Electronic Supplementary Information (ESI)

Stabilization of 11/9-Helical α/β-Peptide Foldamers in Protic Solvents

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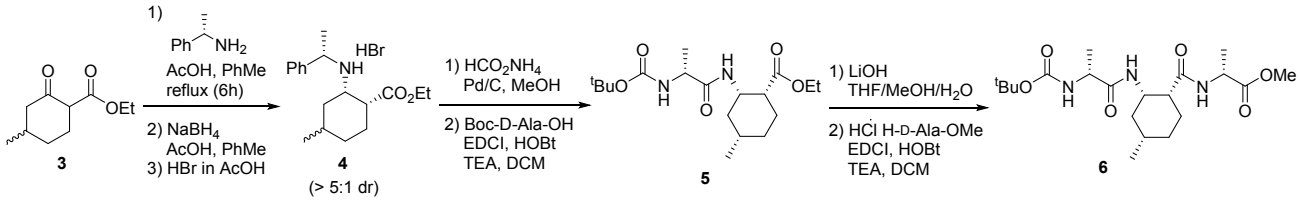
Synthetic procedures

General

L-Alanine and 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. RP-HPLC analysis was performed on the Agilent 1260 infinity series with a UV detector and a C18 column. 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.).

α/β-Peptide trimer 6



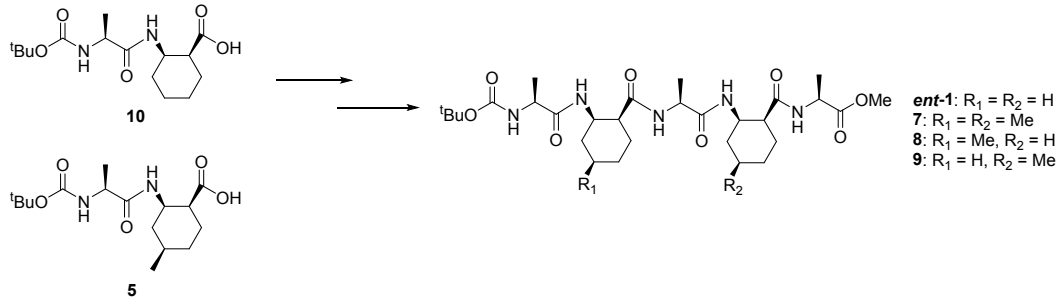
To a solution of racemic β-ketoester **3** in dry toluene, (*R*)-1-phenylethylamine (1.1 eq) and glacial acetic acid (1.1 eq) were added under nitrogen. The reaction mixture was refluxed for 6 h with the removal of water using a Dean-stark trap, and then was cooled in an ice bath. About half of toluene in reaction mixture was evaporated *in vacuo*. After the addition of glacial acetic acid, $NaBH_4$ (2.0 eq) was added to the mixture portionwisely over 2 h (0.5 eq×4) at 0 ℃. The mixture was then further stirred for 2 h at rt, and diluted with excess water in an ice bath. The coolded mixture is basified with 10 M aq. sodium hydroxide to adjust the pH to 9.0 at 0 ℃, and extracted with ethyl acetate. The combined organic fraction was dried over $MgSO_4$, and was concentrated *in vacuo* to give an oily product, which was dissolved in ether, and HBr in acetic acid (1.0 eq) was added dropwisely with stirring. The mixture was stored at room temperature overnight until a white precipitate formed. The precipitate was recrystallized in acetonitrile-ethanol successively to give an epimeric mixture **4** (*ca*. 5:1, ~20% in three steps). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34-7.21 (m, 5H), 4.17 (q, J = 7.2 Hz, 2H), 3.99 (q, J = 6.5 Hz, 1H), 2.97 (s, 1H), 2.45-2.41 (m, 1H), 2.05-2.00 (m, 1H), 1.74-1.24 (m, 12H), 1.13-1.04 (m, 1H), 0.87 (d, J = 6.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.2, 145.8, 128.4 (2C), 126.8, 126.6 (2C), 59.8, 54.2, 53.8, 41.2, 38.6, 32.2, 30.4, 27.7, 25.4, 22.3, 14.4 (peaks for the minor epimer were omitted.)

To a two-necked round flask charged with **4**, 10% Pd/C (~20% wt) and MeOH were added under the nitrogen stream, and then HCO_2NH_4 (5.0 eq) was added. The reaction mixture was refluxed for 8 h, cooled, and filtered through Celite pad. The filtrate was concentrated *in vacuo*, basified with aq. $NaHCO_3$, and then extracted with ethyl acetate. The combined organic fraction was dried over $MgSO_4$, filtered, and concentrated *in vacuo* to give a crude product, which was directly added to a mixture of Boc-D-Ala-OH (1.0 eq), EDCI (1.5 eq), HOBt (1.3 eq), Et_3N (1.1 eq) in dichloromethane. The reaction mixture was stirred for 2 d at rt, diluted with excess ethyl acetate, washed successively with aqueous 10% citric acid, aqueous saturated sodium carbonate, and brine. The organic layer was dried over $MgSO_4$, filtered and was concentrated *in vacuo* to give a crude product, which was purified by flash column chromatography by elution of 4:1 to 2:1 ethyl acetate in hexanes to give **5**. ^{1}H NMR

(400 MHz, $CDCl_3$) δ 7.00 (d, J = 4.3 Hz, 1H), 5.05 (s, 1H), 4.23-3.99 (m, 4H), 2.77 (s, 1H), 2.23-2.19 (m, 1H), 1.70-1.20 (m, 20H), 0.95-0.76 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.0, 171.6, 155.2, 79.8, 60.5, 50.3, 48.1, 43.1, 37.3, 31.9, 30.4, 28.3 (3C), 27.9, 22.1, 19.1, 14.2.

To a mixture of dimer **5** in methanol and THF, a solution of LiOH (5 eq) in H_2O was added with stirring at 0 °C. The mixture was stirred at 0 °C overnight. The solvent was evaporated off, and the mixture was acidified with 1 *N* HCl to pH 1. The turbid mixture was extracted with ethyl acetate. The combined organic layer was washed brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo* to give an acid, which was directly coupled with alanine methyl ester hydrochloride by EDCI-mediated coupling method described above. The crude product was purified by flash column chromatography by elution of 4:1 to 1:1 ethyl acetate in hexanes to give **6**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 (d, J = 9.7 Hz, 1H), 7.12 (d, J = 7.4 Hz, 1H), 5.06 (d, J = 6.5 Hz, 1H), 4.58 (quintet, J = 7.0 Hz, 1H), 4.14 (m, 1H), 3.94 (quintet, J = 6.8 Hz, 1H), 3.77 (s, 3H), 2.62 (m, 1H), 1.96 (m, 1H), 1.86-1.30 (m, 21H), 0.92 (d, J = 6.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.8, 174.4, 172.5, 155.8, 80.0, 52.7, 51.0, 48.8, 48.3, 43.0, 36.0, 32.1, 29.4, 28.3 (3C), 27.2, 22.2, 17.7, 16.2. HRMS (ESI) *m/z* Calcd. for $C_{20}H_{35}N_3O_6$ $[M+Na]^+$ 436.2418, found 436.2419.

α/β-Peptide pentamers 1, *ent*-1, 7-9



The synthesis and the spectral data of two pentamers containing *cis*-ACHC residue, **1** and ***ent*-1** were reported previously.[S1] Three pentamers containing *cis*,*cis*-mACHC residue, **7-9** were synthesized from dipeptide fragments **5** and **10** by a solution-phase fragment coupling strategy mediated by EDCI.

Boc-Ala-*cis*,*cis*-mACHC-Ala-*cis*,*cis*-mACHC-Ala-OMe (7)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (d, J = 7.8 Hz, 1H), 7.82 (d, J = 10.0 Hz, 1H), 7.60 (d, J = 5.1 Hz, 1H), 7.52 (d, J = 10.2 Hz, 1H), 5.10 (d, J = 5.8 Hz, 1H), 4.61 (quintet, J = 7.6 Hz, 1H), 4.20-4.04 (m, 4H), 3.76 (s, 3H), 2.60-2.57 (m, 2H), 2.04-1.17 (m, 32H), 0.94 (d, J = 6.1 Hz, 3H), 0.90 (d, J = 6.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.3, 175.3, 174.8, 174.2, 172.8, 155.8, 79.9, 52.6, 51.8, 51.3, 49.4, 48.7, 48.5, 43.0, 42.6, 36.0, 35.8, 32.3, 31.9, 29.5, 29.2, 28.3 (3C), 27.0, 26.8, 22.5, 22.2, 17.8, 16.6, 16.0. HRMS (ESI) *m/z* Calcd. for $C_{31}H_{53}N_5O_8$ $[M+Na]^+$ 646.3786, found 646.3787.

Boc-Ala-*cis*,*cis*-mACHC-Ala- *cis*-ACHC-Ala-OMe (8)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, J = 7.7 Hz, 1H), 7.84 (d, J = 10.0 Hz, 1H), 7.63 (d, J = 5.2 Hz, 1H), 7.52 (d, J = 10.2 Hz, 1H), 5.16 (d, J = 5.9 Hz, 1H), 4.61 (quintet, J = 7.6 Hz, 1H), 4.20-4.06 (m, 4H), 3.76 (s, 3H), 2.61 (m, 2H), 2.29-1.18 (m, 33H), 0.90 (d, J = 6.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.3, 175.3, 174.8, 174.4, 172.8, 155.8, 80.0, 52.6, 51.8, 51.3, 49.4, 48.7, 48.6, 43.7, 42.6, 36.0, 31.9, 29.2, 28.3 (3C), 27.6, 27.3, 26.9, 25.4, 22.5, 20.8, 17.8, 16.6, 16.0. HRMS (ESI) *m/z* Calcd. for $C_{30}H_{51}N_5O_8$ $[M+Na]^+$ 632.3630, found 632.3631.

Boc-Ala-*cis*-ACHC-Ala-*cis*,*cis*-mACHC-Ala-OMe (9)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, *J* = 7.7 Hz, 1H), 7.81 (d, *J* = 9.9 Hz, 1H), 7.61 (d, *J* = 4.9 Hz, 1H), 7.52 (d, *J* = 10.2 Hz, 1H), 5.16 (d, *J* = 5.8 Hz, 1H), 4.60 (quintet, *J* = 7.6 Hz, 1H), 4.17-4.06 (m, 4H), 3.76 (s, 3H), 2.62-2.59 (m, 2H), 2.22-1.24 (m, 33H), 0.94 (d, *J* = 6.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.3, 175.3, 174.7, 174.3, 172.9, 155.8, 80.0, 52.6, 51.8, 51.3, 49.3, 48.6 (2C), 43.5, 43.0, 35.8, 32.3, 29.6, 28.3 (3C), 27.9, 27.1 (2C), 25.2, 22.2, 20.8, 17.7, 16.7, 15.9. HRMS (ESI) *m/z* Calcd. for $C_{30}H_{51}N_5O_8$ $[M+Na]^+$ 632.3630, found 632.3631.

