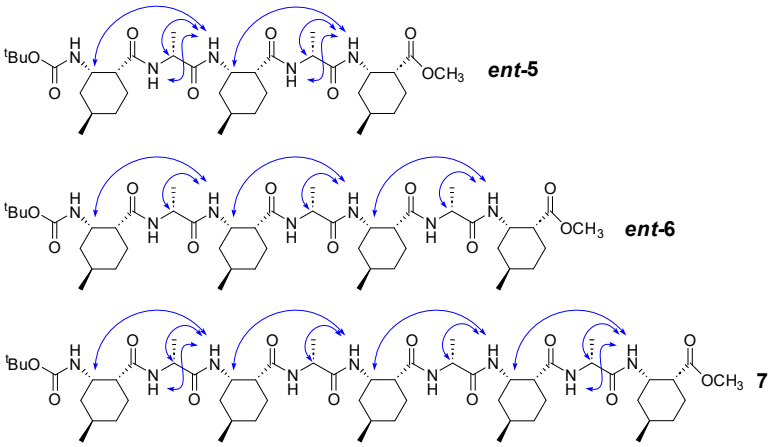


Figure S3. Characteristic NOEs for the 11/9-helix observed in the ROESY spectra of pentamer ***ent*-5**, heptamer ***ent*-6** and nonamer **7** in CD_3CN.

Two-dimensional NMR Spectra

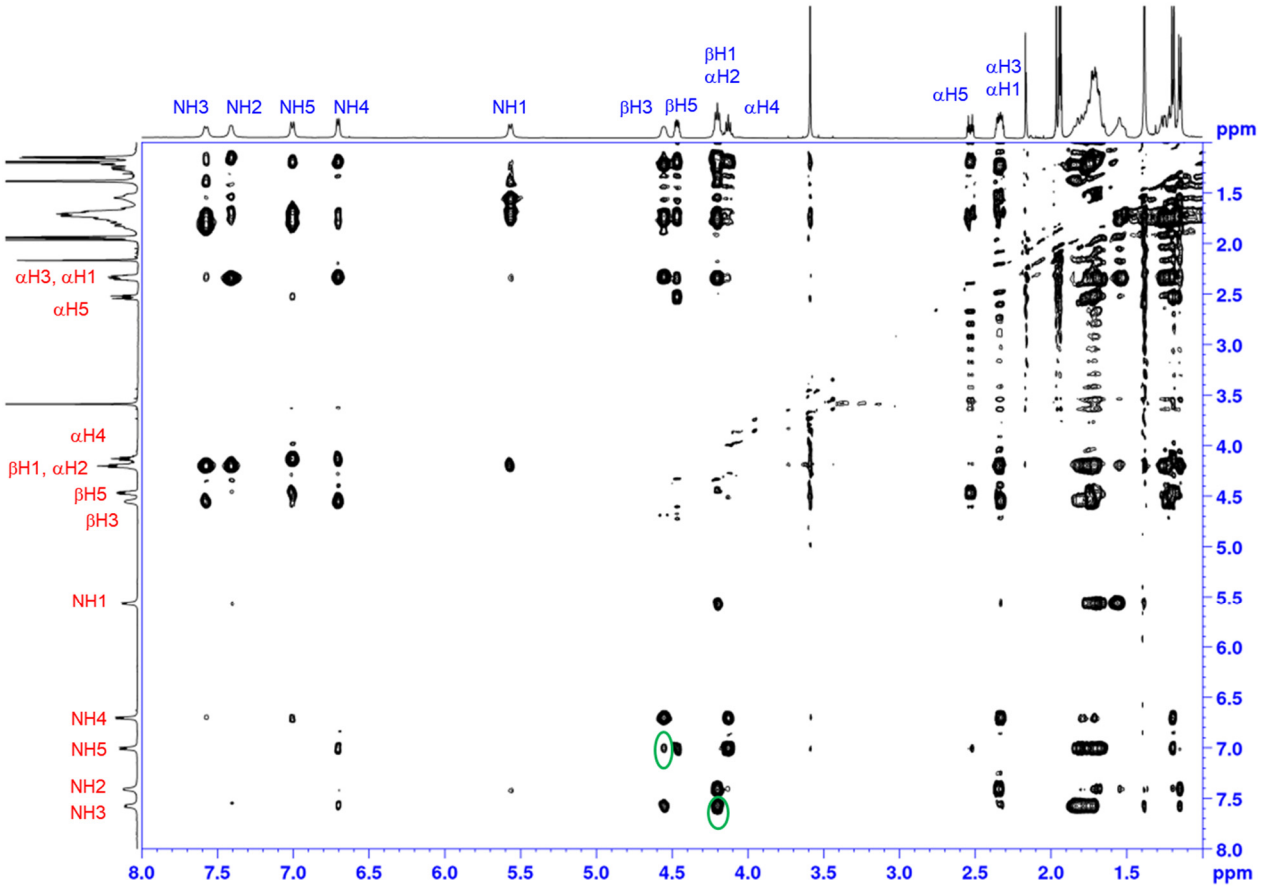


Figure S4. ROESY spectrum of ***ent*-5** in CD_3CN. Green circles indicate nonsequential NOEs: β-residue $C_\beta H(i)$–NH(i+2).

Table S1. Inter-residue NOEs observed for ***ent*-5** in CD_3CN. Characteristic NOEs for the 9/11-helix are highlighted yellow.

Residue	H atom	Residue	H atom	Intensity
β-residue (1)	NH	α-residue (2)	NH	W
β-residue (1)	$C_\alpha H$	α-residue (2)	NH	S
β-residue (1)	$C_\beta H$	β-residue (3)	NH	M*
α-residue (2)	NH	β-residue (3)	NH	W
α-residue (2)	$C_\alpha H$	β-residue (3)	NH	M*
β-residue (3)	NH	α-residue (4)	NH	W
β-residue (3)	$C_\alpha H$	α-residue (4)	NH	S
β-residue (3)	$C_\beta H$	α-residue (4)	NH	S
β-residue (3)	$C_\beta H$	β-residue (5)	NH	W
α-residue (4)	NH	β-residue (5)	NH	M
α-residue (4)	$C_\alpha H$	β-residue (5)	NH	S

W: weak; M: medium; S: strong.
* Ambiguous NOEs because of overlap with other NOEs

