Supporting Information

New Preorganized γ-Amino Acids as Foldamer Building Blocks

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I. Materials and Instrumentation

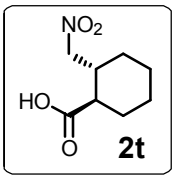
Proton nuclear magnetic resonance (^{1}H NMR) spectra were recorded on Bruker AC-300 (300 MHz) spectrometers. Chemical shifts were recorded in parts per million (ppm, δ) relative to tetramethylsilane (δ 0.00). ^{1}H NMR splitting patterns are designated as singlet (s), doublet (d), triplet (t), or quartet (q). All first-order splitting patterns were assigned on the basis of the appearance of the multiplet. Splitting patterns that could not be easily interpreted are designated as multiplet (m) or broad (br). Carbon nuclear magnetic resonance (^{13}C NMR) spectra were recorded on a Bruker AC-300 (75 MHz) spectrometer. Mass spectra (MS) were obtained using an electrospray ionization (ESI) mass spectrometer. Flasks were oven-dried overnight and cooled under a stream of nitrogen. All reagents were purchased from Aldrich Chemical Company. Flash chromatography was performed using silica gel 60 Å (32-63 mesh) from Sorbent Technologies. Reactions were monitored by thin layer chromatography (TLC) using 0.25 mm E. Merck pre-coated silica gel 60 (particle size 0.040–0.063 mm). Visualization was performed using a UV lamp or potassium permanganate stain.

II. General Procedure for Organocatalytic Michael Reaction of a Nitromethane with 1-Cyclohexene-1-Carboxaldehyde

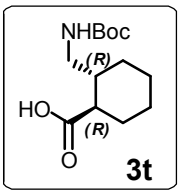
To a 20 mL vial equipped with a small magnetic stir bar was added 0.4 mmol of amine catalyst **A** (325 mg, 20 mol %) in EtOH (8.6 mL), 0.2 mmol benzoic acid (63 mg, 10 mol %) and 5.0 mmol 1-cyclohexene-1-carboxaldehyde (582 μL, 1.0 equiv.). The mixture was stirred at room temperature for about 1 min, and then 6.0 mmol nitromethane (806 μL, 3.0 equiv.) was added. The total volume of the reaction mixture was about 10 mL ([1-cyclohexene-1-carboxaldehyde] in reaction mixture ~ 0.5 M). The mixture was stirred at room temperature. Reaction progress was monitored by ^{1}H NMR analysis of the crude reaction mixture. Specifically, 50 μL crude reaction mixture was mixed with 500 μL $CDCl_3$ for ^{1}H NMR analysis. After NMR data showed that the reaction was complete, excess $NaBH_4$ (9 mmol, 306 mg) was added, followed by 10 mL MeOH, and the mixture was stirred for a few minutes. [These aldehydes were rapidly reduced to the corresponding *trans* and *cis* γ-nitro alcohols **1t** and **1c** to avoid epimerization adjacent to the aldehyde group. HPLC analysis of the *trans* γ-nitro aldehyde indicated that this molecule was generated in 99% *ee*. HPLC conditions: Chiracel OD-H column, λ=220 nm, hexane/isopropanol (v/v: 97/3), flow rate = 1.0 mL/min; t = 30.5 min, 34.5 min (99% *ee*). The *ee* of *cis* γ-nitro alcohol **1c** (> 95% *ee*) was determined by ^{1}H NMR analysis of the unpurified product generated by coupling *cis* γ-nitro acid **2c** to L-alanine methyl ester]. The mixture was then slowly poured into a 100 mL beaker containing 20 mL 1 M NH_4Cl at 0 °C. The resulting mixture was extracted with EtOAc (about 3 x 10 mL). Extraction of the product into the organic phase was monitored

by TLC. The EtOAc layers were collected, washed with 30 mL brine, dried over $MgSO_4$ and filtered. The filtrate was concentrated to give the crude alcohol product, which was purified via SiO_2 column chromatography eluting with EtOAc/hexane to give the nitro alcohols **1t** and **1c**. Diastereomers **1t** and **1c** were difficult to separate on a preparative scale, so the mixture of these δ-nitro alcohols was treated with $H_2Cr_2O_7$ in acetone, which quantitatively generated the corresponding γ-nitro carboxylic acids **2t** and **2c**. These diastereomers could be separated by chromatography and crystallization (major isomer **2t** is a white solid, while **2c** is an oil).

(1R,2R)-2-(nitromethyl)cyclohexanecarboxylic acid (2t): To 6.1 mmol alcohol **(1t and 1s)** dissolved in 60 mL acetone at 0 °C was added 9.1 mmol H2Cr2O7 (18 mL Jones reagent). The mixture was stirred for 5 h, during which time the mixture warmed to room temperature. Excess isopropanol was added, and the mixture was stirred for 10 min. The mixture was filtered, and the solution was diluted with 40 mL 1 N HCl and extracted with Et2O. The combined organic layer was washed with brine, dried over MgSO4, filtered and concentrated to give a viscous oil, from which the residue was purified via column chromatography eluting with EtOAc/hexane (1:10 to1:3; v/v) to give pure product as a white solid. ^{1}H NMR (300 MHz, CDCl3) δ 4.75 (m, 1H), 4.33(m, 1H), 3.65 (m, 2H), 2.10 (m, 1H), 1.77(m, 2 H), 1.54 (m, 1H), 1.42 (m, 2H), 1.25 (m, 2H).

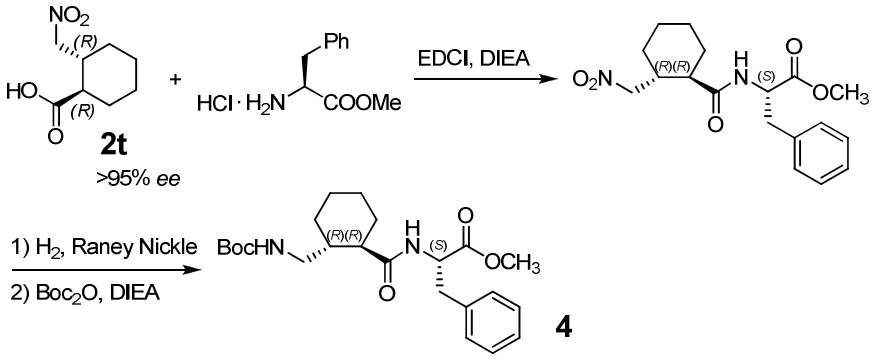


(1R,2R)-2-((tert-butoxycarbonylamino)methyl)cyclohexanecarboxylic acid (3t): γ-nitro acid **2t** (5.1 mmol) was dissolved in methanol (10 mL), and flask was flushed with N2. To the flask was added Pd/C (0.1 g), and the flask was attached to a Parr apparatus and shaken for 24 hours at a H2 pressure of 40 psi. The reaction mixture was filtered through a pad of celite and concentrated to give a white solid. This solid was suspended in anhydrous CH2Cl2 (20 mL) and stirred vigorously. TMSCl (1.29 mL, 10.2 mmol) was added in one portion, and the mixture was stirred at room temperature for 2 h. The mixture was cooled to 0 °C, and DIEA (1.59 mL, 9.1 mmol) and Boc2O (1.7 g, 7.7 mmol) were added sequentially. The reaction mixture was allowed to warm to room temperature and stirred for 12 h. The resulting mixture was concentrated to provide a yellow oil, which was then dissolved in EtOAc (50 mL). To this solution, water was added (20 mL), and the solution was acidified with 1 N HCl. The separated organic layer was dried (MgSO4), filtered and concentrated to give a white solid. The residue was purified via column chromatography eluting with EtOAc/hexane (1:10 to1:1; v/v) to give the desired product as a white solid in 80 % yield.