Circular dichroism experiments

Circular Dichroism spectra were measured by using JASCO-815 spectrometer at 298K. The spectra were obtained using 1-mm path length cell, wavelength range of 190 to 260 nm with 0.1 nm data interval, 1.0 nm bandwidth, and 200 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 various solvents.

Crystallization

X-ray quality crystals of **1** were grown from EtOAc/n-pentane mixture. Crystals of **6** and **9** were grown by solvent diffusion in $CHCl_3$/Et_2O/n-pentane solutions.

Crystal Structure Report

- **Boc-D-Ala-(1*R*,2*S*)-ACHC-D-Ala-(1*R*,2*S*)-ACHC-D-Ala-OMe (1)**

Data Collection

A colorless crystal with approximate dimensions 0.2 × 0.1 × 0.1 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 150 K and centered in the X-ray beam by using a video camera.

The crystal evaluation and data collection were performed on a Bruker D8 Venture diffractometer with Mo K_α (λ = 0.71073 Å) radiation and the diffractometer to crystal distance of 4.00 cm.

The initial cell constants were obtained from two 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 3 seconds per frame. The reflections were successfully indexed by an automated indexing routine built in the APEXII program. The final cell constants were calculated from a set of 9760 strong reflections from the actual data collection.

The data were collected by using the half sphere data collection routine to survey the reciprocal space to the extent of a half sphere to a resolution of 0.81 Å. A total of 200536 data were harvested by collecting 18 sets of frames with 0.5º scans in ω and φ with an exposure time 5 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.[S2]

Structure Solution and Refinement

The systematic absences in the diffraction data were uniquely consistent for the space group $P2_12_12_1$ that yielded chemically reasonable and computationally stable results of refinement.[S3,4]

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 386 parameters against 5268 data resulted in residuals *R* (based on F^2 for $I \geq 2\sigma$) and *wR* (based on F^2 for all data) of 0.0275 and 0.0686, respectively. The final difference Fourier map was featureless.

Summary

Crystal Data for $C_{29}H_{49}N_5O_8$ (M =595.73): orthorhombic, space group $P2_12_12_1$ (no. 19), a = 9.7107(7) Å, b = 17.8054(12) Å, c = 18.6925(14) Å, V = 3232.0(4) Å^3, Z = 4, T = 150.0 K, μ(MoKα) = 0.089 mm^{-1}, *Dcalc* = 1.224 g/mm^3, 200536 reflections measured ($4.35 \leq 2\Theta \leq 48.65$), 5268 unique ($R_{int}$ = 0.0423, R_{sigma} = 0.0098) which were used in all calculations. The final R_1 was 0.0275 ($I > 2\sigma(I)$) and wR_2 was 0.0686 (all data).

Table S1. Crystal data and structure refinement for **1**.

Empirical formula	$C_{29}H_{49}N_5O_8$
Formula weight	595.73
Temperature/K	150.0
Crystal system	orthorhombic
Space group	$P2_12_12_1$
a/Å	9.7107(7)
b/Å	17.8054(12)
c/Å	18.6925(14)
α/°	90
β/°	90
γ/°	90
Volume/Å^3	3232.0(4)
Z	4
ρ_{calc}mg/mm^3	1.224
m/mm^{-1}	0.089
F(000)	1288.0
Crystal size/mm^3	0.2 × 0.1 × 0.1
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection	4.358 to 48.656°
Index ranges	$-11 \leq h \leq 11$, $-20 \leq k \leq 20$, $-21 \leq l \leq 21$
Reflections collected	200536
Independent reflections	5268 [R_{int} = 0.0423, R_{sigma} = 0.0098]
Data/restraints/parameters	5268/0/386
Goodness-of-fit on F^2	1.053
Final R indexes [I>=2σ (I)]	R_1 = 0.0275, wR_2 = 0.0670
Final R indexes [all data]	R_1 = 0.0299, wR_2 = 0.0686
Largest diff. peak/hole / e Å^{-3}	0.21/-0.24

Flack parameter -0.06(14)

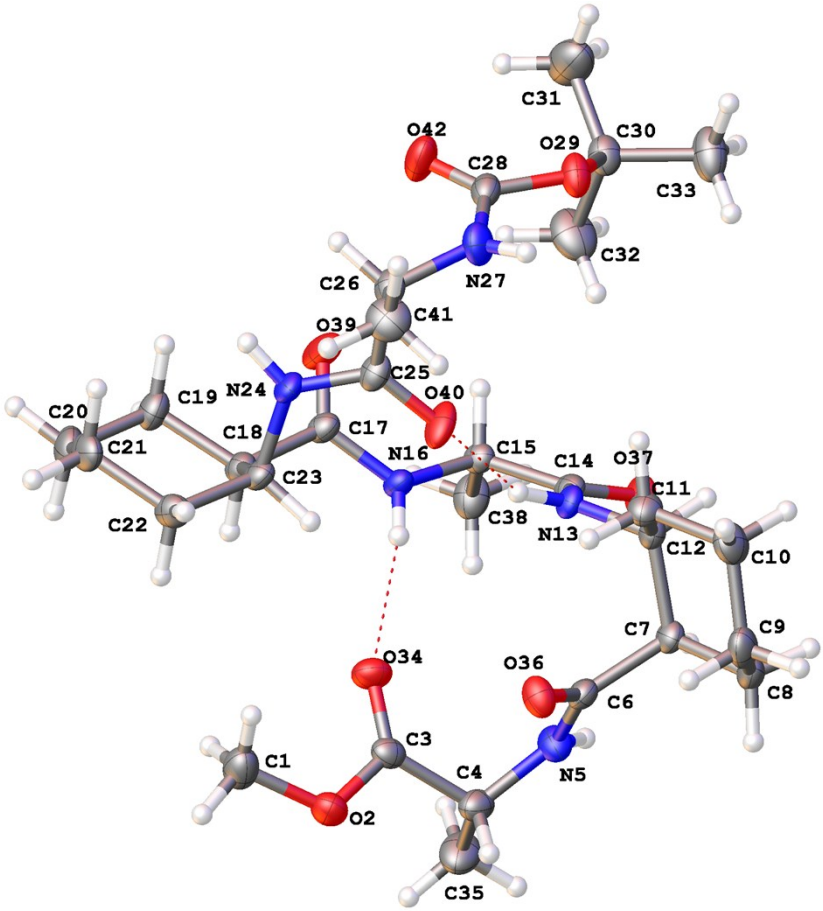


Figure S1. Molecular drawing of **1**. Dashed lines indicate hydrogen bonds.

Table S2. Fractional Atomic Coordinates ($\times 10^4$) and Equivalent Isotropic Displacement Parameters ($Å^2 \times 10^3$) for **1**. U_{eq} is defined as 1/3 of of the trace of the orthogonalised U_{IJ} tensor.

Atom	***x***	***y***	***z***	**U(eq)**
C1	10939(3)	8817.3(13)	6173.7(14)	39.4(6)
C3	9618(2)	9883.6(12)	6450.1(10)	24.8(5)
C4	9678(2)	10728.4(12)	6563.9(11)	28.8(5)
C6	8396(2)	10725.0(11)	7680.8(11)	23.0(4)
C7	7227(2)	11077.9(11)	8102.7(11)	23.6(4)
C8	7769(2)	11551.3(12)	8731.1(12)	29.1(5)
C9	8265(2)	11082.6(13)	9363.6(12)	33.4(5)
C10	7149(3)	10539.8(14)	9610.8(12)	35.7(5)
C11	6716(2)	10023.2(12)	8999.0(11)	29.1(5)
C12	6195(2)	10478.1(10)	8365.3(11)	23.0(4)
C14	4943(2)	10202.8(10)	7264.9(11)	21.8(4)
C15	4631(2)	9653.8(11)	6659.5(11)	22.0(4)
C17	5379(2)	8373.2(11)	6402.7(11)	23.4(4)
C18	6603(2)	7858.2(11)	6265.6(11)	23.2(4)
C19	6138(2)	7141.8(11)	5887.5(12)	30.3(5)
C20	7340(3)	6608.7(13)	5746.1(13)	37.9(6)

C21	8101(2)	6424.7(12)	6434.1(13)	33.9(5)
C22	8590(2)	7144.9(12)	6797.3(13)	30.0(5)
C23	7412(2)	7687.5(11)	6956.0(11)	23.7(4)
C25	6206(2)	7773.1(11)	8106.0(11)	25.1(5)
C26	5586(2)	7324.8(11)	8723.6(11)	26.8(5)
C28	3267(2)	7820.6(11)	8774.6(11)	25.8(5)
C30	1461(2)	8773.3(12)	8678.4(11)	29.6(5)
C31	244(3)	8275.3(16)	8537.3(19)	57.3(8)
C32	2098(3)	9090.2(16)	8007.9(14)	50.0(7)
C33	1057(3)	9401.4(14)	9182.6(13)	43.8(6)
C35	9616(3)	11110.3(14)	5833.2(13)	43.5(6)
C38	4384(3)	10064.8(13)	5958.1(12)	34.9(5)
C41	6733(3)	7143.1(14)	9245.8(13)	39.6(6)
N5	8549.3(19)	10983.4(10)	7005.0(9)	27.9(4)
N13	5802.6(17)	9982.5(9)	7777.5(9)	21.9(4)
N16	5694.7(16)	9085.8(9)	6582.1(9)	21.4(4)
N24	6544.5(18)	7381.8(9)	7524.4(9)	23.6(4)
N27	4521(2)	7761.7(10)	9077(1)	32.3(4)
O2	10872.3(15)	9614.8(8)	6324.5(8)	32.3(4)
O29	2550.8(17)	8380.9(8)	9083.1(8)	31.2(4)
O34	8591.1(15)	9508.7(8)	6435.7(8)	32.2(4)
O36	9163.9(16)	10240.7(8)	7915.7(8)	29.9(3)
O37	4375.0(16)	10826.6(7)	7268.6(8)	30.5(4)
O39	4195.1(16)	8156.4(8)	6356.7(11)	45.5(5)
O40	6440.9(19)	8447.6(8)	8183.4(8)	36.7(4)
O42	2844.2(17)	7411.5(9)	8308.3(10)	43.8(4)

Table S3. Anisotropic Displacement Parameters ($Å^2 \times 10^3$) for **1**. The Anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U_{11}+2hka^*b^*U_{12}+\ldots]$.