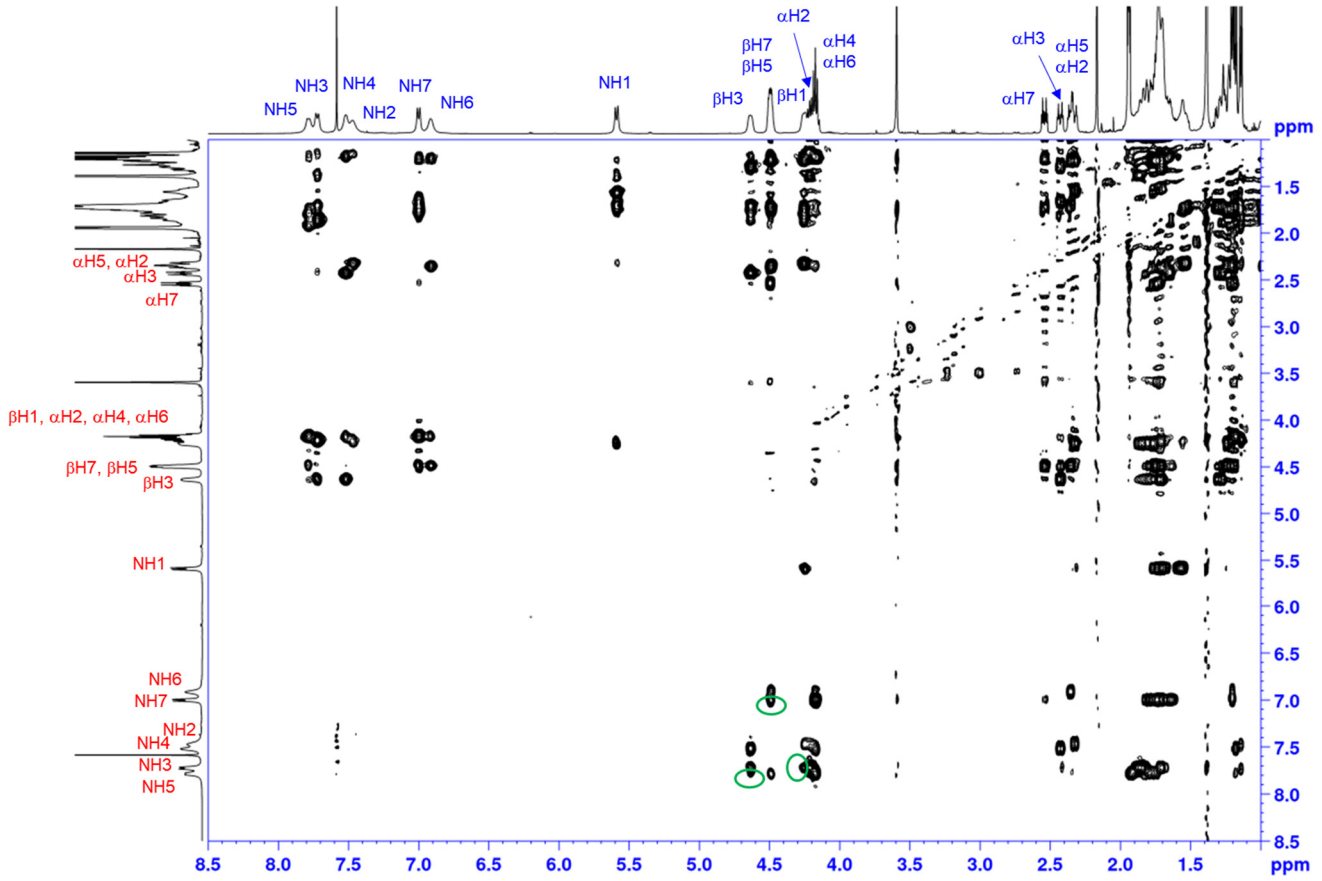


Figure S5. ROESY spectrum for ***ent*-6** in CD_3CN. Green circles indicate nonsequential NOEs: β-residue $C_\beta H(i)$–NH(i+2).

Table S2. Inter-residue NOEs observed of ***ent*-6** in CD_3CN. Characteristic NOEs for the 9/11-helix are highlighted yellow.

Residue	H atom	Residue	H atom	Intensity
β-residue (1)	$C_\alpha H$	α-residue (2)	NH	S
β-residue (1)	$C_\beta H$	β-residue (3)	NH	M*
α-residue (2)	$C_\alpha H$	β-residue (3)	NH	M*
β-residue (3)	$C_\alpha H$	α-residue (4)	NH	S
β-residue (3)	$C_\beta H$	α-residue (4)	NH	S
β-residue (3)	$C_\beta H$	β-residue (5)	NH	W
α-residue (4)	$C_\alpha H$	β-residue (5)	NH	S
β-residue (5)	NH	α-residue (6)	NH	W
β-residue (5)	$C_\alpha H$	α-residue (6)	NH	S
β-residue (5)	$C_\beta H$	α-residue (6)	NH	S*
β-residue (5)	$C_\beta H$	β-residue (7)	NH	M*
α-residue (6)	$C_\alpha H$	β-residue (7)	NH	S

W: weak; M: medium; S: strong.
* Ambiguous NOEs because of overlap with other NOEs

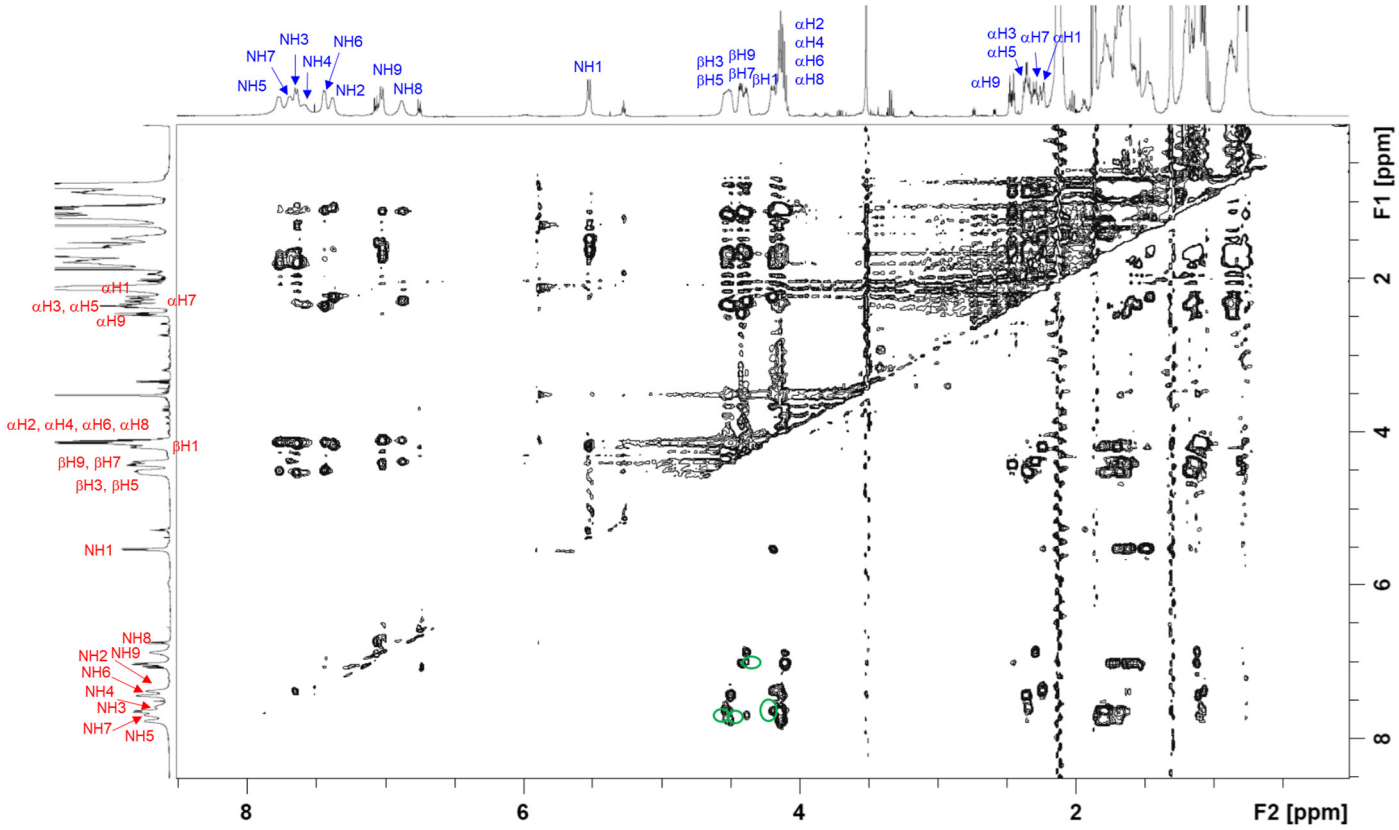


Figure S6. ROESY spectrum of **7** in CD_3CN. Green circles indicate nonsequential NOEs: β-residue $C_\beta H(i)$–NH(i+2).

Table S3. Inter-residue NOEs observed for ***ent*-6** in CD_3CN. Characteristic NOEs for the 9/11-helix are highlighted yellow.