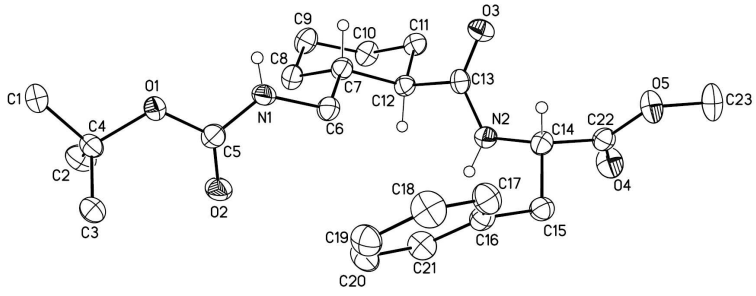
TLC Rf = 0.3 (EtOAc/hexanes, v/v, 1:1). ^{1}H NMR (300 MHz, CDCl3), δ 6.40 (m, 1H), 4.83 (m, 1H), 3.10 (m, 3H), 1.56 (m, 8H), 1.43 (s, 9H).

III. Stereochemistry Determination:



Compound **2t**, generated from Michael Reaction of a nitromethane with 1-cyclohexene-1-carboxaldehyde, was coupled to (L)-phenylalanine methyl ester to afford coupling product**.** The L-phenylalanine/γ-dipeptide **4** was prepared in an efficient one-pot operation involving nitro group reduction followed by Boc protection.

The absolute configuration of **2t** was established as (*R,R*) via the crystal structure of L-phenylalanine/γ-dipeptide derivative **4**.



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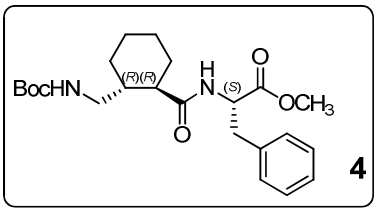
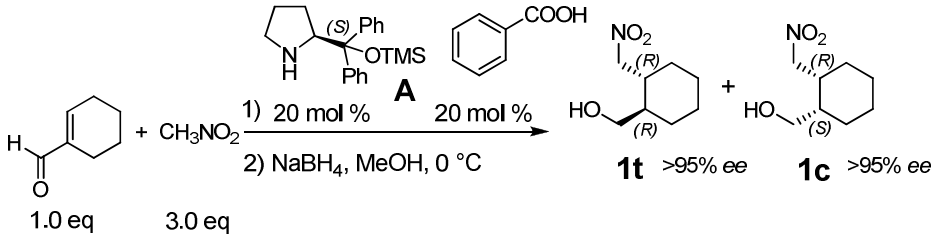


We observed that the minor γ-nitro aldehyde stereoisomer generated by the Michael addition could be converted to the major γ-nitro aldehyde isomer by treatment with DBU, which suggests that γ-nitro carboxylic acid **2c** has the *S* configuration at the ring carbon bearing the carboxyl group. This deduction was confirmed by oligomer crystal structures **5** and **6** discussed below.

IV. Solvent Effects

Our methodology development efforts were motivated by results from Hayashi et al.[8] and Wang et al.[9]; these groups simultaneously reported that pyrrolidine **A** catalyzes a highly enantioselective Michael addition of nitromethane to β-substituted propenal derivatives. Use of benzoic acid as a co-catalyst proved to be necessary for high yields, and simple alcohols were superior as reaction media to nonpolar or polar aprotic solvents. For the Michael reaction of a nitromethane with 1-cyclohexene-1-carboxaldehyde, we found that the desired Michael product was obtained with excellent enantioselectivity (>95% *ee*), but only moderate diastereoselectivity (**1t:1c** = 4.5:1) when 20 mol% (*S*)-**A** and 10 mol% benzoic acid were employed. To improve the diastereomeric ratio, the reaction conditions were examined in detail. It was found that both the co-catalyst and solvent used in the reaction are important. The diastereomeric ratio was improved to 7:1 (**1t:1c**) by using 20 mol% benzoic acid. After screening the solvents (EtOH, MeOH, *i*-PrOH and CH_2Cl_2), we found that excellent yield and moderate diastereomeric ratio were achieved when EtOH was employed (Table S1).

Table S1



Entry	solvents	Yield (%)[a]	dr (1t:1c)[a]
1	MeOH	65	5:1
2	EtOH	91	7:1
3	*i*-PrOH	99	5:1
4	CH_2Cl_2	10	9:1

a. Determined from H NMR of the crude reaction mixture after 24 hours

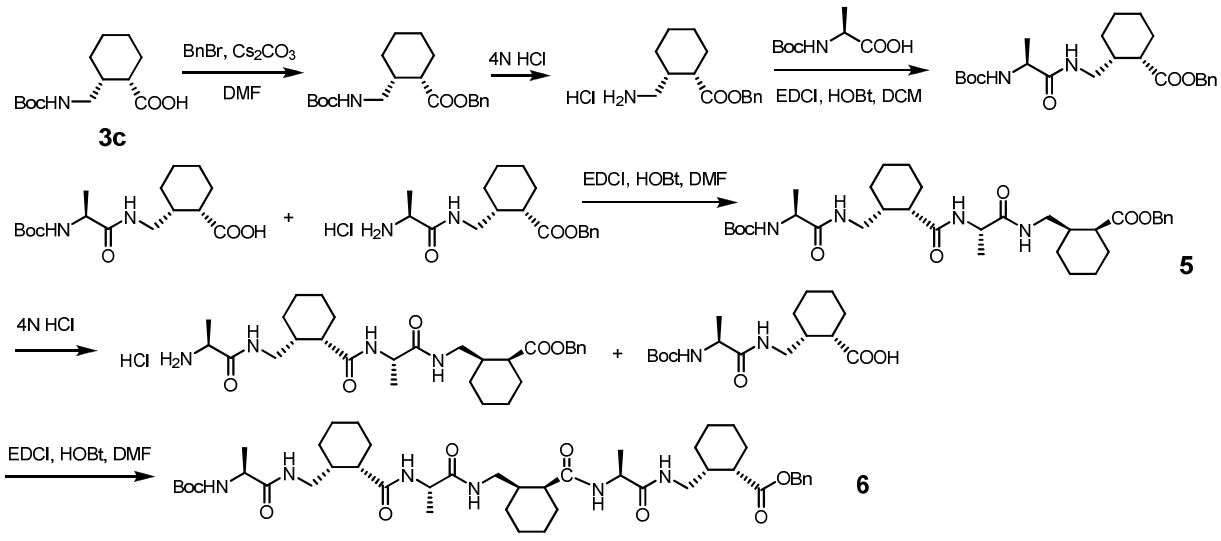
V. Peptide Synthesis and Purification

Peptides **5** and **6** were synthesized by conventional solution phase methods using a fragment condensation strategy. The tert-butyloxycarbonyl group (Boc) was used for N-terminal protection, and the C-terminal was protected as a benzy ester (OBn). Deprotection at the N-terminus was performed using 4N HCl in dioxane, and hydrogenation was done to remove the C-terminal protecting groups.