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
C1	32.0(13)	35.5(13)	50.7(15)	-11.4(11)	-2.2(11)	3.1(10)
C3	24.2(11)	30.2(11)	20(1)	0.5(9)	2.1(8)	-2.8(9)
C4	31.4(11)	29.1(11)	25.9(11)	-0.8(9)	3.4(9)	-6.7(9)
C6	26.0(11)	16.7(10)	26.3(11)	-0.6(8)	0.1(9)	-2.4(9)
C7	26.6(11)	15.8(9)	28.6(11)	-0.3(8)	1.5(9)	2.0(8)
C8	25.5(11)	21.7(10)	40.0(12)	-9.9(10)	5.6(10)	-1.3(9)
C9	34.5(13)	34.8(12)	31.1(12)	-14.2(10)	-0.4(10)	1.5(10)
C10	42.1(14)	40.4(13)	24.5(11)	-4.6(10)	3.7(10)	1.8(11)
C11	35.7(12)	25.9(11)	25.7(11)	2.0(9)	4.3(9)	-3.1(10)
C12	25.6(11)	17.5(9)	25.9(10)	-3.2(8)	2.3(9)	0.9(8)
C14	21.3(10)	15.1(10)	29.1(11)	3.2(8)	3.0(8)	-0.8(8)
C15	21.1(10)	16.8(9)	28.1(10)	3.0(8)	-0.7(9)	2.1(8)
C17	23.2(11)	16.8(10)	30.3(11)	2.1(8)	-1.5(9)	-1.0(8)
C18	24.7(10)	16.0(9)	29.1(11)	1.9(8)	1.5(9)	-0.4(8)
C19	35.9(13)	20.1(10)	34.9(12)	-4.2(9)	-3.4(10)	1.9(9)
C20	47.5(15)	24.4(11)	41.7(14)	-8.3(10)	7.0(12)	3.2(11)
C21	31.4(12)	20.4(11)	49.9(14)	-2.3(10)	7.9(11)	8.3(9)
C22	23.7(11)	24.4(10)	42.1(13)	3.3(10)	2.3(10)	3.5(9)
C23	24.0(11)	15.5(9)	31.6(11)	0.6(8)	1.1(9)	-1.1(8)
C25	30.8(12)	17(1)	27.6(11)	1.5(8)	-6.0(9)	3.9(9)
C26	33.9(12)	19.9(10)	26.5(11)	0.8(9)	1.5(9)	4.2(9)

C28	33.5(12)	18.3(10)	25.5(10)	-0.1(9)	5.6(9)	-0.5(9)
C30	37.2(12)	26.6(11)	25.0(11)	1.9(9)	0.7(10)	6.6(10)
C31	33.7(14)	45.9(16)	92(2)	-9.5(16)	-2.6(15)	4.5(12)
C32	64.3(18)	52.7(16)	33.1(13)	12.9(12)	8.6(13)	13.2(14)
C33	63.4(18)	34.1(13)	34.0(13)	0.4(10)	0.7(12)	20.3(12)
C35	63.2(18)	34.1(13)	33.2(13)	5.4(11)	11.9(12)	-6.1(12)
C38	46.2(14)	27.9(11)	30.7(12)	2.4(10)	-4.6(10)	8.2(11)
C41	45.2(15)	37.6(13)	36.0(13)	12.4(11)	-4.6(11)	6.2(11)
N5	33.2(10)	23.3(8)	27.2(9)	5.2(7)	3.2(8)	4.2(8)
N13	27.1(9)	12.2(7)	26.5(9)	-0.7(7)	-0.7(7)	2.3(7)
N16	17.4(8)	16.4(8)	30.6(9)	-0.6(7)	-0.8(7)	-0.6(7)
N24	28.3(9)	13.0(8)	29.5(9)	-0.4(7)	1.9(8)	-2.0(7)
N27	38.5(11)	33.4(10)	24.9(9)	-7.6(8)	-0.4(8)	5.4(9)
O2	23.3(7)	33.4(8)	40.4(9)	-3.7(7)	3.4(7)	-0.9(7)
O29	42.7(9)	26.3(8)	24.8(7)	-2.3(6)	2.3(7)	10.5(7)
O34	24.1(8)	34.0(8)	38.7(9)	-6.2(7)	3.1(7)	-6.6(7)
O36	33.0(8)	29.8(8)	26.9(7)	2.2(6)	1.4(6)	11.4(7)
O37	38.0(9)	16.6(7)	36.9(8)	0.6(6)	-1.1(7)	8.9(6)
O39	24.1(8)	21.5(8)	91.0(14)	-9.3(8)	-1.6(9)	-2.0(7)
O40	64.6(11)	14.3(7)	31.1(8)	0.4(6)	0.7(8)	3.0(8)
O42	37.1(9)	32.1(9)	62.1(11)	-21.9(9)	-5.6(9)	1.6(7)

Table S4. Bond Lengths for **1**.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
C1	O2	1.449(3)	C17	N16	1.348(3)
C3	C4	1.520(3)	C17	O39	1.216(3)
C3	O2	1.330(3)	C18	C19	1.526(3)
C3	O34	1.200(3)	C18	C23	1.541(3)
C4	C35	1.527(3)	C19	C20	1.527(3)
C4	N5	1.445(3)	C20	C21	1.519(3)
C6	C7	1.518(3)	C21	C22	1.527(3)
C6	N5	1.353(3)	C22	C23	1.526(3)
C6	O36	1.222(2)	C23	N24	1.461(3)
C7	C8	1.539(3)	C25	C26	1.527(3)
C7	C12	1.544(3)	C25	N24	1.332(3)
C8	C9	1.525(3)	C25	O40	1.231(2)
C9	C10	1.524(3)	C26	C41	1.516(3)
C10	C11	1.527(3)	C26	N27	1.453(3)
C11	C12	1.521(3)	C28	N27	1.347(3)
C12	N13	1.460(3)	C28	O29	1.346(3)
C14	C15	1.526(3)	C28	O42	1.208(3)
C14	N13	1.330(3)	C30	C31	1.501(4)
C14	O37	1.240(2)	C30	C32	1.507(3)
C15	C38	1.521(3)	C30	C33	1.514(3)
C15	N16	1.453(2)	C30	O29	1.477(3)
C17	C18	1.523(3)			

Table S5. Bond Angles for **1**.

Atom	Atom	Atom	Angle/°	Atom	Atom	Atom	Angle/°
O2	C3	C4	110.19(18)	C19	C18	C23	111.94(16)
O34	C3	C4	125.9(2)	C18	C19	C20	111.94(18)
O34	C3	O2	123.84(19)	C21	C20	C19	111.06(18)
C3	C4	C35	108.30(17)	C20	C21	C22	110.28(18)
N5	C4	C3	111.18(17)	C23	C22	C21	112.64(18)
N5	C4	C35	109.90(19)	C22	C23	C18	110.13(17)
N5	C6	C7	115.26(18)	N24	C23	C18	112.86(16)
O36	C6	C7	124.19(18)	N24	C23	C22	109.73(16)
O36	C6	N5	120.55(19)	N24	C25	C26	116.16(17)
C6	C7	C8	111.55(17)	O40	C25	C26	119.61(18)
C6	C7	C12	111.33(16)	O40	C25	N24	124.1(2)
C8	C7	C12	110.99(17)	C41	C26	C25	107.97(18)
C9	C8	C7	113.58(17)	N27	C26	C25	110.15(17)
C10	C9	C8	110.93(19)	N27	C26	C41	110.16(18)
C9	C10	C11	110.54(18)	O29	C28	N27	110.18(18)
C12	C11	C10	110.73(17)	O42	C28	N27	124.3(2)
C11	C12	C7	113.58(18)	O42	C28	O29	125.5(2)
N13	C12	C7	110.37(16)	C31	C30	C32	113.5(2)
N13	C12	C11	110.55(15)	C31	C30	C33	110.0(2)
N13	C14	C15	118.03(16)	C32	C30	C33	110.3(2)
O37	C14	C15	119.32(18)	O29	C30	C31	112.01(19)
O37	C14	N13	122.64(18)	O29	C30	C32	107.97(19)
C38	C15	C14	111.26(16)	O29	C30	C33	102.50(17)
N16	C15	C14	112.26(16)	C6	N5	C4	120.64(18)
N16	C15	C38	111.19(17)	C14	N13	C12	121.87(16)
N16	C17	C18	115.57(17)	C17	N16	C15	121.24(17)
O39	C17	C18	122.33(18)	C25	N24	C23	122.74(17)
O39	C17	N16	122.10(19)	C28	N27	C26	119.64(17)
C17	C18	C19	110.52(17)	C3	O2	C1	115.31(17)
C17	C18	C23	112.07(17)	C28	O29	C30	120.10(16)

Table S6. Torsion Angles for **1**.

A	B	C	D	Angle/°	A	B	C	D	Angle/°
C3	C4	N5	C6	60.6(3)	C32	C30	O29	C28	-57.2(2)
C4	C3	O2	C1	-177.22(18)	C33	C30	O29	C28	-173.69(19)
C6	C7	C8	C9	-75.9(2)	C35	C4	N5	C6	-179.55(19)
C6	C7	C12	C11	75.8(2)	C38	C15	N16	C17	-91.1(2)
C6	C7	C12	N13	-49.0(2)	C41	C26	N27	C28	-163.17(19)
C7	C6	N5	C4	175.96(17)	N5	C6	C7	C8	-113.3(2)
C7	C8	C9	C10	-54.1(2)	N5	C6	C7	C12	122.16(19)
C7	C12	N13	C14	-74.7(2)	N13	C14	C15	C38	-147.25(18)
C8	C7	C12	C11	-49.1(2)	N13	C14	C15	N16	-21.9(2)
C8	C7	C12	N13	-173.94(16)	N16	C17	C18	C19	-165.48(17)
C8	C9	C10	C11	58.0(2)	N16	C17	C18	C23	68.9(2)
C9	C10	C11	C12	-58.2(3)	N24	C25	C26	C41	96.5(2)
C10	C11	C12	C7	54.4(2)	N24	C25	C26	N27	-143.20(19)
C10	C11	C12	N13	179.12(17)	N27	C28	O29	C30	153.54(18)

C11 C12 N13 C14	158.76(18)	O2 C3 C4 C35	85.5(2)
C12 C7 C8 C9	48.8(2)	O2 C3 C4 N5	-153.65(18)
C14 C15 N16 C17	143.54(18)	O29 C28 N27 C26	-165.22(17)
C15 C14 N13 C12	178.02(17)	O34 C3 C4 C35	-90.8(3)
C17 C18 C19 C20	-179.59(18)	O34 C3 C4 N5	30.0(3)
C17 C18 C23 C22	177.68(16)	O34 C3 O2 C1	-0.8(3)
C17 C18 C23 N24	54.7(2)	O36 C6 C7 C8	66.8(2)
C18 C17 N16 C15	173.97(17)	O36 C6 C7 C12	-57.8(3)
C18 C19 C20 C21	55.5(3)	O36 C6 N5 C4	-4.1(3)
C18 C23 N24 C25	-108.4(2)	O37 C14 C15 C38	33.9(3)
C19 C18 C23 C22	52.9(2)	O37 C14 C15 N16	159.28(17)
C19 C18 C23 N24	-70.2(2)	O37 C14 N13 C12	-3.2(3)
C19 C20 C21 C22	-56.3(3)	O39 C17 C18 C19	14.8(3)
C20 C21 C22 C23	57.1(3)	O39 C17 C18 C23	-110.8(2)
C21 C22 C23 C18	-54.9(2)	O39 C17 N16 C15	-6.3(3)
C21 C22 C23 N24	69.9(2)	O40 C25 C26 C41	-79.1(2)
C22 C23 N24 C25	128.4(2)	O40 C25 C26 N27	41.2(3)
C23 C18 C19 C20	-53.9(2)	O40 C25 N24 C23	9.1(3)
C25 C26 N27 C28	77.8(2)	O42 C28 N27 C26	16.8(3)
C26 C25 N24 C23	-166.23(17)	O42 C28 O29 C30	-28.5(3)
C31 C30 O29 C28	68.5(3)		

- **Boc-D-Ala-(1*R*,2*S*,4*S*)-mACHC-D-Ala-OMe (6)**

Data Collection

A colorless crystal with approximate dimensions 0.26 × 0.1 × 0.1 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 K and centered in the X-ray beam by using a video camera.