Residue	H atom	Residue	H atom	Intensity
β-residue (1)	$C_\alpha H$	α-residue (2)	NH	S
β-residue (1)	$C_\beta H$	β-residue (3)	NH	S
α-residue (2)	$C_\alpha H$	β-residue (3)	NH	M*
α-residue (2)	NH	β-residue (3)	NH	M
β-residue (3)	$C_\alpha H$	α-residue (4)	NH	M
β-residue (3)	$C_\beta H$	α-residue (4)	NH	S
β-residue (3)	$C_\beta H$	β-residue (5)	NH	M
α-residue (4)	$C_\alpha H$	β-residue (5)	NH	S
β-residue (5)	$C_\alpha H$	α-residue (6)	NH	S
β-residue (5)	$C_\beta H$	α-residue (6)	NH	S
β-residue (5)	$C_\beta H$	β-residue (7)	NH	W*
α-residue (6)	$C_\alpha H$	β-residue (7)	NH	S
β-residue (7)	$C_\alpha H$	α-residue (8)	NH	S
β-residue (7)	$C_\beta H$	α-residue (8)	NH	S
β-residue (7)	$C_\beta H$	β-residue (9)	NH	W
α-residue (8)	$C_\alpha H$	β-residue (9)	NH	W

W: weak; M: medium; S: strong.
* Ambiguous NOEs because of overlap with other NOEs

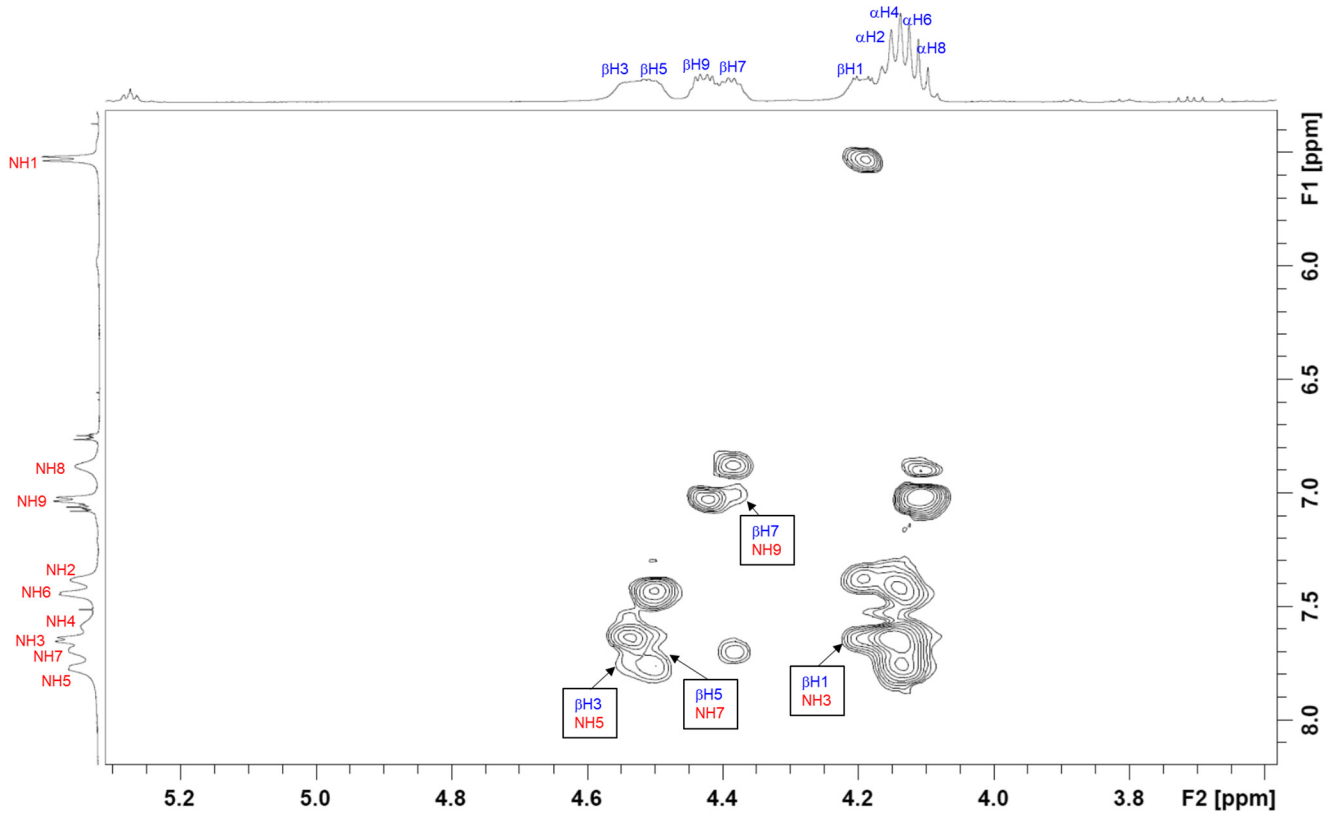


Figure S7. Partial ROESY spectrum for **7** in CD_3CN, indicating nonsequential NOEs: β-residue $C_\beta H(i)$–NH(i+2).

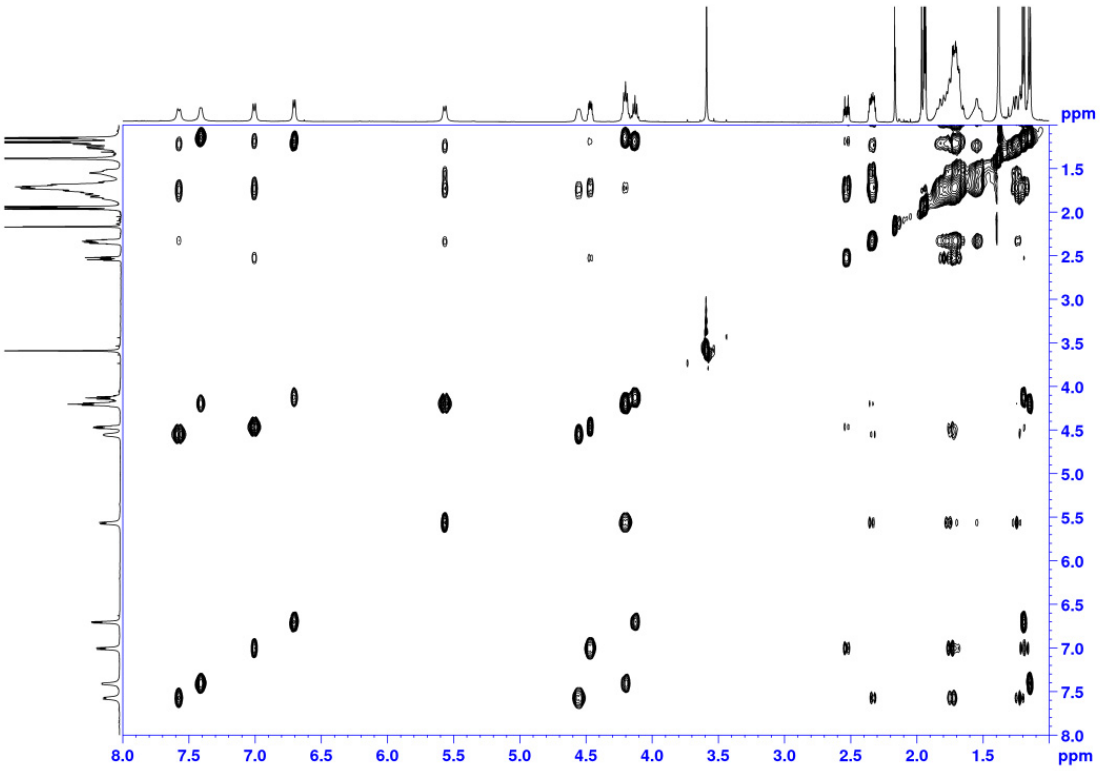


Figure S8. TOCSY spectrum of ***ent*-5** in CD_3CN.