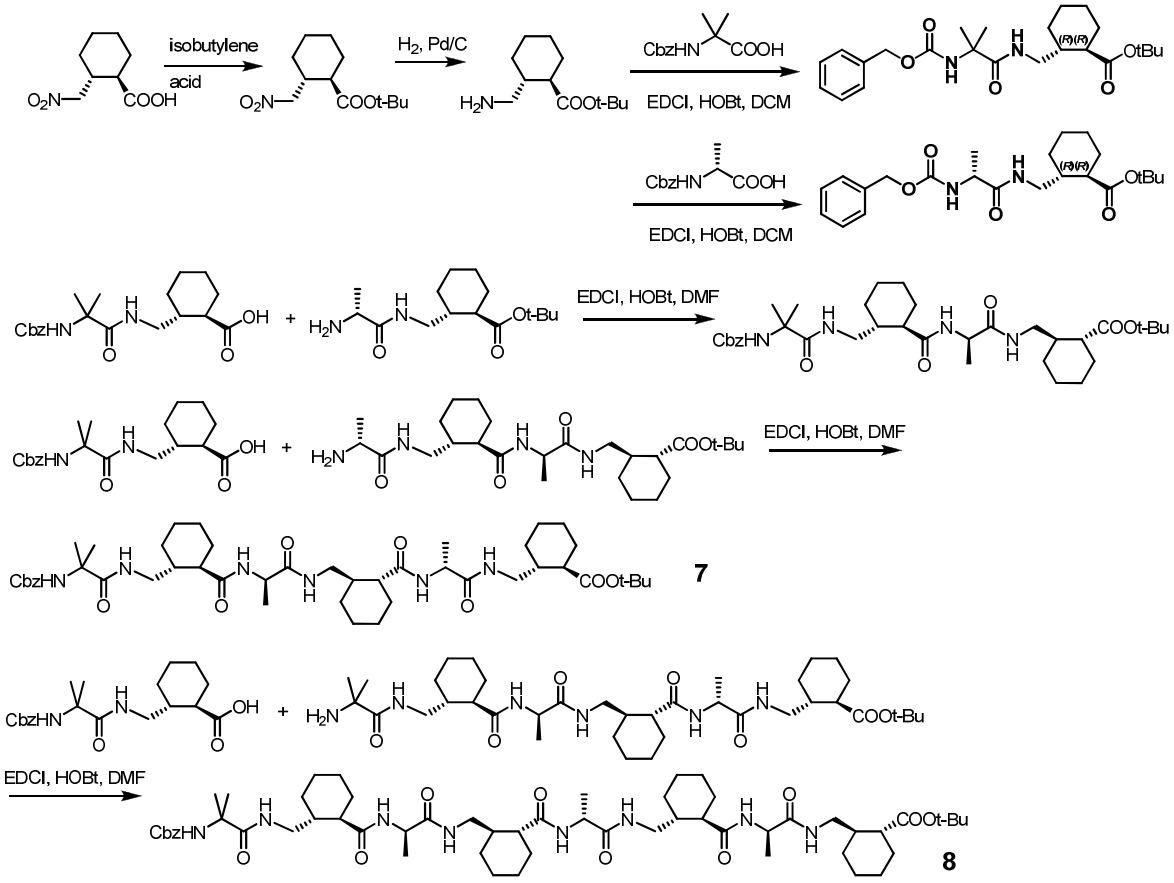
Peptides **7** and **8** were synthesized by conventional solution phase methods using a fragment condensation strategy. The Carboxybenzyl group (Cbz) was used for N-terminal protection, and the C-terminal was protected as a tert-butyl ester (OtBu). Deprotection at the C-terminus was performed using 4N HCl in dioxane, and hydrogenation was done to remove the N-terminal protecting groups.

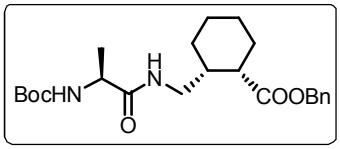
Boc or Cbz-protected amino acids, *N,N*-Diisopropylethylamine (DIEA), and coupling reagents (N,N-dimethylamino) propyl-3-ethylcarbodiimide hydrochloride (EDCI▪HCl) and Hydroxybenzotriazole (HOBt) were purchased from Sigma-Aldrich and Chem-Impex.

Scheme S1 Synthesis of Peptides **5** and **6**



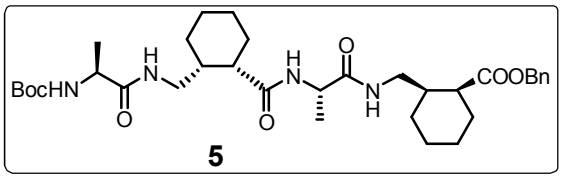
Scheme S2 Synthesis of Peptides **7** and **8**





Boc-(L)Ala-γ(II)-OBn: Boc-(L)-Ala-OH (284 mg, 1.5 mmol) was added directly to a solution of HCl·NH2-γ(II)-OBn (426 mg, 1.5 mmol), EDCI (345 mg, 1.8 mmol), and *N,N*-diisopropylethylamine (392 µL, 2.25 mmol) in CH2Cl2 (10 mL). The resulting solution was stirred for one day at room temperature. The reaction mixture was diluted with EtOAc, washed with aqueous 10% aqueous citric acid, saturated aqueous NaHCO3 and then brine. The organic layer was dried over MgSO4, filtered and concentrated to give a residue that was purified via column chromatography eluting with EtOAc and hexanes to yield the desired product (596 mg, 95% yield). ^{1}H NMR (300 MHz, CDCl3) δ 7.37-7.3 (m, 5H), 6.28(br, 1H), 5.13 (s, 2H), 4.97 (br, 1H), 4.05 (m, 1H), 3.43 (m, 1H), 3.04 (m, 1H), 2.71 (m, 1H), 1.98 (m, 1H), 1.91 (m, 1H), 1.61 (m, 4H), 1.49-1.37 (m, 3H), 1.43 (s, 9H), 1.34-1.26 (m, 1H), 1.29 (d, *J* = 7.1 Hz, 3H); ^{13}C NMR: (75.4 MHz, CDCl3) δ 174.50, 172.69, 155.65, 136.23, 128.84, 128.49, 128.45, 101.14, 80.21, 66.29, 50.37, 42.86, 41.53, 38.39, 28.52, 26.97, 26.81, 23.88, 23.36, 18.58; HRMS *m/z* (ESI): calcd. for: C23H34N2O5Na [M+Na]+441.2360, found 441.2363.

Boc-(L)Ala-γ(II)-(L)Ala-γ(II)-OBn (5): Dipeptide Boc-(L)Ala-γ(II)-OBn was dissolved in methanol, and flask was flushed with N2. To the flask was added 10% Pd/C, and the flask was attached to a Parr apparatus and shaken for 6-7 hours at a H2 pressure of 10 psi. The reaction mixture was then filtered through a pad of celite and concentrated to give Boc-(L)Ala-γ(II)-OH as a white solid, the crude product was carried on without any purification.



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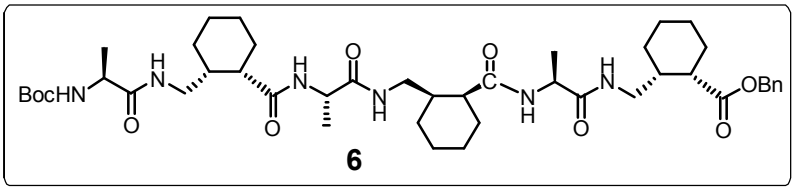
Boc-(L)Ala-γ(II)-OBn (1 equiv.) was treated with 4.0 M HCl in dioxane (~10 eq). The mixture was stirred for 30 min and then concentrated under a nitrogen gas stream to give the HCl salt form of the amine, which was coupled with Boc-(L)Ala-γ(II)-OH by a general peptide coupling method to give the desired product as a white solid. The X-ray quality crystal was grown by slow evaporation of a dichloroethane/heptane solution. 1H NMR (300 MHz, CDCl3) 8.06 (br, 1H), 7.74 (d, *J* = 7.2 Hz, 1H), 7.37-7.31 (m, 5 H), 6.30 (br, 1H), 5.13 (s, 2H), 4.94 (d, *J* = 8.0 Hz, 1H), 4.23 (p, *J* = 7.2 Hz, 1H), 4.09 (p, *J* = 7.2 Hz, 1H), 3.43 (m, 2H), 3.06 (m, 1H), 2.80 (m, 1H), 2.46 (m, 1H), 2.36 (m, 1H), 2.26 (m, 1H), 2.01 (m, 1H), 1.90 (m, 1H), 1.93-1.55 (m, 7H), 1.48-1.20 (m, 23 H). 13C NMR: (75.4 MHz, cdcl3) delta 176.18, 175.12, 174.59, 173.23, 156.12, 136.22, 128.82, 128.47, 128.40, 80.37, 66.32, 50.86, 49.40, 44.01, 42.83, 41.69, 40.36, 38.26, 36.21, 28.47, 26.93, 26.74, 26.68, 25.50, 23.80, 23.44, 22.03, 17.81, 17.45; HRMS *m/z* (ESI): calcd. for: C34H54N4O7 [M+H]+ 629.3909, found 629.3908.