The crystal evaluation and data collection were performed on a Bruker D8 Venture diffractometer with Mo K_α (λ = 0.71073 Å) radiation and the diffractometer to crystal distance of 4.00 cm.

The initial cell constants were obtained from two 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. The final cell constants were calculated from a set of 9940 strong reflections from the actual data collection.

The data were collected by using the half sphere data collection routine to survey the reciprocal space to the extent of a half sphere to a resolution of 0.81 Å. A total of 42177 data were harvested by collecting 6 sets of frames with 0.5º scans in ω and φ with an exposure time 10 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.[S2]

Structure Solution and Refinement

The systematic absences in the diffraction data were uniquely consistent for the space group $P2_12_12_1$ that yielded chemically reasonable and computationally stable results of refinement.[S3,4]

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 269 parameters against 4720 data resulted in residuals *R* (based on F^2 for $I \geq 2\sigma$) and *wR* (based on F^2 for all data) of 0.0355 and 0.0779, respectively. The final difference Fourier map was featureless.

Summary

Crystal Data for $C_{20}H_{35}N_3O_6$ (M =413.51): orthorhombic, space group $P2_12_12_1$ (no. 19), a = 9.1953(5) Å, b = 15.9688(8) Å, c = 16.3770(9) Å, V = 2404.8(2) Å^3, Z = 4, T = 100.0 K, μ(MoKα) = 0.084 mm^{-1}, *Dcalc* = 1.142 g/mm^3, 42177 reflections measured ($4.974 \leq 2\Theta \leq 51.968$), 4720 unique ($R_{int}$ = 0.0693, R_{sigma} = 0.0344) which were used in all calculations. The final R_1 was 0.0355 ($I > 2\sigma(I)$) and wR_2 was 0.0779 (all data).

Table S7. Crystal data and structure refinement for **6**.

Empirical formula	$C_{20}H_{35}N_3O_6$
Formula weight	413.51
Temperature/K	100.0
Crystal system	orthorhombic
Space group	$P2_12_12_1$
a/Å	9.1953(5)
b/Å	15.9688(8)
c/Å	16.3770(9)
α/°	90
β/°	90
γ/°	90
Volume/Å^3	2404.8(2)
Z	4
ρ_{calc}mg/mm^3	1.142
m/mm^{-1}	0.084
F(000)	896.0
Crystal size/mm^3	0.26 × 0.105 × 0.097
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection	4.974 to 51.968°
Index ranges	$-11 \leq h \leq 11$, $-19 \leq k \leq 19$, $-20 \leq l \leq 20$
Reflections collected	42177
Independent reflections	4720 [R_{int} = 0.0693, R_{sigma} = 0.0344]
Data/restraints/parameters	4720/70/269
Goodness-of-fit on F^2	1.052
Final R indexes [I>=2σ (I)]	R_1 = 0.0355, wR_2 = 0.0719
Final R indexes [all data]	R_1 = 0.0525, wR_2 = 0.0779
Largest diff. peak/hole / e Å^{-3}	0.18/-0.22
Flack parameter	0.1(4)

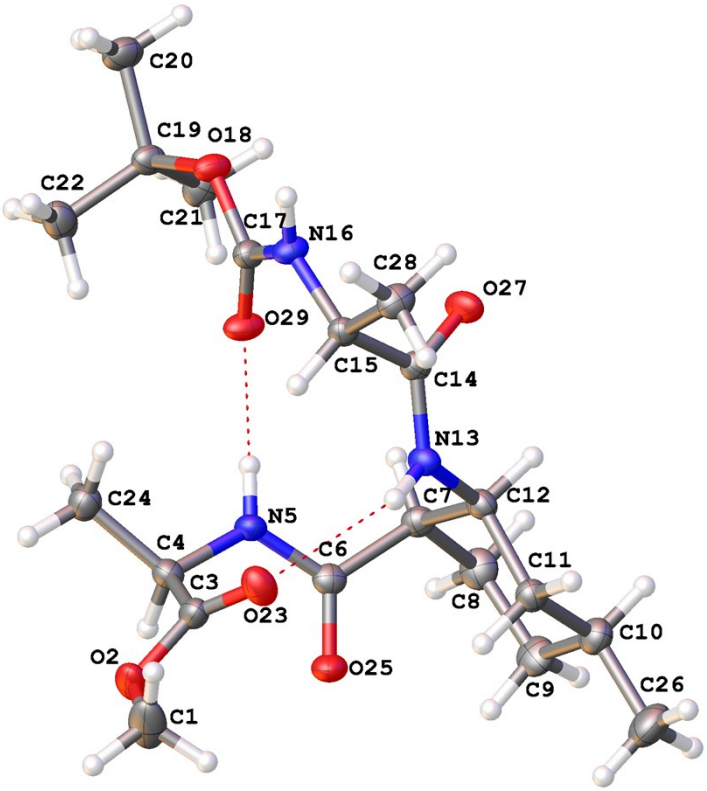


Figure S2. Molecular drawing of **6**. Dashed lines indicate hydrogen bonds.

Table S8. Fractional Atomic Coordinates ($\times 10^4$) and Equivalent Isotropic Displacement Parameters ($Å^2 \times 10^3$) for **6**. U_{eq} is defined as 1/3 of of the trace of the orthogonalised U_{IJ} tensor.

Atom	***x***	***y***	***z***	**U(eq)**
O2	4690(2)	3488.1(10)	556.2(10)	35.0(5)
O18	4136.7(17)	4304.3(9)	5003.2(9)	23.9(4)
O23	4931.1(18)	2636.9(10)	1638.1(9)	30.4(4)
O25	8367.3(19)	3091.4(10)	1475.8(9)	29.0(4)
O27	6442.2(18)	2200.3(11)	4570.1(9)	29.6(4)
O29	5463.8(19)	3969.1(9)	3872.1(9)	27.0(4)
N5	6867(2)	3767.0(11)	2341.9(11)	20.9(4)
N13	6478(2)	2063.3(11)	3189.9(11)	20.3(4)
N16	3825(2)	3068.9(11)	4418.9(11)	21.5(4)
C1	3891(4)	2835.9(17)	136.7(17)	47.6(8)
C3	5153(3)	3302.2(15)	1307.2(13)	24.7(5)
C4	5930(3)	4044.7(14)	1684.7(14)	23.1(5)
C6	7995(3)	3253.6(14)	2184.3(13)	21.3(5)
C7	8735(2)	2871.4(14)	2928.6(14)	22.3(5)
C8	10388(3)	2787.2(16)	2835.0(16)	30.3(6)
C9	10865(3)	2088.2(16)	2257.1(16)	31.9(6)
C10	10161(3)	1247.9(15)	2458.3(15)	29.7(6)
C11	8504(3)	1343.1(15)	2490.3(14)	23.6(5)
C12	8059(2)	1997.5(14)	3117.2(14)	21.5(5)
C14	5818(2)	2216.9(13)	3905.7(13)	19.9(5)
C15	4188(2)	2386.7(13)	3868.8(13)	20.1(5)
C17	4545(3)	3793.3(13)	4386.9(13)	21.2(5)
C19	4614(3)	5190.6(14)	5005.9(14)	22.9(5)

C20	3885(3)	5528.3(15)	5772.6(15)	33.1(6)
C21	6251(3)	5248.1(16)	5086.1(17)	33.0(6)
C22	4023(3)	5622.7(16)	4251.7(15)	33.5(6)
C24	4824(3)	4680.0(15)	1998.6(14)	28.0(6)
C26	10618(3)	566.6(17)	1856.5(18)	43.5(7)
C28	3363(3)	1603.8(15)	4130.2(14)	26.9(6)

Table S9. Anisotropic Displacement Parameters ($Å^2 \times 10^3$) for **6**. The Anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U_{11}+2hka^*b^*U_{12}+\ldots]$.