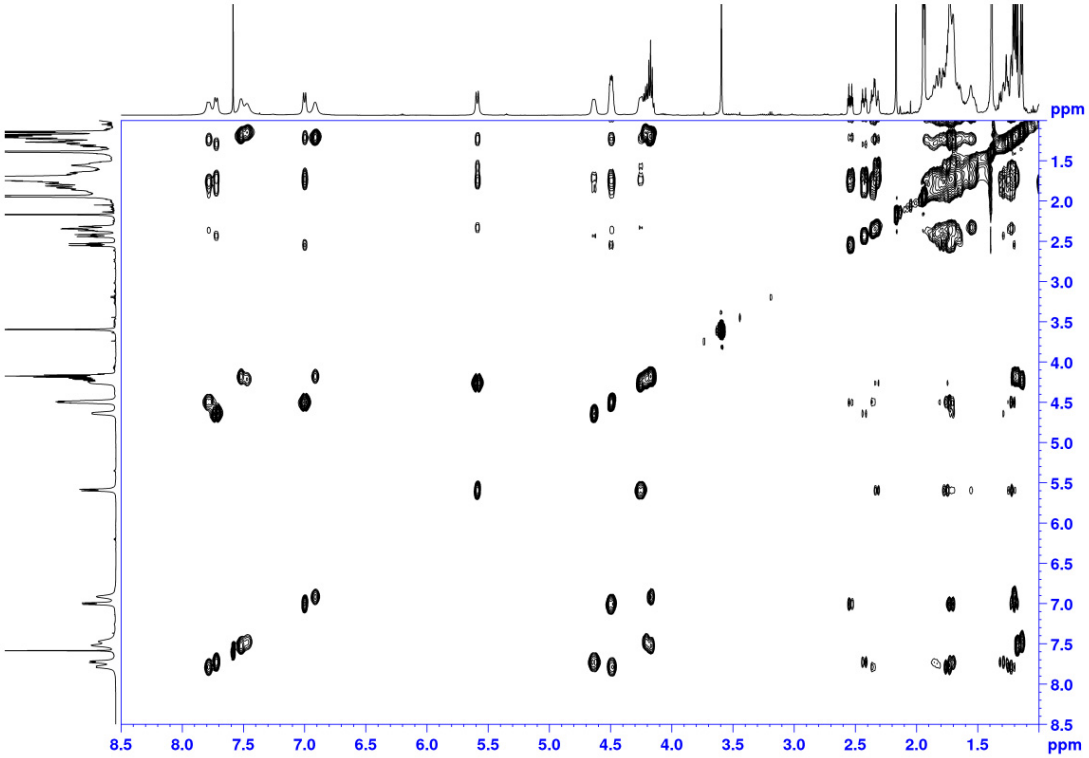


Figure S9. TOCSY spectrum of ***ent*-6** in CD_3CN.

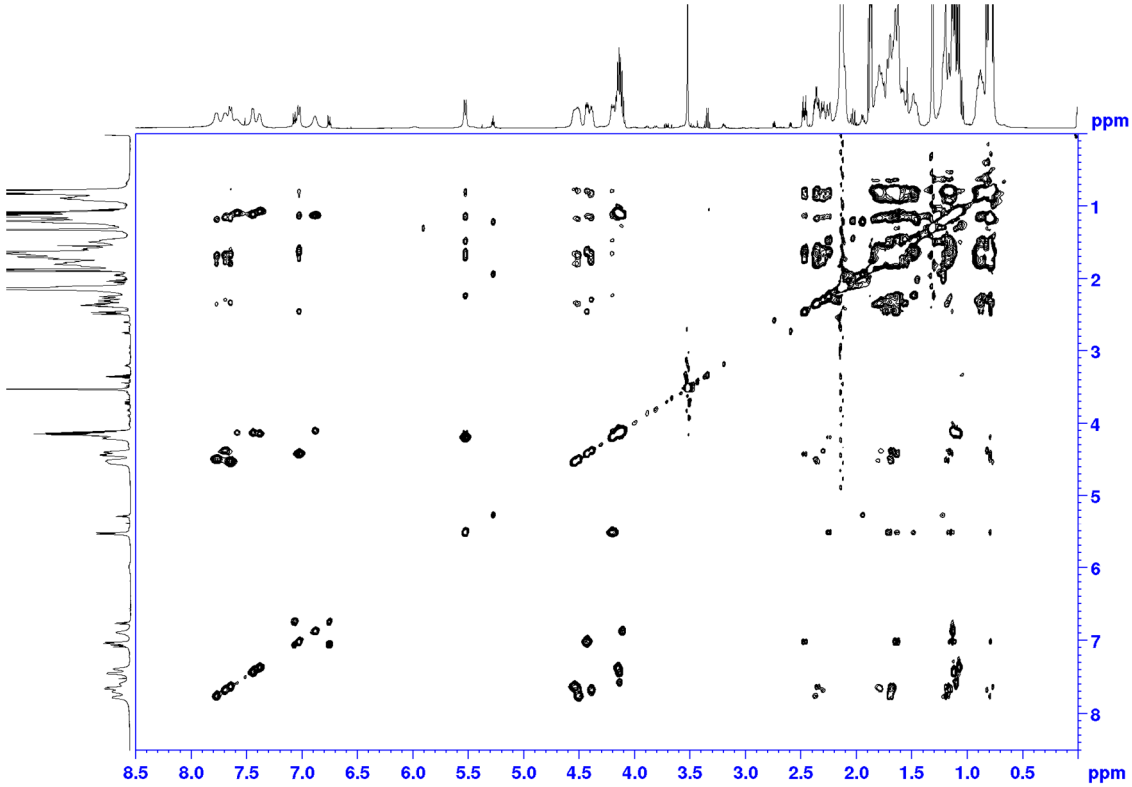


Figure S10. TOCSY spectrum of **7** in CD_3CN.

Crystallization and X-ray structural analysis

Table S4. Crystallization conditions and CCDC deposition numbers.

CCDC number[a]	compound	crystallization condition
1498493	***rac*-5**	Solvent diffusion ($CHCl_3$/*n*-pentane)
1577177	***rac*-6**	Solvent diffusion ($CHCl_3$/*n*-pentane)
2045065	***rac*-7**	Solvent diffusion ($CHCl_3$/*n*-pentane)

a. Deposition number at the Cambridge Crystallographic Data Centre (CCDC).

Crystal Structure Report

♦ Racemate of 1:1 α/β-peptide pentamers (*rac*-5)

Data Collection

A colorless crystal with approximate dimensions 0.60 x 0.32 x 0.10 mm^3 was selected under oil under ambient conditions and attached to the tip of a MiTeGen MicroMount©. The crystal was mounted in a stream of cold nitrogen at 100(1) K and centered in the X-ray beam by using a video camera.

The crystal evaluation and data collection were performed on a Bruker Quazar SMART APEXII diffractometer with Mo K_α (λ = 0.71073 Å) radiation and the diffractometer to crystal distance of 4.96 cm.[S3]

The initial cell constants were obtained from three series of ω scans at different starting angles. Each series consisted of 12 frames collected at intervals of 0.5º in a 6º range about ω with the exposure time of 10 seconds per frame. The reflections were successfully indexed by an automated indexing routine built in the APEXII program suite. The final cell constants were calculated from a set of 5401 strong reflections from the actual data collection.