Boc-(L)Ala-γ(II)-(L)Ala-γ(II)-(L)Ala-γ(II)-(L)Ala-γ(II)-OBn (6): Tetramer Boc-(L)Ala-γ(II)-(L)Ala-γ(II)-OBn (1.0 equiv) was treated with 4.0 M HCl in dioxane (~10 eq). The mixture was stirred for 30 min and then concentrated under a nitrogen gas stream to give the HCl salt form of the amine, which was coupled with Boc-(L)Ala-γ(II)-OH by a general peptide coupling method to give the desired product as white solid. The X-ray quality crystal was grown by slow evaporation of a dichloroethane/heptane solution. 1H NMR (300 MHz, CDCl3) 8.50 (m, 2H), 8.11 (m, 2H), 7.39-7.29 (m, 5 H), 6.19 (br, 1H), 5.13 (s, 2H), 5.00 (d, *J* = 7.8 Hz, 1H), 4.24 (p, *J* = 7.2 Hz, 1H), 4.10 (p, *J* = 7.2 Hz, 2H), 3.55-3.35 (m, 3H), 3.06 (m, 1H), 2.84 (m, 1H), 2.57-2.17 (m, 5H), 2.06-1.11(m,44H); 13C NMR: (75.4 MHz, cdcl3) delta 176.79, 176.58, 176.06, 175.75, 174.60, 173.33, 156.13, 139.61, 128.84, 128.49, 128.41, 80.46, 66.33, 51.04, 50.27, 49.86, 44.82, 44.15, 42.82, 41.64, 39.61, 39.52, 38.30,



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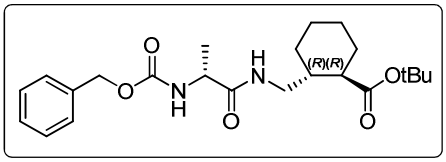
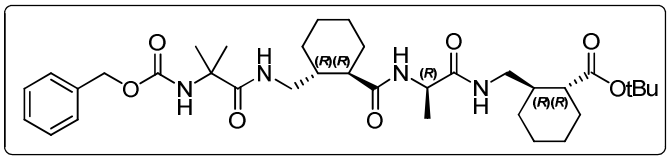
36.21, 35.74, 29.91, 28.93, 28.65, 28.45, 27.05, 26.94, 26.70, 26.52, 25.80, 25.71, 23.76, 23.49, 21.91, 21.69, 17.65, 17.45, 17.01; HRMS *m/z* (ESI): calcd. for: C45H71N6O9 [M+H]+ 839.5278, found 839.5258.

Cbz-(D)Ala-γ(III)-Ot-Bu: (*D*)-Cbz-Ala-OH (327 mg, 1.46 mmol) was added directly to a solution of (*R,R*)-NH2-γ(III)-Ot-Bu (312 mg, 1.46 mmol), EDCI (336 mg, 1.75 mmol), and *N,N*-diisopropylethylamine (305 µL,1.75 mmol) in CH2Cl2 (10 mL). The resulting solution was stirred for 24 hr at room temperature. The reaction mixture was diluted with EtOAc, washed with 1 M aqueous NaHSO4 and then brine. The organic layer was collected and dried over Na2SO4, filtered and concentrated to give a residue that was purified via column chromatography to yield the desired product (550 mg, 90% yield) as white foam. TLC Rf = 0.65 (EtOAc/hexanes, v/v, 1:1). 1H NMR (300 MHz, CDCl3) δ7.35 (m, 5H), 6.24 (broad, 1H), 5.42 (d, *J* = 6.0 Hz, 1H), 5.11 (s, 2H), 4.20 (p, *J* = 7.0 Hz, 1H), 3.25 (m, 1H), 3.14 (m, 1H), 1.93 (m, 2H), 1.80-1.64 (m, 4H), 1.45 (s, 9H), 1.38 (d, *J* = 7.1 Hz, 3H), 1.28-0.79 (m, 4H); 13C NMR: (75.4 MHz, cdcl3) delta 175.50, 172.40, 156.10, 136.44, 128.76, 128.42, 128.27, 80.83, 67.18, 50.88, 48.42, 43.66, 39.66, 30.01, 29.65, 28.28, 25.49, 25.43, 19.12; HRMS *m/z* (ESI): calcd. for: C23H35N2O5 [M+H]+ 419.2541, found 419.2546, calcd. for: C23H34N2O5Na [M+Na]+ 441.2360, found 441.2363.

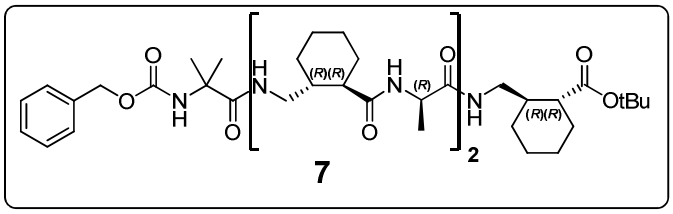


Cbz-Aib-γ(III)-(D)Ala-γ(III)-Ot-Bu: Cbz-Aib-γ(III)-OH (207 mg, 0.55 mmol) was added directly to a solution of NH2-(D)Ala-γ(III)-Ot-Bu (156 mg, 0.55 mmol), EDCI (127 mg, 0.66 mmol), HOBt (82 mg, 0.61 mmol), and *N,N*-diisopropylethylamine (115 µL, 0.66 mmol) in DMF (5 mL). The resulting solution was stirred for 24 h at room temperature. The reaction mixture was diluted with EtOAc, washed with 1 M aqueous NaHSO4, saturated aqueous NaHCO3 and brine. The organic layer was collected and dried over MgSO4, filtered and concentrated to give a residue that was purified via column chromatography to yield the desired product as white foam (301 mg, 85% yield). TLC Rf = 0.10 (EtOAc/hexanes, v/v, 1:1). 1H NMR (300 MHz, CDCl3) δ 7.51 (broad, 1H), 7.34 (m, 5H), 6.37 (broad, 1H), 6.29 (d, *J* = 8.3 Hz, 1H), 5.90 (s, 1H), 5.09, 4.92 (AB, *JAB* = 11.9 Hz, 2H), 4.54 (p, *J*= 7.4 Hz, 1H), 3.77 (m, 1H), 3.29 (m, 1H), 3.05 (m, 1H), 2.80 (m, 1H), 2.10-0.70 (m, 38H); 13C NMR: (75.4 MHz, cdcl3) delta 175.92, 175.82, 174.95, 173.00, 155.95, 136.13, 128.81, 128.55,128.52, 80.48, 67.09, 57.08, 49.21, 48.52, 43.67, 42.90, 39.37, 38.96, 30.83, 30.33, 29.68, 29.26, 28.22,



25.84, 25.70, 25.65, 25.58, 25.47, 18.78; HRMS *m/z* (ESI): calcd. for C35H54N4O7Na [M+Na]+ 665.3885, found 665.3882.

Cbz-Aib-γ(III)-(D)Ala-γ(III)-(D)Ala-γ(III)-Ot-Bu (7): Cbz-Aib-γ(V)-Ala-γ(V)-OH (167 mg, 0.28 mmol) was added directly to a solution of NH2-Ala-γ(V)-Ot-Bu (82 mg, 0.29 mmol), EDCI (66 mg, 0.34 mmol), HOBt (46 mg, 0.34 mmol), and *N,N*-diisopropylethylamine (59 µL, 0.34 mmol) in DMF (3 mL). The resulting solution was stirred for two days at room temperature.The reaction mixture was diluted with EtOAc, washed with 1 M aqueous NaHSO4, saturated aqueous NaHCO3 and then brine. The organic layer was collected and dried over MgSO4, filtered and concentrated to give a residue that was purified via column chromatography to yield the desired product (194 mg, 80% yield) as a white solid. 1H NMR (300 MHz, CDCl3) δ 7.86 (broad, 1H), 7.45 (broad, 1H), 7.36 (m, 5H), 6.91 (broad, 1H), 6.61 (d, *J* = 6.4 Hz, 1H), 6.51 (broad, 1H), 5.48 (s, 1H), 5.12, 5.08 (AB, *JAB* = 12.6 Hz, 2H), 4.36 (m, 2H), 3.76 (m, 1H), 3.54 (m, 1H), 3.18 (m, 2H), 2.89 (m, 2H), 2.06-0.86 (m, 51H); HRMS *m/z* (ESI): calcd. for: C46H72N6O9Na [M+Na]+ 875.5253, found 875.5276.