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
O2	53.3(12)	30.9(9)	20.9(8)	-4.4(7)	-13.6(8)	11.2(9)
O18	30.6(9)	19.9(8)	21.2(8)	-3.7(7)	7.4(7)	-3.6(7)
O23	37.9(11)	27.2(9)	26.2(9)	1.2(7)	-9.0(8)	-1.9(8)
O25	34.4(10)	32.1(9)	20.3(8)	1.4(7)	7.7(7)	6.8(8)
O27	26.4(9)	44.1(11)	18.3(8)	-2.7(7)	-5.1(7)	5.5(8)
O29	33.3(10)	24.2(8)	23.5(8)	-2.9(7)	11.7(8)	-4.6(8)
N5	23.3(11)	24.5(10)	14.9(9)	-1.9(8)	0.2(8)	2.1(8)
N13	17.6(9)	26.5(10)	16.8(9)	-0.7(8)	-1.8(8)	-0.4(8)
N16	20(1)	23(1)	21.6(10)	-3.7(8)	5.7(8)	-2.1(8)
C1	70(2)	36.7(16)	36.0(15)	-13.7(13)	-31.2(15)	13.6(15)
C3	27.4(13)	26.7(13)	20.1(11)	-2(1)	-1.8(10)	8.2(11)
C4	26.0(13)	25.0(12)	18.4(11)	1.7(10)	0.4(10)	2.4(10)
C6	21.5(12)	20.7(12)	21.8(12)	-0.2(9)	1.5(10)	-3.8(10)
C7	21.4(12)	24.9(12)	20.7(12)	-3.6(9)	-1.2(9)	-0.9(10)
C8	20.4(13)	34.3(14)	36.1(14)	1.0(11)	-3.8(11)	-3.2(11)
C9	18.4(13)	39.7(15)	37.8(14)	1.8(12)	2.0(11)	2.5(12)
C10	25.9(13)	33.3(14)	29.9(13)	-0.4(11)	-0.9(11)	6.9(12)
C11	25.4(13)	22.6(12)	22.7(12)	-0.6(9)	-1.3(10)	1.2(11)
C12	20.3(12)	25.6(12)	18.5(11)	1.9(10)	-1.8(9)	0.9(10)
C14	22.3(12)	17.8(11)	19.5(11)	-1.6(9)	-0.6(10)	-1.6(10)
C15	23.5(12)	19.8(11)	17.1(11)	-1.5(9)	-1.3(10)	0.4(10)
C17	25.3(13)	19.5(11)	19.0(11)	-0.3(9)	2.2(10)	1.5(10)
C19	29.4(13)	18.4(11)	21.0(11)	-2.9(9)	2.4(10)	-1.3(10)
C20	43.0(17)	27.6(13)	28.8(14)	-6.3(11)	6.4(12)	1.7(12)
C21	30.0(14)	26.2(13)	42.8(15)	-8.4(12)	-4.3(12)	-1.7(12)
C22	46.3(17)	25.6(13)	28.5(13)	0.2(11)	-6.8(12)	2.7(13)
C24	31.4(14)	26.0(12)	26.6(12)	-2(1)	-2.6(11)	4.4(11)
C26	38.6(17)	42.3(16)	49.6(17)	-7.9(14)	6.5(14)	13.7(14)
C28	26.2(14)	24.0(12)	30.6(13)	-2.2(10)	3.9(11)	-3.7(11)

Table S10. Bond Lengths for **6**.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
O2	C1	1.448(3)	C4	C24	1.526(3)
O2	C3	1.335(3)	C6	C7	1.523(3)
O18	C17	1.351(3)	C7	C8	1.534(3)
O18	C19	1.482(3)	C7	C12	1.559(3)
O23	C3	1.210(3)	C8	C9	1.528(4)
O25	C6	1.237(3)	C9	C10	1.526(4)

O27	C14	1.230(3)	C10	C11	1.532(3)
O29	C17	1.226(3)	C10	C26	1.527(3)
N5	C4	1.448(3)	C11	C12	1.521(3)
N5	C6	1.347(3)	C14	C15	1.524(3)
N13	C12	1.462(3)	C15	C28	1.524(3)
N13	C14	1.343(3)	C19	C20	1.522(3)
N16	C15	1.453(3)	C19	C21	1.514(3)
N16	C17	1.334(3)	C19	C22	1.516(3)
C3	C4	1.516(3)			

Table S11. Bond Angles for **6**.

Atom	Atom	Atom	Angle/°	Atom	Atom	Atom	Angle/°
C3	O2	C1	116.1(2)	C26	C10	C11	111.5(2)
C17	O18	C19	119.78(17)	C12	C11	C10	111.0(2)
C6	N5	C4	120.13(18)	N13	C12	C7	110.37(18)
C14	N13	C12	122.24(19)	N13	C12	C11	111.83(19)
C17	N16	C15	120.78(18)	C11	C12	C7	111.96(18)
O2	C3	C4	110.6(2)	O27	C14	N13	123.9(2)
O23	C3	O2	123.6(2)	O27	C14	C15	119.8(2)
O23	C3	C4	125.7(2)	N13	C14	C15	116.3(2)
N5	C4	C3	110.11(18)	N16	C15	C14	109.58(18)
N5	C4	C24	110.46(18)	N16	C15	C28	109.06(18)
C3	C4	C24	110.10(19)	C28	C15	C14	109.41(19)
O25	C6	N5	121.3(2)	O29	C17	O18	124.5(2)
O25	C6	C7	122.9(2)	O29	C17	N16	124.6(2)
N5	C6	C7	115.74(19)	N16	C17	O18	110.87(19)
C6	C7	C8	113.4(2)	O18	C19	C20	102.15(18)
C6	C7	C12	109.84(18)	O18	C19	C21	110.66(19)
C8	C7	C12	109.66(19)	O18	C19	C22	109.02(19)
C9	C8	C7	114.2(2)	C21	C19	C20	110.2(2)
C10	C9	C8	112.8(2)	C21	C19	C22	113.6(2)
C9	C10	C11	110.0(2)	C22	C19	C20	110.7(2)
C9	C10	C26	111.7(2)				

Table S12. Torsion Angles for **6**.

A	B	C	D	Angle/°	A	B	C	D	Angle/°
O2	C3	C4	N5	-159.21(19)	C8	C7	C12	N13	-178.71(18)
O2	C3	C4	C24	78.8(2)	C8	C7	C12	C11	-53.4(2)
O23	C3	C4	N5	23.0(3)	C8	C9	C10	C11	53.8(3)
O23	C3	C4	C24	-99.0(3)	C8	C9	C10	C26	178.2(2)
O25	C6	C7	C8	38.6(3)	C9	C10	C11	C12	-57.8(3)
O25	C6	C7	C12	-84.5(3)	C10	C11	C12	N13	-176.75(19)
O27	C14	C15	N16	43.6(3)	C10	C11	C12	C7	58.8(3)
O27	C14	C15	C28	-75.9(3)	C12	N13	C14	O27	-10.5(3)
N5	C6	C7	C8	-143.3(2)	C12	N13	C14	C15	171.92(19)
N5	C6	C7	C12	93.5(2)	C12	C7	C8	C9	49.7(3)
N13	C14	C15	N16	-138.64(19)	C14	N13	C12	C7	-90.3(2)
N13	C14	C15	C28	101.8(2)	C14	N13	C12	C11	144.4(2)

C1	O2	C3	O23	-0.5(3)	C15	N16	C17	O18	-173.64(18)
C1	O2	C3	C4	-178.3(2)	C15	N16	C17	O29	5.8(3)
C4	N5	C6	O25	9.0(3)	C17	O18	C19	C20	178.29(19)
C4	N5	C6	C7	-169.06(19)	C17	O18	C19	C21	-64.4(3)
C6	N5	C4	C3	63.4(3)	C17	O18	C19	C22	61.1(3)
C6	N5	C4	C24	-174.8(2)	C17	N16	C15	C14	51.5(3)
C6	C7	C8	C9	-73.5(3)	C17	N16	C15	C28	171.2(2)
C6	C7	C12	N13	-53.4(2)	C19	O18	C17	O29	10.8(3)
C6	C7	C12	C11	71.9(2)	C19	O18	C17	N16	-169.82(18)
C7	C8	C9	C10	-51.5(3)	C26	C10	C11	C12	177.6(2)

• **Boc- L-Ala-(1*S*,2*R*)-ACHC-L-Ala-(1*S*,2*R*,4*R*)-mACHC-L-Ala-OMe (9)**

Data Collection

A colorless crystal with approximate dimensions 0.1 × 0.1 × 0.1 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 K and centered in the X-ray beam by using a video camera.

The crystal evaluation and data collection were performed on a Bruker D8 Venture diffractometer with Cu K_α (λ = 1.54178 Å) radiation and the diffractometer to crystal distance of 4.00 cm.

The initial cell constants were obtained from three series of ω scans at different starting angles. Each series consisted of 20-30 frames collected at intervals of 0.5º in 10-15º range about ω with the exposure time of 5 seconds per frame. The reflections were successfully indexed by an automated indexing routine built in the APEXII program. The final cell constants were calculated from a set of 9583 strong reflections from the actual data collection.

The data were collected by using the half sphere data collection routine to survey the reciprocal space to the extent of a half sphere to a resolution of 0.81 Å. A total of 16765 data were harvested by collecting 6 sets of frames with 1º scans in ω and φ with an exposure time 10-20 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.[S2]

Structure Solution and Refinement

The systematic absences in the diffraction data were uniquely consistent for the space group $P2_12_12_1$ that yielded chemically reasonable and computationally stable results of refinement.[S3,4]

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 469 parameters against 7221 data resulted in residuals *R* (based on F^2 for $I \geq 2\sigma$) and *wR* (based on F^2 for all data) of 0.0351 and 0.0857, respectively. The final difference Fourier map was featureless.

Summary

Crystal Data for $C_{31}H_{52}Cl_3N_5O_8$ (*M* =729.12): orthorhombic, space group $P2_12_12_1$ (no. 19), *a* = 9.5052(17) Å, *b* = 17.583(3) Å, *c* = 23.471(4) Å, *V* = 3922.8(11) Å^3, *Z* = 4, *T* = 100.0 K, μ(CuKα) = 2.533 mm^{-1}, *Dcalc* = 1.235 g/mm^3, 16765 reflections measured (6.28 ≤ 2Θ ≤ 144.676), 7221 unique (R_{int} = 0.0320, R_{sigma} = 0.0389) which were used in all calculations. The final R_1 was 0.0682 (I > 2σ(I)) and wR_2 was 0.1943 (all data).

Table S13. Crystal data and structure refinement for **9**.

Empirical formula	$C_{31}H_{52}Cl_3N_5O_8$
Formula weight	729.12
Temperature/K	100.0
Crystal system	orthorhombic
Space group	$P2_12_12_1$
a/Å	9.5052(17)
b/Å	17.583(3)
c/Å	23.471(4)
α/°	90
β/°	90
γ/°	90
Volume/Å^3	3922.8(11)
Z	4
ρ_{calc}mg/mm^3	1.235
m/mm^{-1}	2.533
F(000)	1552.0
Crystal size/mm^3	0.1 × 0.1 × 0.1
Radiation	CuKα (λ = 1.54178)
2Θ range for data collection	6.28 to 144.676°
Index ranges	-4 ≤ h ≤ 11, -21 ≤ k ≤ 21, -28 ≤ l ≤ 28
Reflections collected	16765
Independent reflections	7221 [R_{int} = 0.0320, R_{sigma} = 0.0389]
Data/restraints/parameters	7221/3/469
Goodness-of-fit on F^2	1.041
Final R indexes [I>=2σ (I)]	R_1 = 0.0682, wR_2 = 0.1889
Final R indexes [all data]	R_1 = 0.0711, wR_2 = 0.1943
Largest diff. peak/hole / e Å^{-3}	1.22/-0.53
Flack parameter	0.053(9)

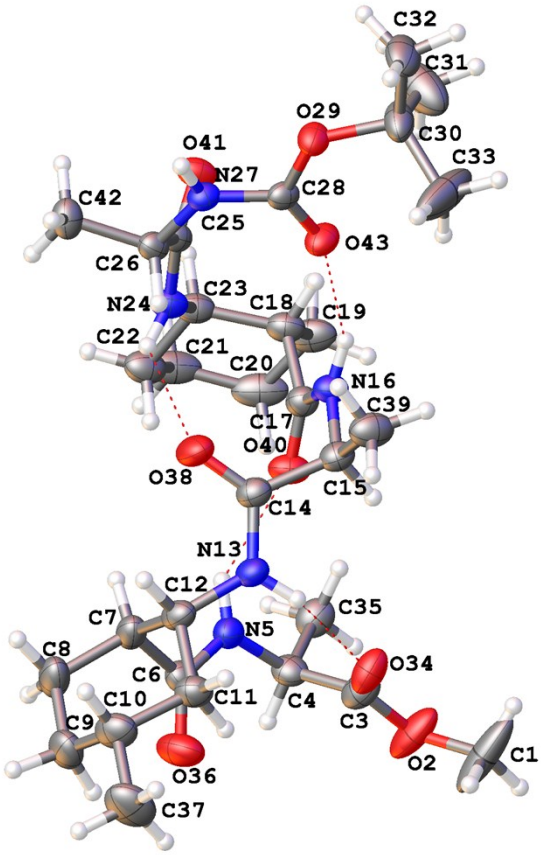


Figure S3. Molecular drawing of **9**. Dashed lines indicate hydrogen bonds. A co-crystallized solvent molecule was omitted for clarity.