The data were collected by using the full sphere data collection routine to survey the reciprocal space to the extent of a full sphere to a resolution of 0.83 Å. A total of 27470 data were harvested by collecting 6 sets of frames with 0.5º scans in ω and φ with exposure times of 30 sec per frame. These highly redundant datasets were corrected for Lorentz and polarization effects. The absorption correction was based on fitting a function to the empirical transmission surface as sampled by multiple equivalent measurements.[S4]

Structure Solution and Refinement

The systematic absences in the diffraction data were consistent for the space groups $P\bar{1}$ and $P1$. The *E*-statistics strongly suggested the centrosymmetric space group $P\bar{1}$ that yielded chemically reasonable and computationally stable results of refinement.[S4-6]

A successful solution by the direct methods provided most non-hydrogen atoms from the *E*-map. The remaining non-hydrogen atoms were located in an alternating series of least-squares cycles and difference Fourier maps. All non-hydrogen atoms were refined with anisotropic displacement coefficients unless specified otherwise. All hydrogen atoms were included in the structure factor calculation at idealized positions and were allowed to ride on the neighboring atoms with relative isotropic displacement coefficients.

The main molecule was disordered over two positions with a ratio of 52.6(6):47.4(6). Atoms C26, C28, O6, and N5 of the main component of the molecule were constrained to have the same anisotropic thermal parameters. Atoms C24A, C25A, O5A, and N4A of the minor component of the molecule were constrained to have the same anisotropic thermal parameters. These molecules were refined with bond distance restraints.

The compound crystalizes as a racemic mixture. The absolute configuration of the arbitrarily chosen enantiomer is C7-*R*, C9-*S*, C13-*S*, C15-*S*, C18-*R*, C20-*S,* C24-*S*, C26-*S,* C29-*R,* C31-*S* and C35-*S.*

There were approximately two solvent molecules (0.54 chloroform and 1.02 dichloromethane) disordered over ten positions also present in the asymmetric unit. A significant amount of time was invested in identifying and refining the disordered molecules. The molecules were modeled based on the solvents used during synthesis and crystallization.

Chloroform molecule containing atom C38 was refined anisotropically with an idealized geometry and anisotropic displacement coefficient restraints to an occupancy of 43.7(4)%.[S9]

Dichloromethane molecule containing atom C39 was refined anisotropically with an idealized geometry and anisotropic displacement coefficient restraints to an occupancy of 18.3(2)%.[S9]

Dichloromethane molecule containing atom C40 was refined anisotropically with an idealized geometry and anistropic displacement coefficient restraints to an occupancy of 20.2(4)%.[S9]

Dichloromethane molecule containing atom C41 was refined isotropically with geometric and thermal displacement parameter constraints to an occupancy of 12.7(3)%.[S9]

Dichloromethane molecule containing atom C42 was refined isotropically with geometric and thermal displacement parameter constraints to an occupancy of 10.7(3)%.[S9]
Chloroform molecule containing atom C43 was refined isotropically with geometric and thermal displacement parameter constraints to an occupancy of 10.5(3)%.[S9]
Dichloromethane molecule containing atom C44 was refined isotropically with geometric and thermal displacement parameter constraints to an occupancy of 6.0(2)%.[S9]
Dichloromethane molecule containing atom C45 was refined isotropically with geometric and thermal displacement parameter constraints to an occupancy of 6.4(2)%.[S9]
Dichloromethane molecule containing atom C46 was refined anisotropically with an idealized geometry and anisotropic displacement coefficient restraints to an occupancy of 18.1(4)%.[S9]
Dichloromethane molecule containing atom C47 was refined isotropically with geometric and thermal displacement parameter constraints to an occupancy of 9.6(2)%.[S9]
The final least-squares refinement of 984 parameters against 11090 data resulted in residuals *R* (based on F^2 for $I \geq 2\sigma$) and *wR* (based on F^2 for all data) of 0.0714 and 0.2099, respectively. The final difference Fourier map was featureless.

Summary
Crystal Data for $C_{36}H_{61}N_5O_8$, 0.54 $CHCl_3$, 1.02 CH_2Cl_2 (M =843.15 g/mol): triclinic, space group P-1 (no. 2), a = 11.974(5) Å, b = 13.462(5) Å, c = 16.117(6) Å, α = 94.77(2)°, β = 103.893(18)°, γ = 115.491(18)°, V = 2224.2(15) Å^3, Z = 2, T = 100.0 K, μ(MoKα) = 0.298 mm^{-1}, *Dcalc* = 1.259 g/cm^3, 27530 reflections measured (2.664° ≤ 2Θ ≤ 56.748°), 11090 unique (R_{int} = 0.0344, R_{sigma} = 0.0640) which were used in all calculations. The final R_1 was 0.0714 (I > 2σ(I)) and wR_2 was 0.2099 (all data).

Table S5. Crystal data and structure refinement for *rac*-5.

Empirical formula	$C_{36}H_{61}N_5O_8$, 0.54 $CHCl_3$, 1.02 CH_2Cl_2
Formula weight	843.15
Temperature/K	100.0
Crystal system	triclinic
Space group	$P\bar{1}$
a/Å	11.974(5)
b/Å	13.462(5)
c/Å	16.117(6)
α/°	94.77(2)
β/°	103.893(18)
γ/°	115.491(18)
Volume/Å^3	2224.2(15)
Z	2
ρ_{calc}g/cm^3	1.259
μ/mm^{-1}	0.298
F(000)	900.0
Crystal size/mm^3	0.6 × 0.32 × 0.1
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	2.664 to 56.748
Index ranges	-15 ≤ h ≤ 15, -17 ≤ k ≤ 18, -21 ≤ l ≤ 21
Reflections collected	27530
Independent reflections	11090 [R_{int} = 0.0344, R_{sigma} = 0.0640]
Data/restraints/parameters	11090/918/984
Goodness-of-fit on F^2	1.064
Final R indexes [I>=2σ (I)]	R_1 = 0.0714, wR_2 = 0.1860
Final R indexes [all data]	R_1 = 0.1124, wR_2 = 0.2099
Largest diff. peak/hole / e Å^{-3}	0.81/-0.75

♦ Racemate of 1:1 α/β-peptide heptamers (*rac*-6)

Data Collection

The diffraction data from yellow crystals (0.08 × 0.06 × 0.03 mm^3) mounted on a MiTeGen MicroMount© were collected at 100 on a ADSC Quantum 210 CCD diffractometer with synchrotron radiation (0.63000 Å) at Supramolecular Crystallography 2D, Pohang Accelerator Laboratory (PAL), Pohang, Korea. The ADSC Q210 ADX program[S10] was used for data collection (detector distance is 63 mm, omega scan; Δω = 1º, exposure time is 1 sec/frame and HKL3000sm (Ver. 703r)[S11] was used for cell refinement, reduction and absorption correction. The crystal structure was solved by the direct method with SHELX-XT (Ver. 2015/4) [S12] and refined by full-matrix least-squares calculations with the SHELX-XL (Ver. 2016/4)[S13] program package.

Structure Solution and Refinement

The systematic absences in the diffraction data were uniquely consistent for the space group Fd-3 that yielded chemically reasonable and computationally stable results of refinement.[S7,13]

A successful solution by the direct methods provided most non-hydrogen atoms from the *E*-map. The remaining non-hydrogen atoms were located in an alternating series of least-squares cycles and difference Fourier maps. All non-hydrogen atoms were refined with anisotropic displacement coefficients. All hydrogen atoms were included in the structure factor calculation at idealized positions and were allowed to ride on the neighboring atoms with relative isotropic displacement coefficients. The final least-squares refinement of 1763 parameters against 21364 data resulted in residuals *R* (based on F^2 for $I \geq 2\sigma$) and *wR* (based on F^2 for all data) of 0.0465 and 0.1685, respectively. The final difference Fourier map was featureless.