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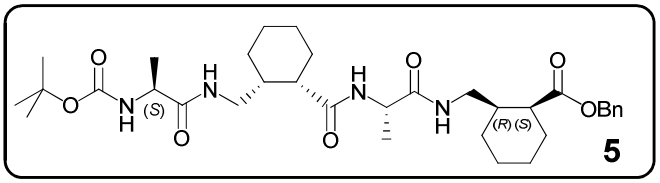
VI. Crystallographic Experimental Section

Crystallization and X-ray Analysis

High-quality crystals of α/γ-peptides 5 and 6 were grown by slow evaporation of chloroform/heptanes/ether or chloroform/heptanes solutions, respectively, and the structures of these oligomers were solved based on X-ray diffraction data. Dr. Ilia Guzei performed the X-ray analysis and solved all structures. The detailed crystallographic experimental section is provided.



5

Data Collection

A colorless crystal with approximate dimensions 0.43 x 0.18 x 0.17 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.

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 0.5° in a 6° 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 suite. The final cell constants were calculated from a set of 9790 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 0.70 Å. A total of 78541 data were harvested by collecting 6 sets of frames with 0.5° scans in ω and φ with exposure times of 15 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. [1]

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 [2].

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 absolute configuration could not be established by anomalous dispersion effects and was assigned based on the synthetic procedure. The absolute configuration is "S" at atoms C6, C15, C17 and C26 and "R" at atoms C10 and C21. There are two intramolecular and two intermolecular hydrogen bonding interactions of the type N-H···O.

The final least-squares refinement of 411 parameters against 4524 data resulted in residuals *R* (based on F^2 for $I \geq 2\sigma$) and *wR* (based on F^2 for all data) of 0.0330 and 0.0925, respectively. The final difference Fourier map was featureless.

The molecular diagram is drawn with 40% probability ellipsoids.

References

[1] Bruker-AXS. (2009) APEX2, SADABS, and SAINT Software Reference Manuals. Bruker-AXS, Madison, Wisconsin, USA.

[2] Sheldrick, G. M. (2008) SHELXL. *Acta Cryst.* **A64**, 112-122.

[3] Guzei, I.A. (2006-2008). Internal laboratory computer programs "Inserter", "FCF_filter", "Modicifer".

[4] Pennington, W.T. (1999) *J. Appl. Cryst.* **32**(5), 1028-1029

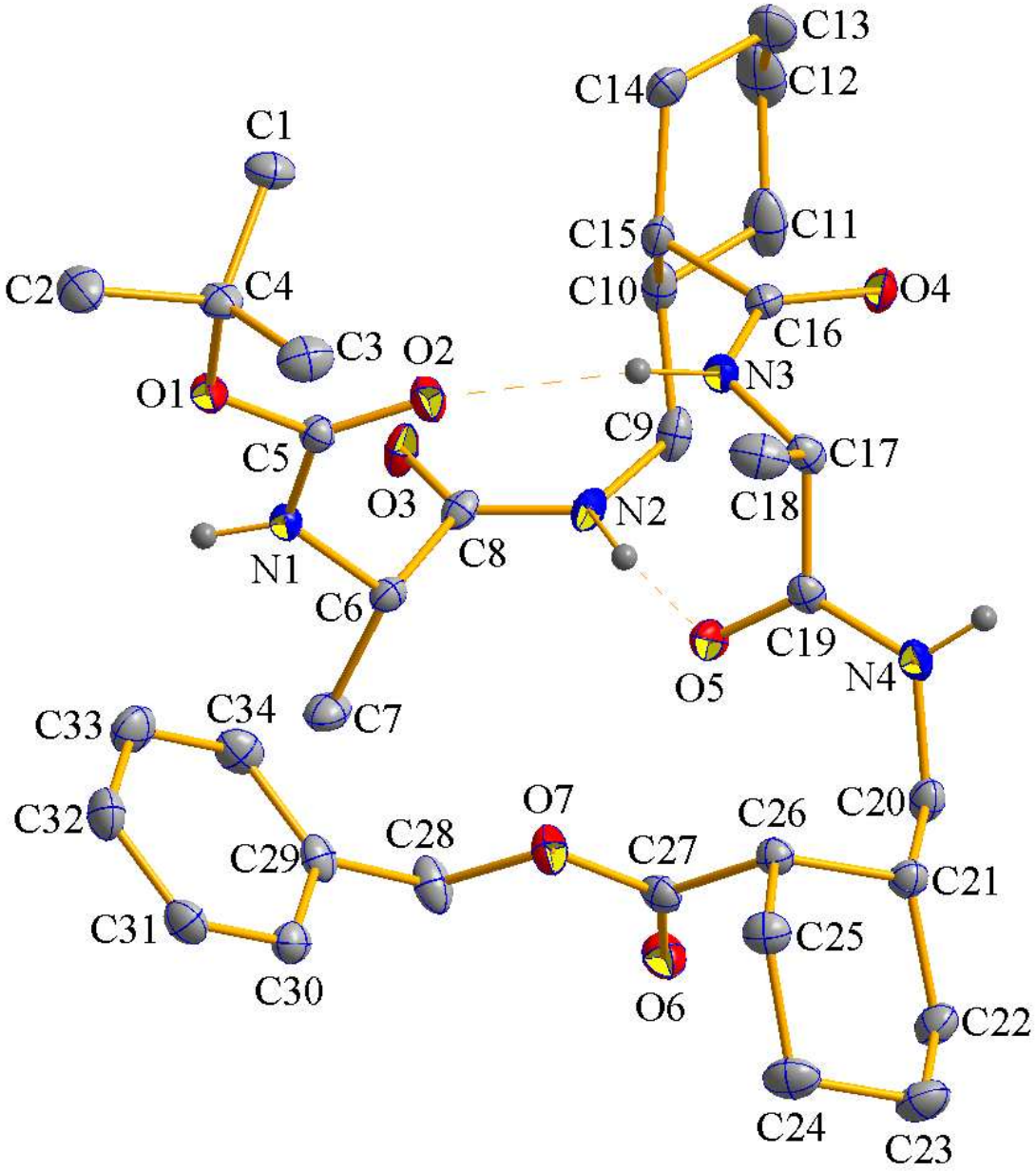


Figure S1. A molecular drawing of Gellman129 [4]. All H atoms attached to carbon atoms are omitted. Two intramolecular hydrogen bonds are shown by dashed lines.

Table S2. Crystal data and structure refinement for gellman129.

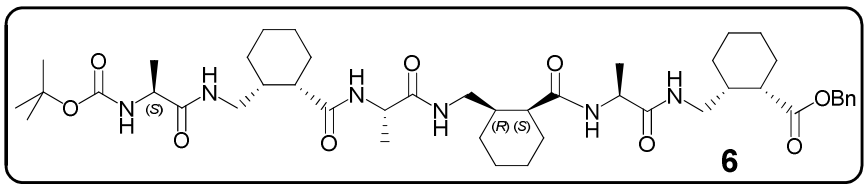
Identification code	gellman129	
Empirical formula	$C_{34}H_{52}N_4O_7$	
Formula weight	628.80	
Temperature	100(1) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	$P2_12_12_1$	
Unit cell dimensions	a = 9.0786(4) Å	α= 90°.
	b = 16.4153(6) Å	β= 90°.
	c = 23.8705(9) Å	γ = 90°.
Volume	3557.4(2) $Å^3$	
Z	4	
Density (calculated)	1.174 Mg/m^3	
Absorption coefficient	0.082 mm^{-1}	
F(000)	1360	
Crystal size	0.43 x 0.18 x 0.17 mm^3	
Theta range for data collection	1.51 to 27.55°.	
Index ranges	-11<=h<=11, -21<=k<=20, -30<=l<=30	
Reflections collected	78541	
Independent reflections	4524 [R(int) = 0.0447]	
Completeness to theta = 25.00°	98.3 %	
Absorption correction	Analytical with SADABS	
Max. and min. transmission	0.9862 and 0.9656	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	4524 / 0 / 411	
Goodness-of-fit on F^2	0.837	
Final R indices [I>2sigma(I)]	R1 = 0.0330, wR2 = 0.0893	
R indices (all data)	R1 = 0.0361, wR2 = 0.0925	
Absolute structure parameter	N/A	
Largest diff. peak and hole	0.224 and -0.154 $e.Å^{-3}$	