Table S14. Fractional Atomic Coordinates ($\times 10^4$) and Equivalent Isotropic Displacement Parameters ($Å^2 \times 10^3$) for **9**. U_{eq} is defined as 1/3 of of the trace of the orthogonalised U_{IJ} tensor.

Atom	***x***	***y***	***z***	**U(eq)**
Cl45	-9656(7)	-9100(5)	-7663(3)	95(2)
Cl46	-12605(7)	-9319(4)	-7680(3)	84.6(19)
Cl47	-10484(13)	-10435(4)	-8059(6)	159(6)
Cl49	-9006(9)	-9470(9)	-8016(6)	261(7)
Cl50	-11800(20)	-9209(10)	-7621(6)	326(9)
Cl51	-11344(8)	-10073(3)	-8557(2)	145(3)
O2	-11105(4)	-12277(3)	-7480.7(16)	66.0(12)
O29	-4330(3)	-7207.8(16)	-6123.6(11)	34.9(6)
O34	-8995(4)	-11868(2)	-7201.5(12)	47.3(8)
O36	-9152(4)	-13051.9(18)	-6017.6(17)	56.9(9)
O38	-6411(4)	-10323.8(17)	-5741.3(14)	48.7(8)
O40	-9682(3)	-10178.2(15)	-6206.6(13)	38.3(6)
O41	-7609(3)	-7716.9(15)	-5138.0(12)	35.6(6)
O43	-6091(3)	-8068.8(16)	-6250.2(11)	36.8(6)
N5	-9808(4)	-11835.8(18)	-6084.6(13)	33.5(7)
N13	-6814(4)	-11296.0(18)	-6346.5(14)	32.8(7)
N16	-7949(4)	-9379.6(18)	-6464.4(14)	31.9(7)
N24	-8022(4)	-8986.1(18)	-5165.4(15)	33.3(7)
N27	-4816(3)	-7995.5(17)	-5430.0(13)	28.5(6)
C1	-10564(8)	-12315(6)	-8059(3)	110(4)
C3	-10183(5)	-12040(3)	-7094.4(19)	43.3(10)

C4	-10867(5)	-12007(2)	-6510.0(18)	36.0(9)
C6	-8925(5)	-12382(2)	-5903.5(17)	37.3(9)
C7	-7682(5)	-12123(2)	-5552.6(17)	39.6(10)
C8	-7177(6)	-12737(3)	-5133.4(19)	50.6(12)
C9	-6387(6)	-13397(3)	-5411(2)	50.1(12)
C10	-5194(6)	-13135(3)	-5810(2)	48.2(11)
C11	-5771(5)	-12568(2)	-6238.3(19)	39.1(9)
C12	-6443(5)	-11882(2)	-5937.7(18)	35.9(9)
C14	-6765(4)	-10558(2)	-6209.1(17)	33.7(8)
C15	-7133(4)	-10010(2)	-6696.2(17)	33.5(8)
C17	-9169(4)	-9535(2)	-6203.6(16)	32.3(8)
C18	-9870(4)	-8872(2)	-5895.0(19)	36.4(9)
C19	-11476(5)	-8842(3)	-5984(2)	46.7(11)
C20	-12278(5)	-9454(3)	-5664(3)	53.9(13)
C21	-11893(5)	-9463(3)	-5043(3)	54.6(14)
C22	-10321(5)	-9571(2)	-4957(2)	43.1(10)
C23	-9527(4)	-8925(2)	-5251.8(18)	34.6(8)
C25	-7183(4)	-8376(2)	-5153.0(14)	28.2(7)
C26	-5615(4)	-8555(2)	-5116.4(15)	28.9(7)
C28	-5162(4)	-7783(2)	-5960.8(15)	28.4(7)
C30	-4500(6)	-6833(3)	-6677.3(18)	47.2(11)
C31	-5922(8)	-6432(4)	-6670(4)	89(3)
C32	-3317(6)	-6247(3)	-6664(2)	54.5(13)
C33	-4258(12)	-7404(5)	-7146(3)	111(4)
C35	-12077(5)	-11428(3)	-6501.8(19)	42.4(10)
C37	-4485(7)	-13804(3)	-6100(3)	66.4(16)
C39	-5811(5)	-9718(3)	-6980(2)	47.3(11)
C42	-5188(5)	-8522(3)	-4489.3(17)	40.5(9)
C44	-10913(13)	-9367(9)	-8117(8)	41(4)
C48	-10731(18)	-9414(10)	-8149(6)	280(30)

Table S15. Anisotropic Displacement Parameters ($Å^2 \times 10^3$) for **9**. The Anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U_{11}+2hka^*b^*U_{12}+\ldots]$.

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
Cl45	62(3)	139(5)	85(3)	-21(3)	-35(3)	2(3)
Cl46	71(3)	105(4)	77(3)	-4(3)	7(3)	19(3)
Cl47	180(9)	73(4)	223(13)	-62(6)	96(9)	-31(5)
Cl49	128(6)	392(16)	264(12)	132(12)	-86(7)	20(8)
Cl50	360(20)	420(20)	196(10)	-110(11)	93(12)	127(17)
Cl51	237(6)	77(2)	121(3)	-51(2)	10(4)	-20(3)
O2	47(2)	99(3)	52.5(19)	-41(2)	-19.6(16)	17(2)
O29	36.7(15)	37.2(13)	30.7(12)	1.6(10)	-0.3(11)	-10.7(12)
O34	38.6(19)	71(2)	32.8(14)	-12.0(14)	-2.8(13)	1.7(16)
O36	60(2)	32.2(15)	79(2)	-1.5(15)	-16.1(19)	3.6(15)
O38	66(2)	34.6(15)	45.6(17)	-8.8(13)	-17.7(15)	-0.8(14)
O40	33.8(15)	27.8(13)	53.3(16)	-5.7(12)	3.8(13)	-1.1(11)
O41	32.8(15)	26.1(12)	47.9(15)	-0.4(11)	10.7(12)	2.0(11)
O43	39.0(16)	38.4(14)	32.9(13)	-3.4(11)	0.4(12)	-14.0(12)
N5	40.1(19)	31.7(16)	28.7(14)	0.1(12)	0.8(13)	-3.4(13)
N13	35.2(18)	29.4(15)	33.7(16)	-5.9(12)	-6.3(13)	-0.7(13)

N16	32.7(18)	26.0(14)	36.8(16)	-3.1(12)	2.4(13)	-2.4(13)
N24	31.2(18)	26.2(15)	42.5(17)	-3.1(13)	4.2(14)	0.3(12)
N27	26.2(16)	27.8(14)	31.4(14)	-4.2(11)	0.7(12)	-4.0(12)
C1	56(4)	217(10)	57(3)	-79(5)	-23(3)	44(5)
C3	40(3)	47(2)	44(2)	-12.4(18)	-11.0(19)	6.8(19)
C4	33(2)	31.5(18)	44(2)	0.6(15)	-3.4(17)	-6.1(16)
C6	44(2)	32(2)	35.4(19)	3.1(15)	5.3(17)	-0.5(17)
C7	55(3)	35(2)	29.3(17)	-1.7(15)	-5.0(17)	11.6(19)
C8	71(3)	49(2)	33(2)	2.2(18)	-7(2)	20(2)
C9	65(3)	41(2)	44(2)	6.8(19)	-8(2)	16(2)
C10	49(3)	38(2)	59(3)	-5(2)	-10(2)	12(2)
C11	40(2)	31.3(18)	46(2)	-4.2(16)	-1.9(18)	3.4(16)
C12	39(2)	30.5(18)	38.2(19)	-6.3(15)	-11.6(17)	4.7(16)
C14	32(2)	31.4(18)	37.9(19)	-5.2(16)	-3.7(16)	0.0(15)
C15	33(2)	31.7(18)	36.2(19)	-5.5(15)	-1.1(16)	-2.3(16)
C17	34(2)	29.9(17)	33.3(17)	-2.3(14)	-1.1(15)	2.2(16)
C18	35(2)	27.7(18)	47(2)	-3.5(16)	2.2(17)	1.8(16)
C19	32(2)	38(2)	71(3)	-13(2)	-3(2)	6.8(18)
C20	29(2)	40(2)	93(4)	-17(2)	10(2)	-1.1(19)
C21	39(3)	38(2)	86(4)	-14(2)	28(3)	-8.4(19)
C22	45(3)	34(2)	51(2)	-1.1(17)	15(2)	-4.8(18)
C23	30(2)	29.2(18)	45(2)	-3.8(15)	5.9(16)	-2.2(16)
C25	32(2)	26.1(17)	26.3(16)	-0.6(13)	6.6(14)	-0.1(14)
C26	32(2)	26.0(15)	28.6(16)	-0.6(13)	6.1(14)	0.6(14)
C28	30.2(19)	27.2(15)	27.9(15)	-4.6(13)	6.7(14)	-1.4(14)
C30	56(3)	53(2)	33(2)	12.7(18)	-9.7(19)	-22(2)
C31	67(4)	75(4)	125(6)	42(4)	-37(4)	-17(4)
C32	67(3)	54(3)	43(2)	14(2)	-3(2)	-26(3)
C33	168(9)	120(6)	47(3)	-38(4)	45(4)	-96(7)
C35	33(2)	52(2)	43(2)	-5.9(19)	2.1(17)	-1.0(19)
C37	68(4)	48(3)	84(4)	5(3)	12(3)	24(3)
C39	47(3)	41(2)	54(2)	-8.7(19)	14(2)	-4(2)
C42	39(2)	50(2)	32.4(19)	5.8(17)	1.0(16)	3.3(19)
C44	29(6)	35(8)	58(11)	0(7)	-13(6)	-10(5)
C48	660(90)	99(14)	91(13)	62(12)	-180(30)	-170(30)