Summary

Crystal Data for $C_{47}H_{79}N_7O_{10}$ (*M* =902.17 g/mol): triclinic, space group P-1 (no. 2), *a* = 18.468(4) Å, *b* = 19.384(4) Å, *c* = 23.636(5) Å, *α* = 99.67(3)°, *β* = 93.03(3)°, *γ* = 106.32(3)°, *V* = 7960(3) $Å^3$, *Z* = 6, *T* = 100 K, μ(synchrotron) = 0.062 mm^{-1}, *Dcalc* = 1.129 g/cm^3, 92826 reflections measured (2.702° ≤ 2Θ ≤ 40.998°), 21364 unique (R_{int} = 0.0577, R_{sigma} = 0.1145) which were used in all calculations. The final R_1 was 0.0465 (I > 2σ(I)) and wR_2 was 0.1685 (all data).

Table S6. Crystal data and structure refinement for *rac*-6.

Empirical formula	$C_{47}H_{79}N_7O_{10}$
Formula weight	902.17
Temperature/K	100
Crystal system	triclinic
Space group	P-1
a/Å	18.468(4)
b/Å	19.384(4)
c/Å	23.636(5)
α/°	99.67(3)
β/°	93.03(3)
γ/°	106.32(3)
Volume/$Å^3$	7960(3)
Z	6
$\rho_{calc}g/cm^3$	1.129
μ/mm^{-1}	0.062
F(000)	2940.0
Crystal size/mm^3	0.08 × 0.06 × 0.03
Radiation	synchrotron (λ = 0.63000)
2Θ range for data collection/°	2.702 to 40.998
Index ranges	-28 ≤ h ≤ 28, -30 ≤ k ≤ 30, -36 ≤ l ≤ 36
Reflections collected	92826
Independent reflections	21364 [R_{int} = 0.0577, R_{sigma} = 0.1145]
Data/restraints/parameters	21364/6/1763
Goodness-of-fit on F^2	0.817
Final R indexes [I>=2σ (I)]	R_1 = 0.0465, wR_2 = 0.1503
Final R indexes [all data]	R_1 = 0.1075, wR_2 = 0.1685
Largest diff. peak/hole / e $Å^{-3}$	0.25/-0.25

♦ Racemate of 1:1 α/β-peptide nonamers (*rac*-7)

Data Collection and Structure Refinement

The crystal structures of ***rac*-7** were determined by standard crystallographic methods. A colorless block-shaped crystal (0.219 × 0.204 × 0.156 mm^3) was used for single-crystal X-ray diffraction. The data were collected at 223(2) K using a Bruker D8 Venture equipped with IμS micro-focus sealed tube Mo Kα (λ= 0.71073 Å) and a PHOTON III M14 detector in Western Seoul Center of Korea Basic Science Institute. Data collection and integration were performed with SMART APEX3 software package (SAINT+).[S10] Absorption correction was performed by multi-scan method implemented in SADABS.[S11] The structure was solved by direct methods and refined by full-matrix least-squares on F2 using SHELXTL program package (version 6.14).[S12] All the non-hydrogen atoms were refined anisotropically, and hydrogen atoms were added to their geometrically ideal positions.

Summary

Crystal Data for $C_{58}H_{97}N_9O_{12}$ (*M* =1112.4 g/mol): monoclinic, space group $P2_1/n$, *a* = 10.7446(12) Å, *b* = 18.069(2) Å, *c* = 37.895(4) Å, *α* = 90°, *β* = 90.547(4)°, *γ* = 90°, *V* = 7356.7(14) $Å^3$, *Z* = 4, *T* = 223(2) K, μ = 0.570 mm^{-1}, *Dcalc* = 1.004 Mg/cm^3, 89374 reflections measured (2.332° ≤ 2Θ ≤ 77.803°), 15366 unique (R_{int} = 0.1302) which were used in all calculations. The final R_1 was 0.1164 (I > 2σ(I)) and wR_2 was 0.4080 (all data).

Table S7. Crystal data and structure refinement for *rac*-7.

Empirical formula	C58 H97 N9 O12 [+ solvent]	
Formula weight	1112.44	
Temperature	223(2) K	
Wavelength	1.54178 Å	
Crystal system	Monoclinic	
Space group	$P2_1/n$	
Unit cell dimensions	a = 10.7446(12) Å	α= 90°.
	b = 18.069(2) Å	β= 90.547(4)°.
	c = 37.895(4) Å	γ = 90°.
Volume	7356.7(14) $Å^3$	
Z	4	
Density (calculated)	1.004 Mg/m^3	
Absorption coefficient	0.570 mm^{-1}	
F(000)	2416	
Crystal size	0.219 x 0.204 x 0.156 mm^3	
Theta range for data collection	2.332 to 77.803°.	
Index ranges	-12<=h<=13, -22<=k<=21, -47<=l<=46	
Reflections collected	89374	
Independent reflections	15366 [R(int) = 0.1302]	
Completeness to theta = 67.679°	98.6 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7541 and 0.6168	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	15366 / 0 / 725	
Goodness-of-fit on F^2	1.481	
Final R indices [I>2sigma(I)]	R1 = 0.1164, wR2 = 0.3559	
R indices (all data)	R1 = 0.2091, wR2 = 0.4080	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.601 and -0.528 $e.Å^{-3}$	