Table S3. Hydrogen bonds for gellman129 [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
N(4)-H(4)...O(3)#1	0.88	1.94	2.821(2)	178.0
N(3)-H(3)...O(2)	0.88	2.18	3.033(2)	164.8
N(2)-H(2)...O(5)	0.88	2.00	2.876(2)	171.6
N(1)-H(1)...O(4)#2	0.88	1.99	2.859(2)	169.6

Symmetry transformations used to generate equivalent atoms:

#1 -x+1,y+1/2,-z+1/2 #2 -x+1,y-1/2,-z+1/2



6

Data Collection

A colorless crystal with approximate dimensions 0.12 x 0.156 x 0.41 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 SMART APEXII diffractometer with Cu K_α (λ = 1.54178 Å) radiation and the diffractometer to crystal distance of 4.03 cm. Bruker SMART APEXII diffractometer with Cu Kα (λ = 1.54178 Å) radiation and the diffractometer to crystal distance of 4.03 cm

The initial cell constants were obtained from three series of ω scans at different starting angles. Each series consisted of 41 frames collected at intervals of 0.6º in a 25º 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 9948 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 0.82 Å. A total of 170064 data were harvested by collecting 19 sets of frames with 0.5º scans in ω with an exposure time 25-50 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. [1]

Structure Solution and Refinement

The systematic absences in the diffraction data and the *E*-statistics were consistent for the space groups $P4_12_11$ and $P4_32_11$. Only the space group $P4_12_11$ yielded chemically reasonable and computationally stable results of refinement [2-4].

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.

There were several disordered and partially occupied solvent molecules also present in the asymmetric unit. A significant amount of time was invested in identifying and refining the disordered molecules. Bond length restraints were applied to model the molecules but the resulting isotropic displacement coefficients suggested the molecules were mobile. In addition, the refinement was computationally unstable. Option SQUEEZE of program PLATON [2] was used to correct the diffraction data for diffuse scattering effects and to identify the solvate molecule. PLATON calculated the upper limit of volume that can be occupied by the solvent to be 1872 $Å^3$, or 17.6% of the unit cell volume. The program calculated 480 electrons in the unit cell for the diffuse species. Please note that all derived results in the following tables are based on the known contents. No data are given for the diffusely scattering species.

The final least-squares refinement of 536 parameters against 9438 data resulted in residuals *R* (based on F^2 for $I \geq 2\sigma$) and *wR* (based on F^2 for all data) of 0.0792 and 0.2246, respectively. The final difference Fourier map was featureless.

The molecular diagram is drawn with 30% probability ellipsoids.

References

[1] Bruker-AXS. (2007) APEX2, SADABS, and SAINT Software Reference Manuals. Bruker-AXS, Madison, Wisconsin, USA.

[2] Sheldrick, G. M. (2008) SHELXL. *Acta Cryst.* **A64**, 112-122.

[3] Dolomanov, O.V.; Bourhis, L.J.; Gildea, R.J.; Howard, J.A.K.; Puschmann, H. "OLEX2: a complete structure solution, refinement and analysis program". *J. Appl. Cryst.* (2009) **42**, *339-341*.

[4] Guzei, I.A. (2006-2008). Internal laboratory computer programs "Inserter", "FCF_filter", "Modicifer".

[5] A.L. Spek (1990) Acta Cryst. A46, C34.

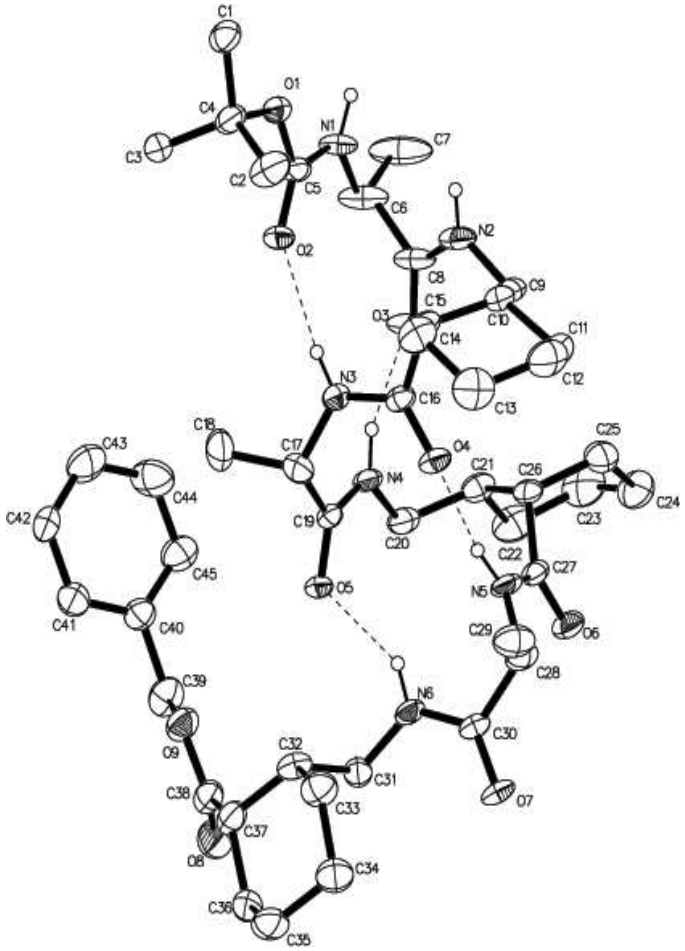


Figure S2. A molecular drawing of Gellman131. All H atoms are attached to C atoms are omitted.

Table S4. Crystal data and structure refinement for gellman131.

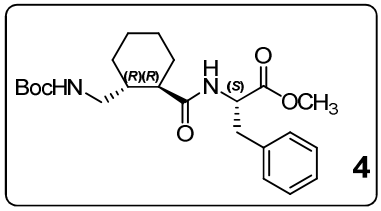
Identification code	gellman131	
Empirical formula	C_{45} H_{70} N_6 O_9	
Formula weight	839.07	
Temperature	100(2) K	
Wavelength	1.54178 Å	
Crystal system	Tetragonal	
Space group	$P4_12_12$	
Unit cell dimensions	a = 15.1846(3) Å	α= 90°.
	b = 15.1846(3) Å	β= 90°.
	c = 46.0450(11) Å	γ = 90°.
Volume	10616.7(4) $Å^3$	
Z	8	
Density (calculated)	1.050 Mg/m^3	
Absorption coefficient	0.593 mm^{-1}	
F(000)	3632	
Crystal size	0.41 x 0.16 x 0.12 mm^3	
Theta range for data collection	3.06 to 66.98°.	
Index ranges	-18<=h<=18, -18<=k<=17, -54<=l<=54	
Reflections collected	170064	
Independent reflections	9438 [R(int) = 0.0349]	
Completeness to theta = 66.98°	99.7 %	
Absorption correction	Numerical with SADABS	
Max. and min. transmission	0.9323 and 0.7932	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	9438 / 0 / 536	
Goodness-of-fit on F^2	0.998	
Final R indices [I>2sigma(I)]	R1 = 0.0792, wR2 = 0.2197	
R indices (all data)	R1 = 0.0832, wR2 = 0.2246	
Absolute structure parameter	0.0(3)	
Largest diff. peak and hole	0.536 and -0.407 $e.Å^{-3}$	

Table S5. Hydrogen bonds for gellman131 [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
N(1)-H(1)...O(6)#1	0.88	1.95	2.801(3)	163.6
N(3)-H(3)...O(2)	0.88	2.12	2.994(3)	173.0
N(4)-H(4)...O(3)	0.88	1.99	2.819(4)	157.6
N(5)-H(5)...O(4)	0.88	2.05	2.903(4)	164.6
N(2)-H(2)...O(7)#1	0.88	2.02	2.810(4)	148.1
N(6)-H(6)...O(5)	0.88	2.02	2.800(3)	147.8

Symmetry transformations used to generate equivalent atoms:

#1 y-1/2,-x+1/2,z-1/4



Data Collection

A colorless crystal with approximate dimensions $0.589 \times 0.119 \times 0.046$ 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 101(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 SMART APEXII diffractometer with Cu K_α (λ = 1.54178 Å) radiation and the diffractometer to crystal distance of 4.03 cm.