Table S16. Bond Lengths for **9**.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
Cl45	C44	1.669(15)	N27	C28	1.342(5)
Cl46	C44	1.910(17)	C3	C4	1.519(6)
Cl47	C44	1.926(19)	C4	C35	1.536(6)
Cl49	C48	1.672(17)	C6	C7	1.510(6)
Cl50	C48	1.643(16)	C7	C8	1.537(6)
Cl51	C48	1.613(15)	C7	C12	1.544(7)
O2	C1	1.453(8)	C8	C9	1.529(7)
O2	C3	1.329(6)	C9	C10	1.541(8)
O29	C28	1.340(5)	C10	C11	1.518(6)
O29	C30	1.466(5)	C10	C37	1.517(7)
O34	C3	1.195(6)	C11	C12	1.536(5)
O36	C6	1.227(5)	C14	C15	1.535(6)

O38	C14	1.220(5)	C15	C39	1.513(6)
O40	C17	1.232(5)	C17	C18	1.526(5)
O41	C25	1.228(5)	C18	C19	1.541(6)
O43	C28	1.222(5)	C18	C23	1.547(6)
N5	C4	1.450(5)	C19	C20	1.518(7)
N5	C6	1.345(6)	C20	C21	1.502(9)
N13	C12	1.451(5)	C21	C22	1.520(7)
N13	C14	1.339(5)	C22	C23	1.530(5)
N16	C15	1.458(5)	C25	C26	1.526(6)
N16	C17	1.340(5)	C26	C42	1.528(5)
N24	C23	1.449(6)	C30	C31	1.524(10)
N24	C25	1.338(5)	C30	C32	1.525(6)
N27	C26	1.445(5)	C30	C33	1.508(8)

Table S17. Bond Angles for **9**.

Atom	Atom	Atom	Angle/°	Atom	Atom	Atom	Angle/°
C3	O2	C1	114.7(5)	O40	C17	N16	121.8(4)
C28	O29	C30	121.8(3)	O40	C17	C18	122.1(4)
C6	N5	C4	120.2(3)	N16	C17	C18	116.1(3)
C14	N13	C12	121.4(3)	C17	C18	C19	113.2(4)
C17	N16	C15	118.4(3)	C17	C18	C23	109.0(3)
C25	N24	C23	122.1(3)	C19	C18	C23	110.1(4)
C28	N27	C26	122.2(3)	C20	C19	C18	114.0(4)
O2	C3	C4	110.2(4)	C21	C20	C19	111.5(4)
O34	C3	O2	124.0(4)	C20	C21	C22	111.7(4)
O34	C3	C4	125.8(4)	C21	C22	C23	109.4(4)
N5	C4	C3	109.4(4)	N24	C23	C18	110.4(3)
N5	C4	C35	111.9(3)	N24	C23	C22	111.6(4)
C3	C4	C35	110.9(4)	C22	C23	C18	112.5(3)
O36	C6	N5	120.4(4)	O41	C25	N24	124.1(4)
O36	C6	C7	123.1(4)	O41	C25	C26	121.1(3)
N5	C6	C7	116.4(3)	N24	C25	C26	114.7(3)
C6	C7	C8	112.4(4)	N27	C26	C25	110.1(3)
C6	C7	C12	111.1(3)	N27	C26	C42	109.0(3)
C8	C7	C12	109.2(4)	C25	C26	C42	107.8(3)
C9	C8	C7	114.5(4)	O29	C28	N27	109.3(3)
C8	C9	C10	113.1(4)	O43	C28	O29	125.3(3)
C11	C10	C9	109.5(4)	O43	C28	N27	125.4(3)
C37	C10	C9	111.5(4)	O29	C30	C31	107.2(5)
C37	C10	C11	111.9(4)	O29	C30	C32	101.8(3)
C10	C11	C12	111.2(4)	O29	C30	C33	109.2(5)
N13	C12	C7	113.3(4)	C31	C30	C32	110.0(5)
N13	C12	C11	110.8(3)	C33	C30	C31	116.8(7)
C11	C12	C7	111.8(3)	C33	C30	C32	110.7(5)
O38	C14	N13	123.6(4)	Cl45	C44	Cl46	104.3(10)
O38	C14	C15	121.5(4)	Cl45	C44	Cl47	94.5(9)
N13	C14	C15	114.9(3)	Cl46	C44	Cl47	100.6(9)
N16	C15	C14	108.7(3)	Cl50	C48	Cl49	118.7(12)
N16	C15	C39	110.3(3)	Cl51	C48	Cl49	115.0(13)
C39	C15	C14	110.6(4)	Cl51	C48	Cl50	112.4(12)

Table S18. Torsion Angles for **9**.

A	B	C	D	Angle/°	A	B	C	D	Angle/°
O2	C3	C4	N5	173.2(4)	C10	C11	C12	C7	-60.5(5)
O2	C3	C4	C35	-62.8(5)	C12	N13	C14	O38	0.1(7)
O34	C3	C4	N5	-7.9(6)	C12	N13	C14	C15	177.7(4)
O34	C3	C4	C35	116.1(5)	C12	C7	C8	C9	-50.1(6)
O36	C6	C7	C8	-27.4(6)	C14	N13	C12	C7	86.0(5)
O36	C6	C7	C12	95.4(5)	C14	N13	C12	C11	-147.4(4)
O38	C14	C15	N16	-40.7(5)	C15	N16	C17	O40	-7.5(6)
O38	C14	C15	C39	80.6(5)	C15	N16	C17	C18	171.4(3)
O40	C17	C18	C19	-42.8(6)	C17	N16	C15	C14	-59.5(4)
O40	C17	C18	C23	80.0(5)	C17	N16	C15	C39	179.1(4)
O41	C25	C26	N27	-38.2(5)	C17	C18	C19	C20	72.9(5)
O41	C25	C26	C42	80.6(4)	C17	C18	C23	N24	52.8(4)
N5	C6	C7	C8	151.7(4)	C17	C18	C23	C22	-72.6(4)
N5	C6	C7	C12	-85.5(4)	C18	C19	C20	C21	52.2(5)
N13	C14	C15	N16	141.7(4)	C19	C18	C23	N24	177.6(3)
N13	C14	C15	C39	-97.1(4)	C19	C18	C23	C22	52.1(4)
N16	C17	C18	C19	138.2(4)	C19	C20	C21	C22	-56.7(5)
N16	C17	C18	C23	-99.0(4)	C20	C21	C22	C23	59.0(5)
N24	C25	C26	N27	145.8(3)	C21	C22	C23	N24	178.0(4)
N24	C25	C26	C42	-95.4(4)	C21	C22	C23	C18	-57.2(5)
C1	O2	C3	O34	0.0(8)	C23	N24	C25	O41	9.9(6)
C1	O2	C3	C4	178.9(6)	C23	N24	C25	C26	-174.3(3)
C4	N5	C6	O36	-12.7(6)	C23	C18	C19	C20	-49.4(5)
C4	N5	C6	C7	168.2(4)	C25	N24	C23	C18	83.7(4)
C6	N5	C4	C3	-77.5(5)	C25	N24	C23	C22	-150.4(3)
C6	N5	C4	C35	159.1(4)	C26	N27	C28	O29	174.0(3)
C6	C7	C8	C9	73.8(6)	C26	N27	C28	O43	-6.0(6)
C6	C7	C12	N13	56.0(4)	C28	O29	C30	C31	65.7(5)
C6	C7	C12	C11	-70.1(4)	C28	O29	C30	C32	-178.8(4)
C7	C8	C9	C10	50.5(6)	C28	O29	C30	C33	-61.8(6)
C8	C7	C12	N13	-179.4(3)	C28	N27	C26	C25	-47.8(4)
C8	C7	C12	C11	54.5(4)	C28	N27	C26	C42	-165.9(3)
C8	C9	C10	C11	-52.7(5)	C30	O29	C28	O43	2.6(6)
C8	C9	C10	C37	-177.1(5)	C30	O29	C28	N27	-177.4(4)
C9	C10	C11	C12	57.7(5)	C37	C10	C11	C12	-178.2(4)
C10	C11	C12	N13	172.1(4)					