Copies of NMR Spectra

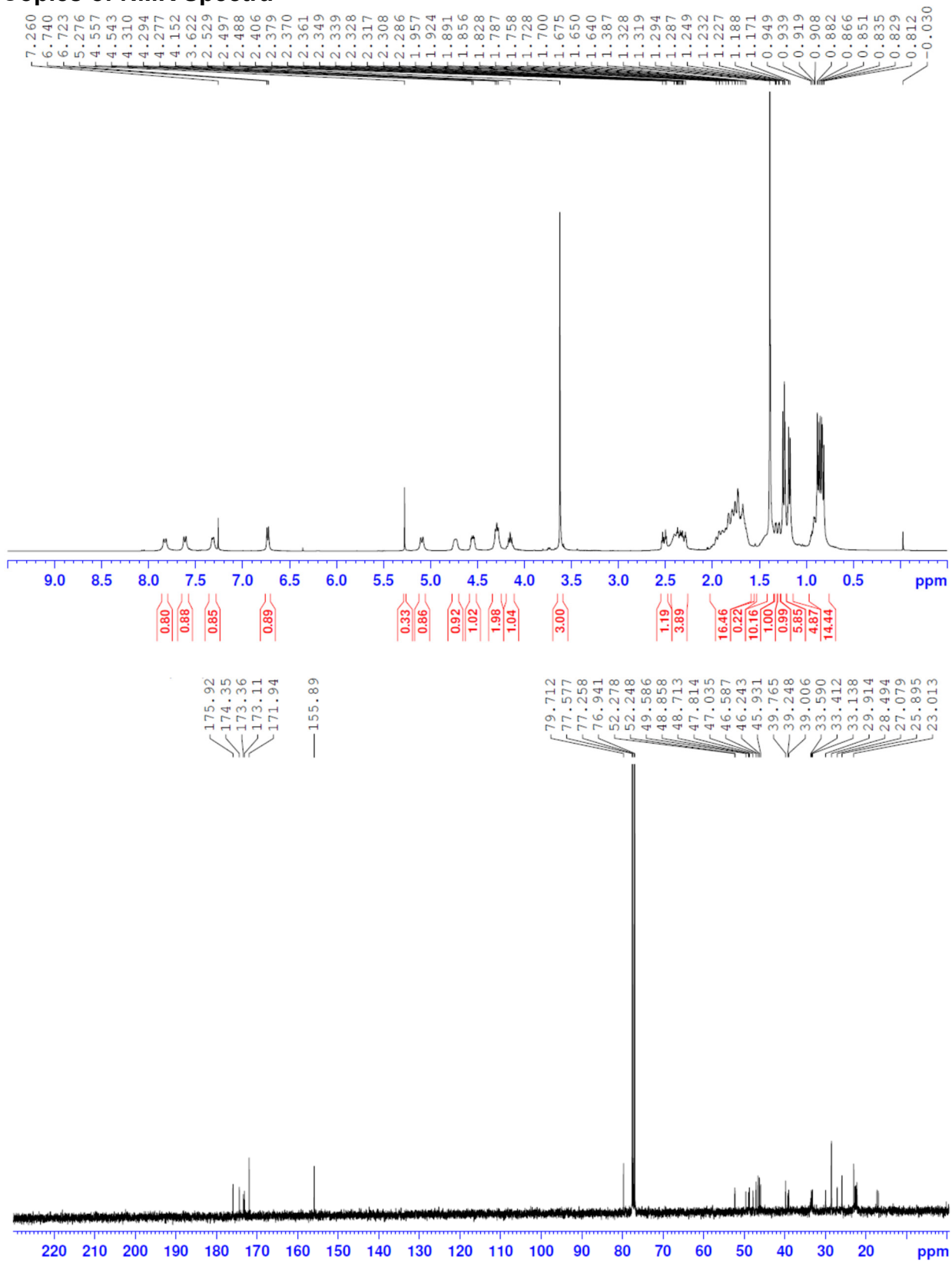


Figure S11. ^{1}H and ^{13}C NMR spectra of ***ent*-5** in $CDCl_3$

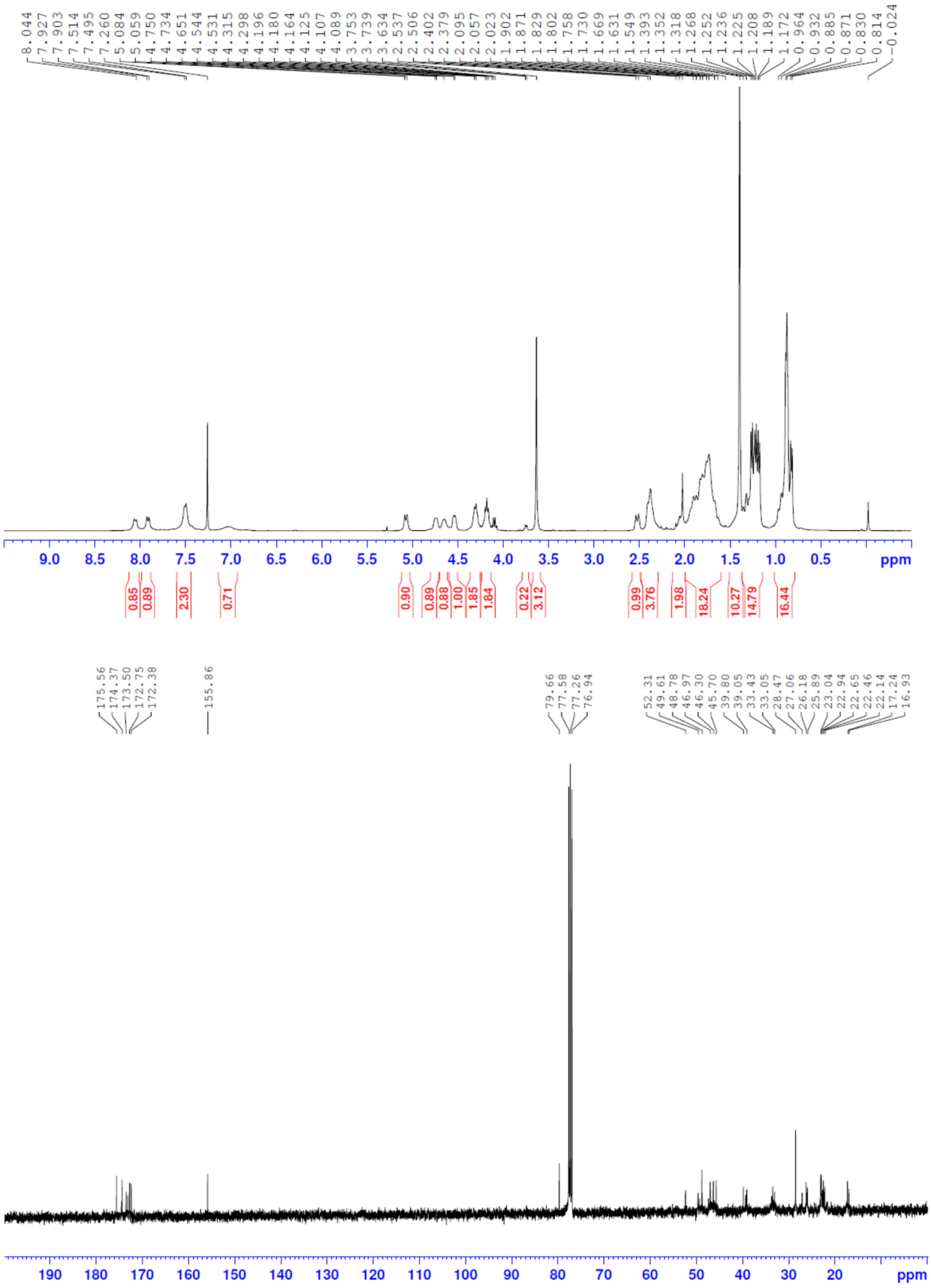


Figure S12. ^{1}H and ^{13}C NMR spectra for ***ent*-6** in $CDCl_3$.