The initial cell constants were obtained from three series of ω scans at different starting angles. Each series consisted of 50 frames collected at intervals of 0.5º in a 25º 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 SMART program. The final cell constants were calculated from a set of 9999 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 0.82 Å. A total of 19713 data were harvested by collecting 15 sets of frames with 0.5º scans in ω 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. [1]

Structure Solution and Refinement

The systematic absences in the diffraction data and the E-statistics were uniquely consistent for the space group $P2_12_12_1$ that yielded chemically reasonable and computationally stable results of refinement [2].

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 276 parameters against 4206 data resulted in residuals *R* (based on F^2 for $I \geq 2\sigma$) and *wR* (based on F^2 for all data) of 0.0412 and 0.0964, respectively. The final difference Fourier map was featureless.

The molecular diagram is drawn with 50% probability ellipsoids.

References

[1] Bruker-AXS. (2007) APEX2, SADABS, and SAINT Software Reference Manuals. Bruker-AXS, Madison, Wisconsin, USA.

[2] Sheldrick, G. M. (2008) SHELXL. *Acta Cryst.* **A64**, 112-122.

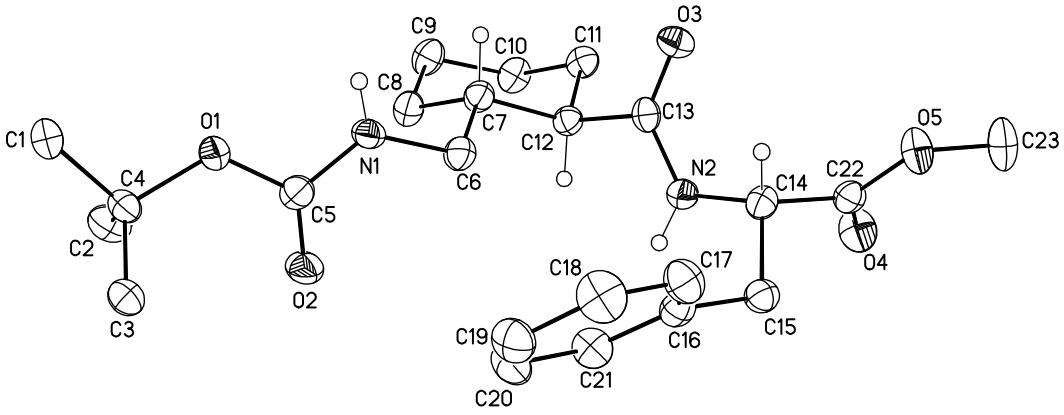


Figure S3. A molecular drawing of Gellman92 shown with 50% probability ellipsoids. All H atoms except those on heteroatoms and chiral centers are omitted.

Table S4. Crystal data and structure refinement for Gellman92.

Identification code	gellman92	
Empirical formula	$C_{23}\ H_{34}\ N_2\ O_5$	
Formula weight	418.52	
Temperature	102(2) K	
Wavelength	1.54178 Å	
Crystal system	Orthorhombic	
Space group	$P2_12_12_1$	
Unit cell dimensions	a = 5.0717(3) Å	α= 90°.
	b = 18.5804(9) Å	β= 90°.
	c = 24.1986(13) Å	γ = 90°.
Volume	2280.3(2) $Å^3$	
Z	4	
Density (calculated)	1.219 Mg/m^3	
Absorption coefficient	0.694 mm^{-1}	
F(000)	904	
Crystal size	0.59 x 0.12 x 0.05 mm^3	
Theta range for data collection	3.00 to 69.52°.	
Index ranges	-6<=h<=5, -22<=k<=22, -29<=l<=29	
Reflections collected	19713	
Independent reflections	4206 [R(int) = 0.0554]	
Completeness to theta = 69.52°	98.8 %	
Absorption correction	Empirical with SADABS	
Max. and min. transmission	0.9688 and 0.6853	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	4206 / 0 / 276	
Goodness-of-fit on F^2	0.989	
Final R indices [I>2sigma(I)]	R1 = 0.0412, wR2 = 0.0932	
R indices (all data)	R1 = 0.0481, wR2 = 0.0964	
Absolute structure parameter	0.0(2)	
Hooft y parameter	0.00(12), Probability of correctness – 100%.	
Largest diff. peak and hole	0.199 and -0.187 $e.Å^{-3}$	

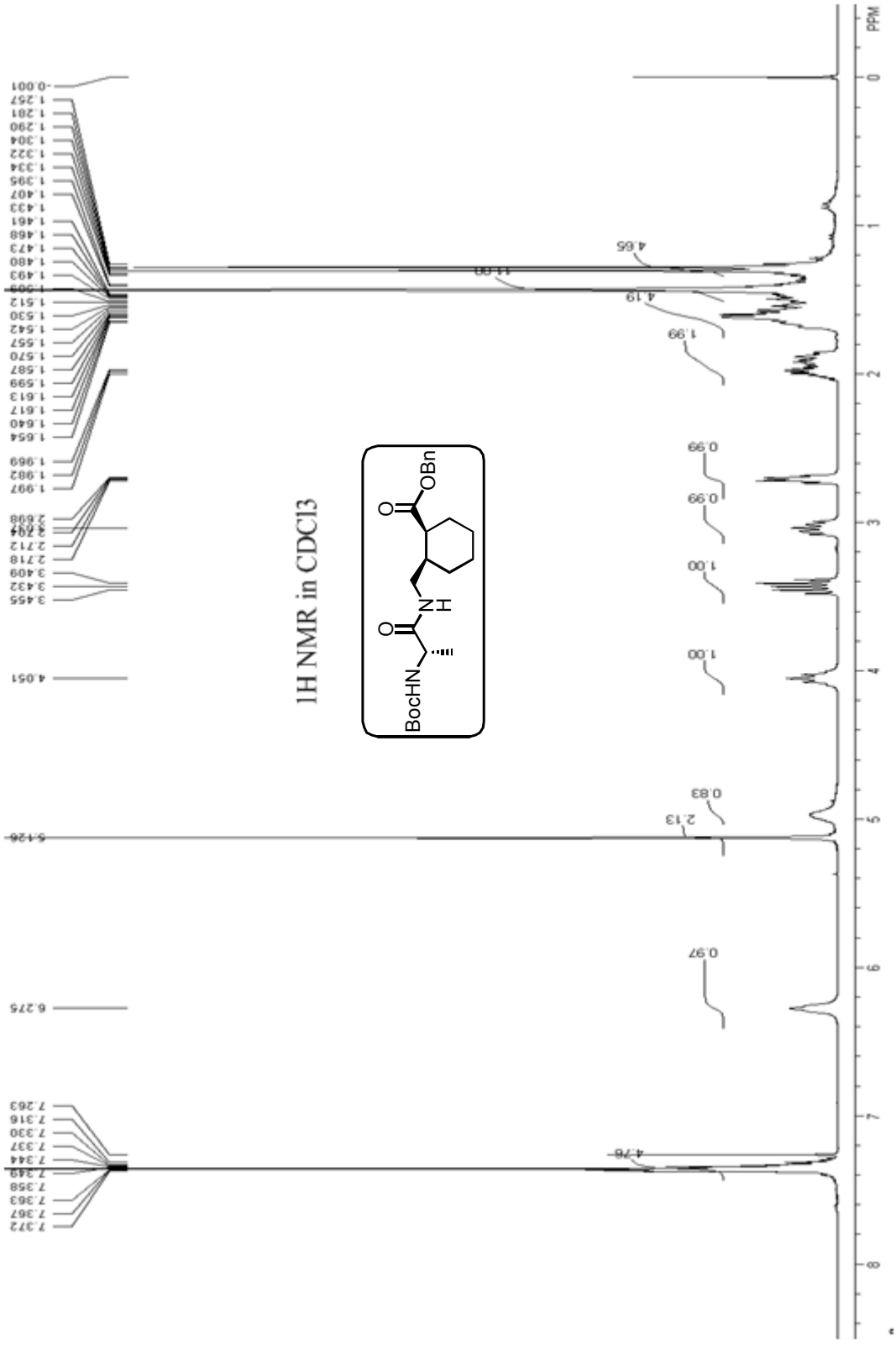
Table S5. Hydrogen bonds for Gellman92 [Å and °].