Copies of high-resolution mass spectra

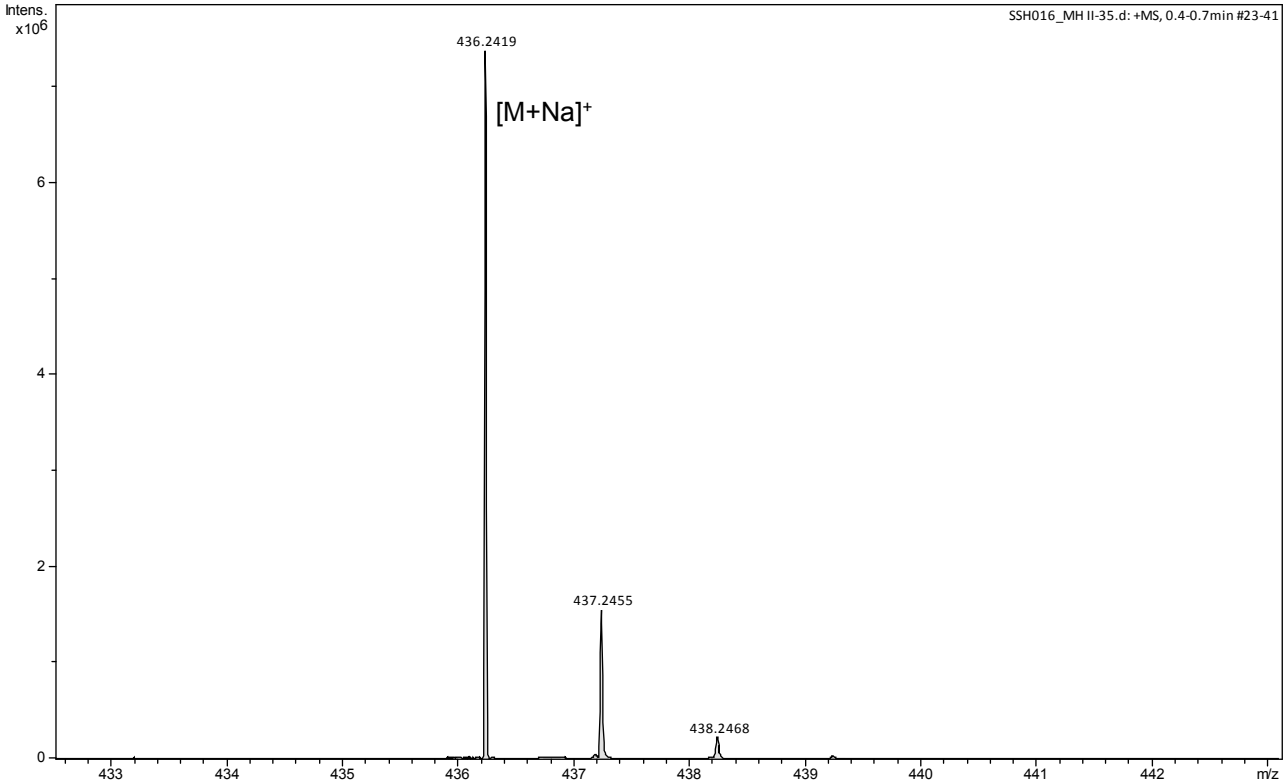


Figure S4. High-resolution mass spectrum for **6**

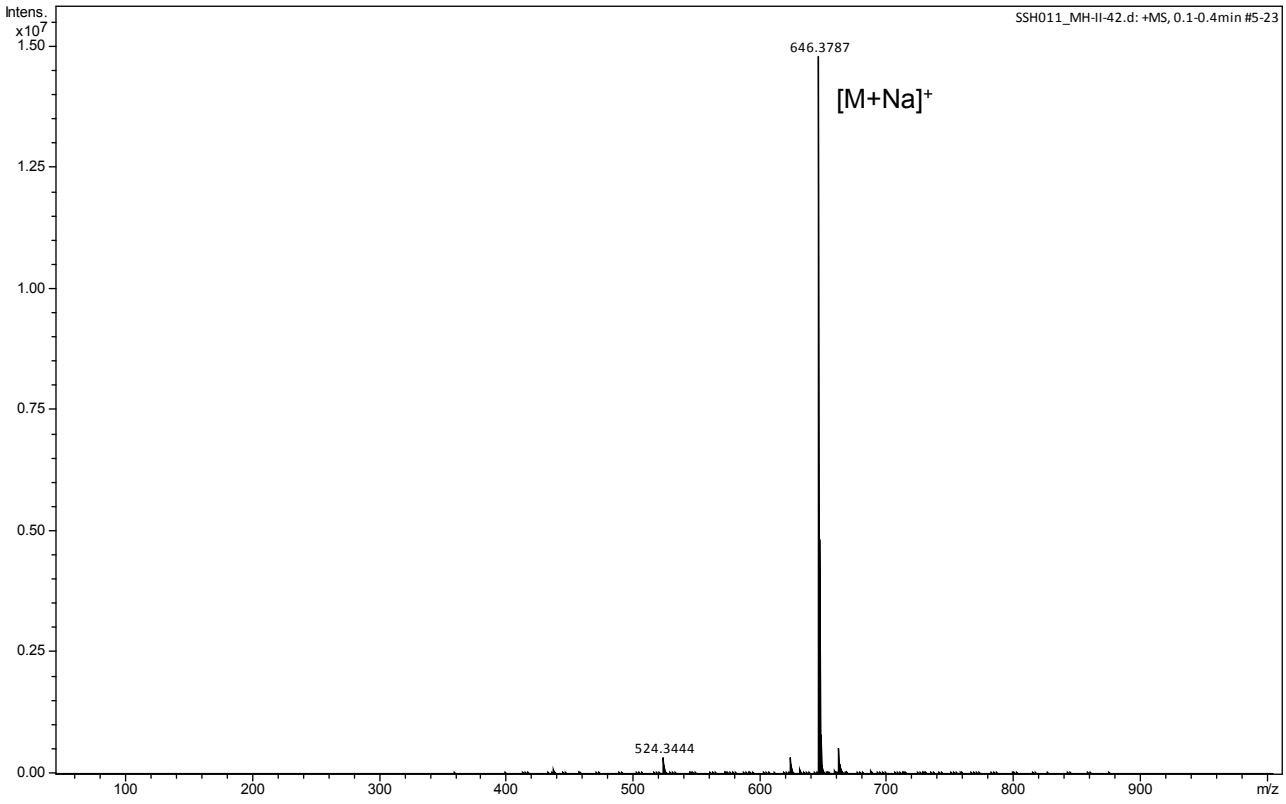


Figure S5. High-resolution mass spectrum for **7**

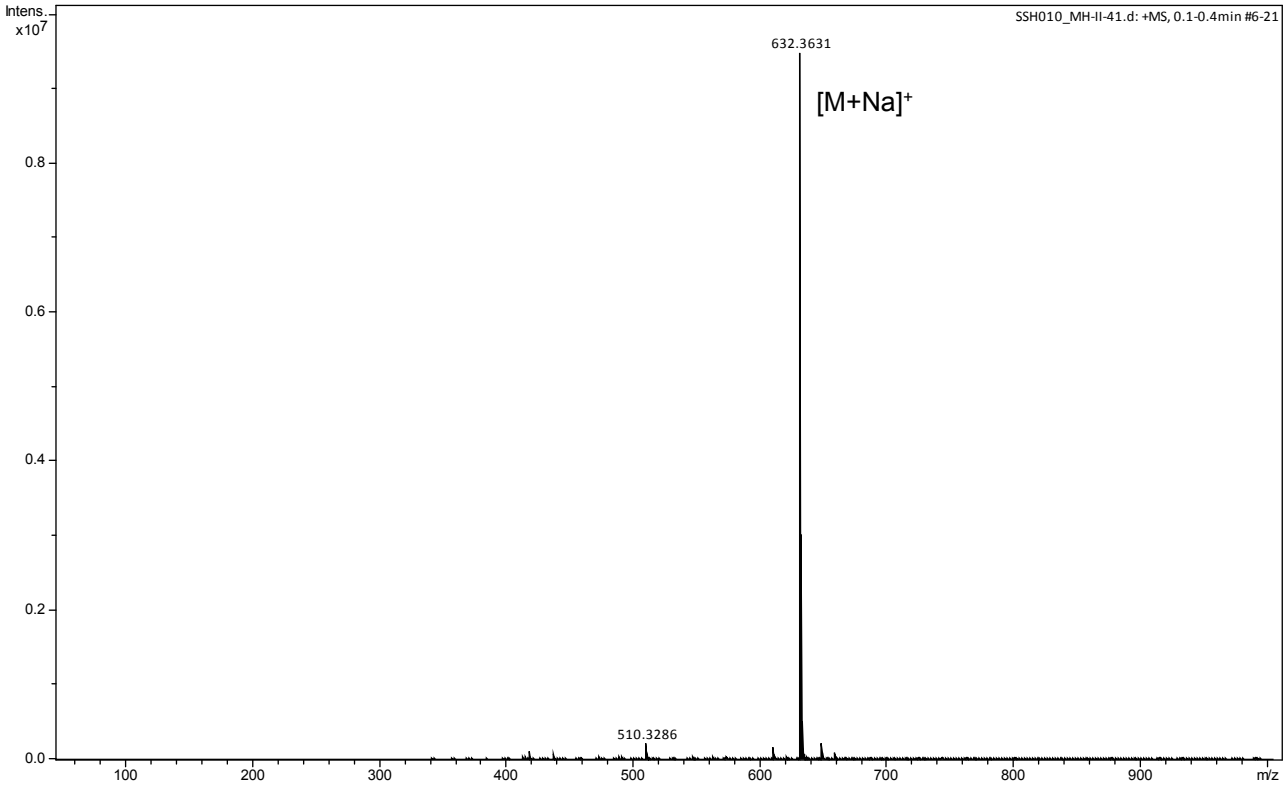


Figure S6. High-resolution mass spectrum for **8**

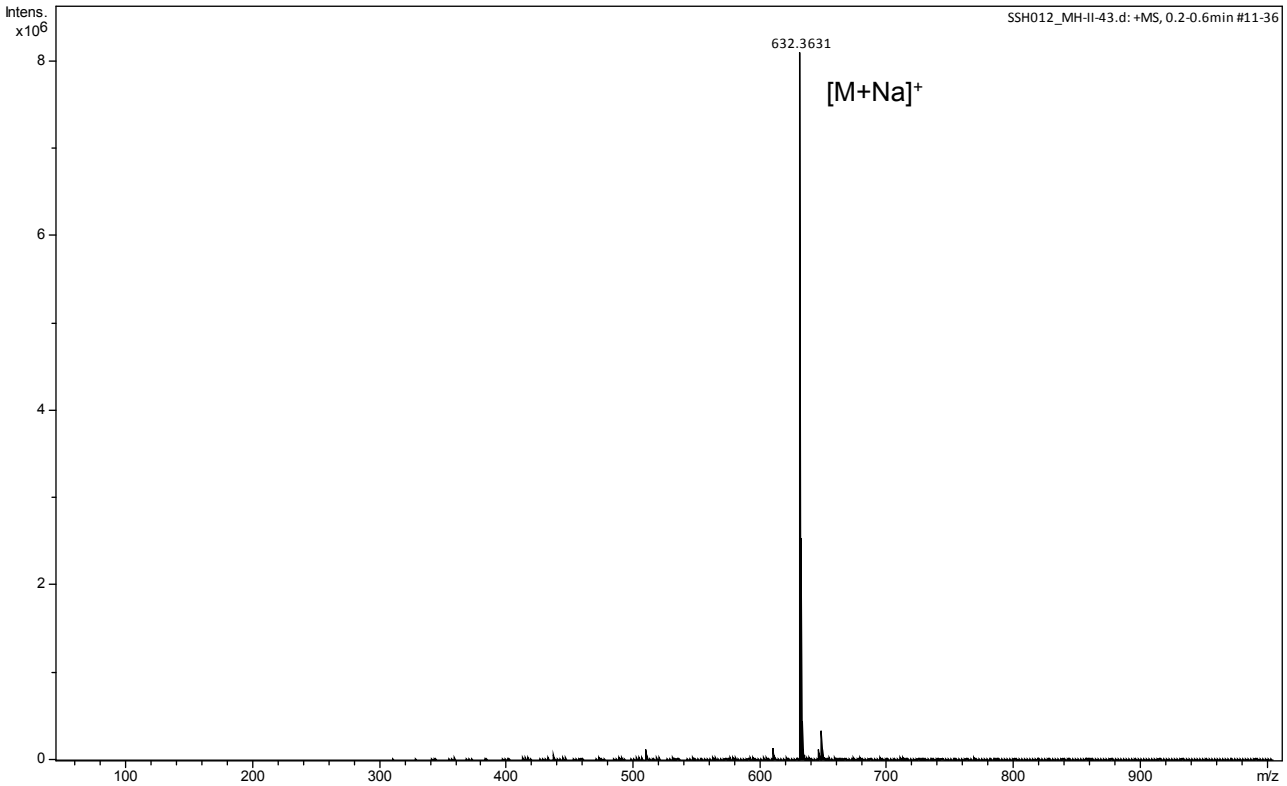


Figure S7. High-resolution mass spectrum for **9**

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