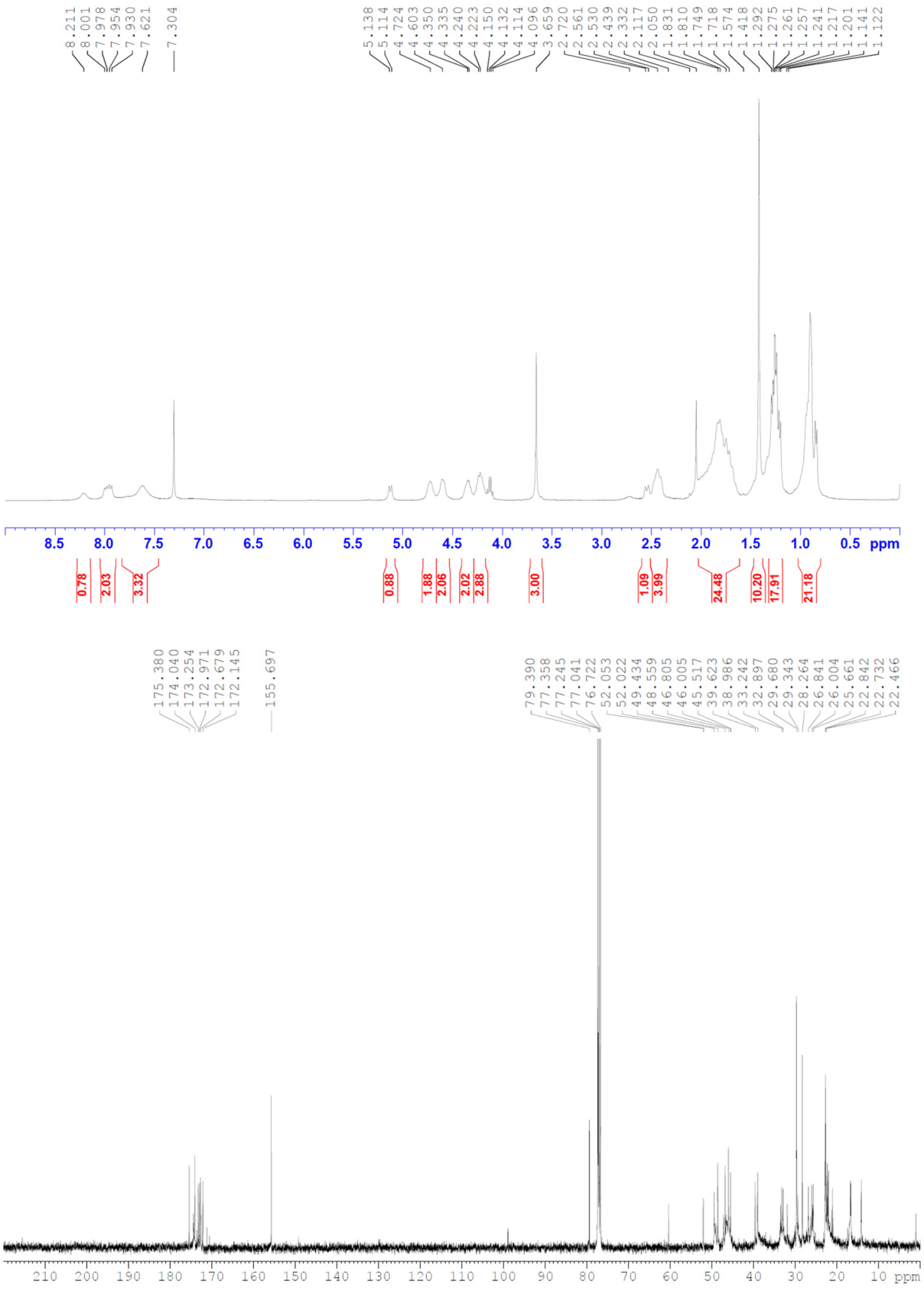


Figure S13. ^{1}H and ^{13}C NMR spectra for **7** in $CDCl_3$.

Copies of High-resolution Mass Spectra

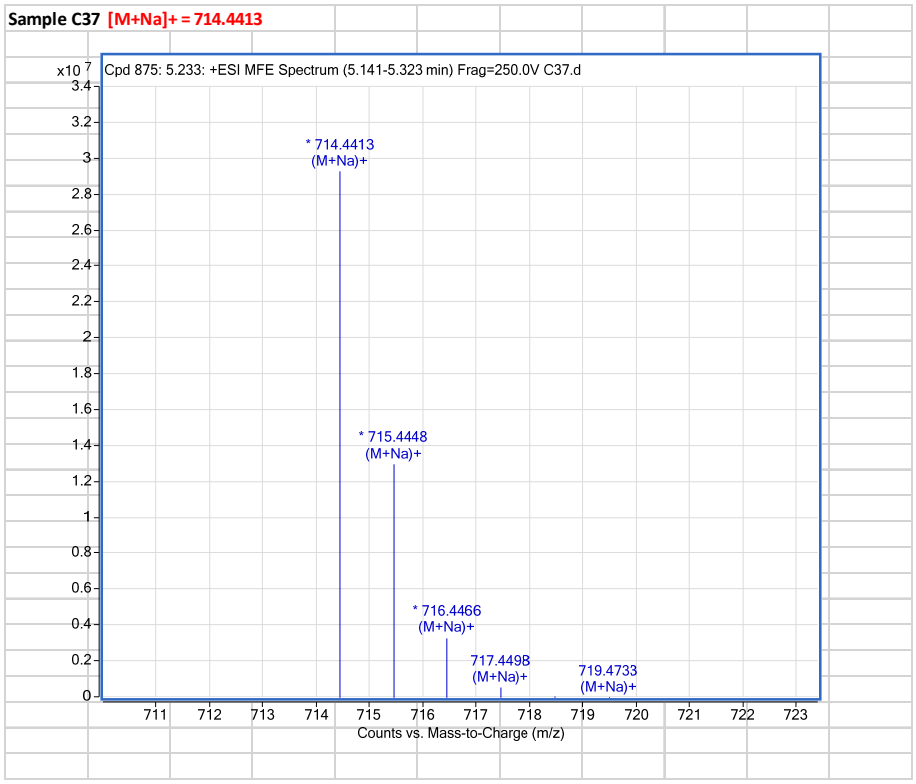


Figure S14. HRMS spectrum of ***ent*-5**.

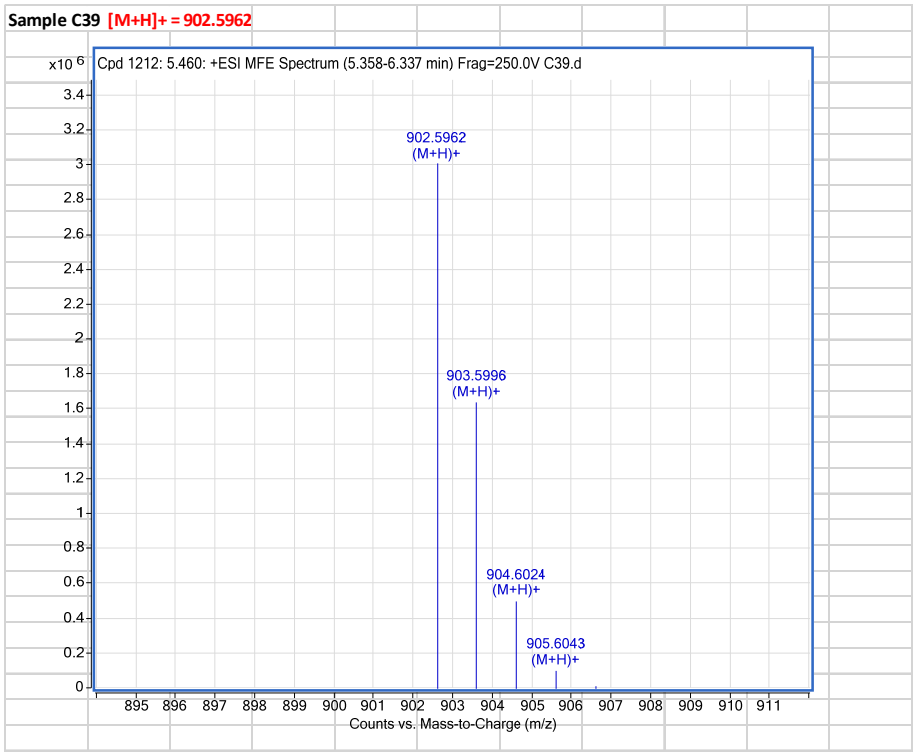


Figure S15. HRMS spectrum of ***ent*-6**.

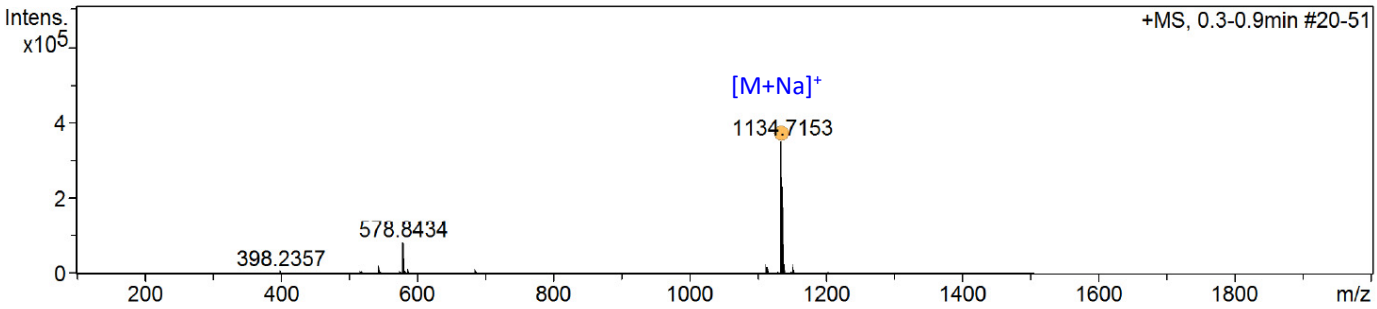


Figure S16. HRMS spectrum of **7**.

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