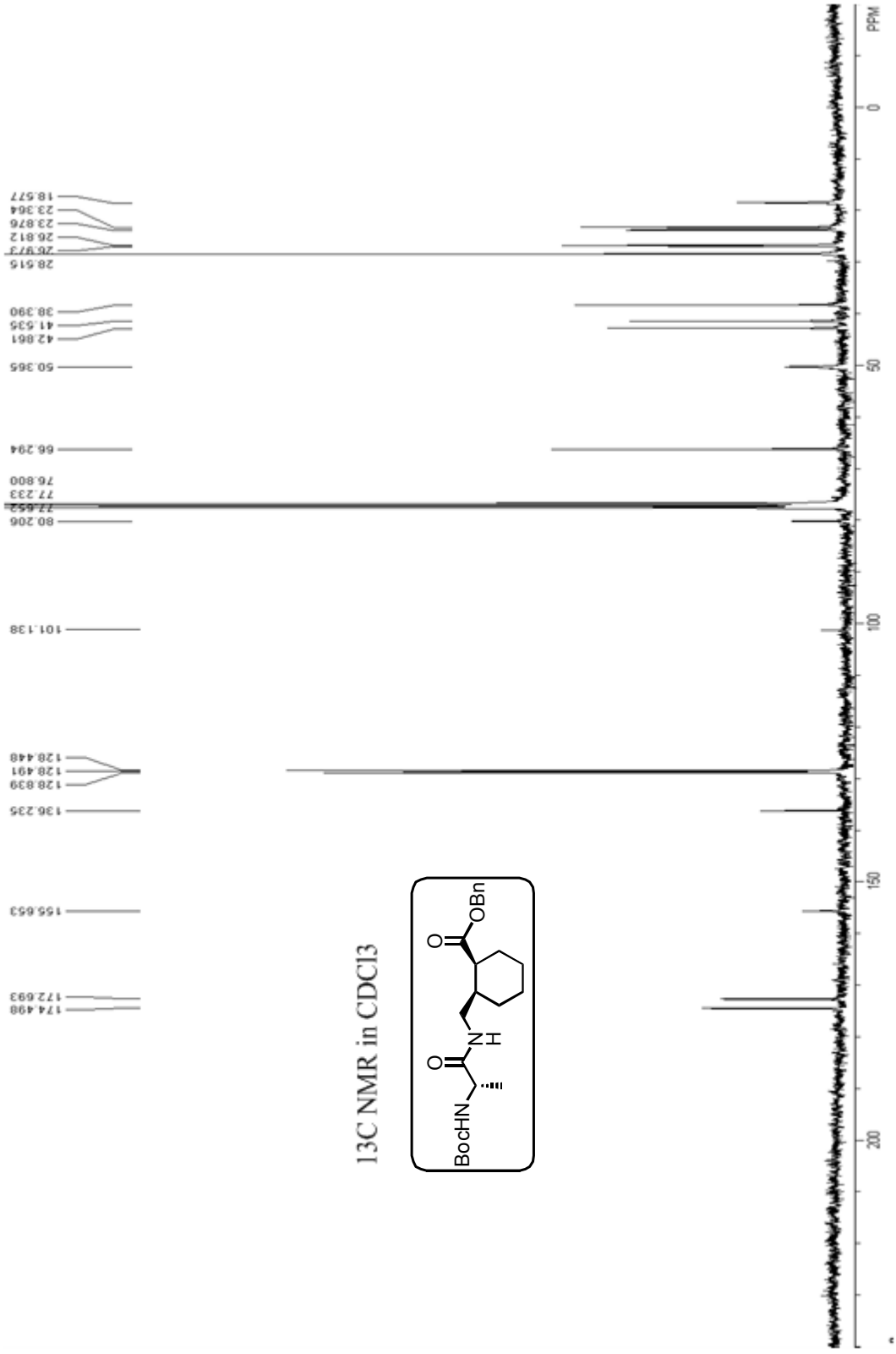
D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
N(1)-H(1)...O(2)#1	0.88	2.12	2.925(2)	151.0
N(2)-H(2)...O(3)#2	0.88	2.14	3.022(2)	178.4

Symmetry transformations used to generate equivalent atoms:

#1 x-1,y,z #2 x+1,y,z

VII. ^{1}H NMR and ^{13}C NMR spectra

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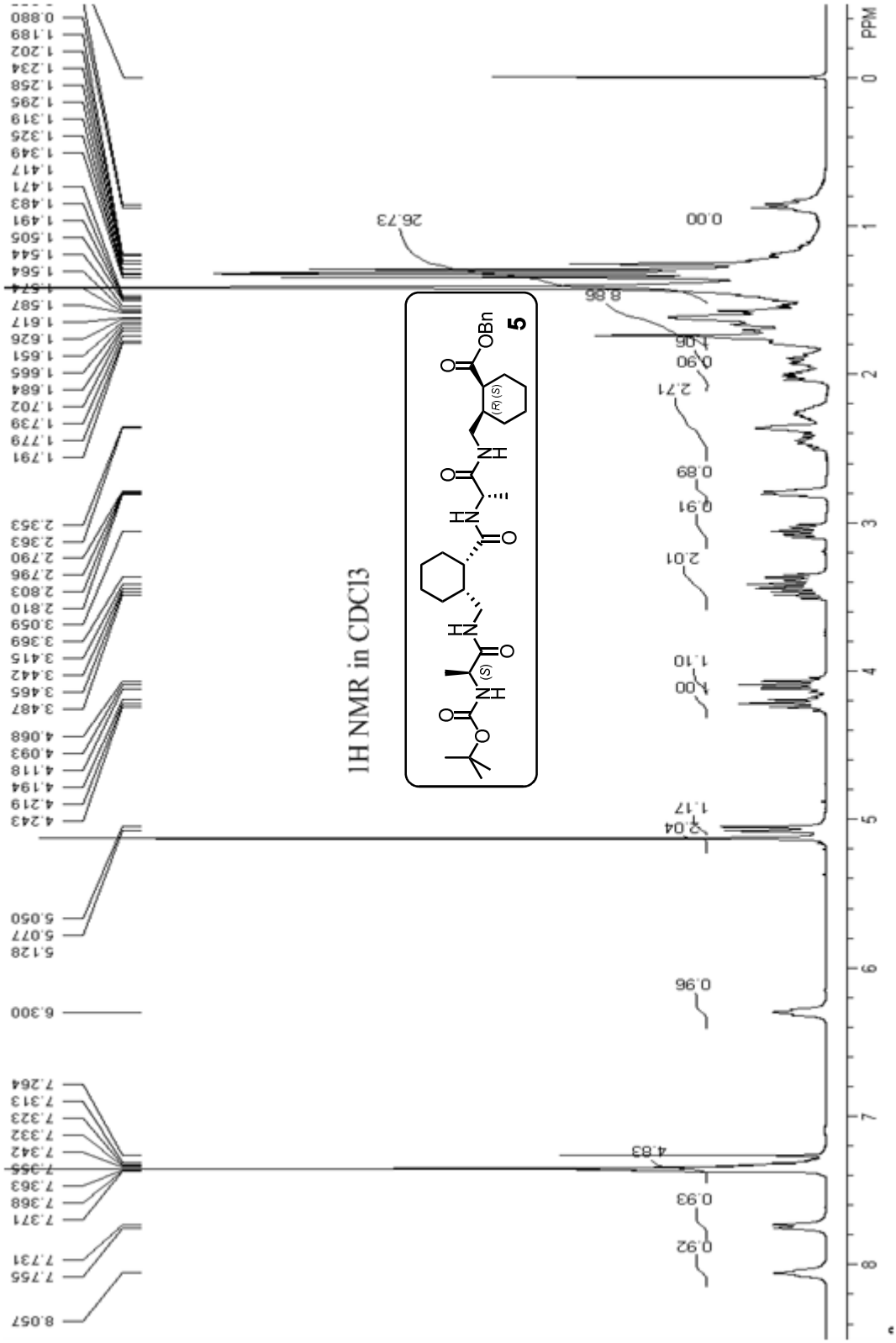
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OBn
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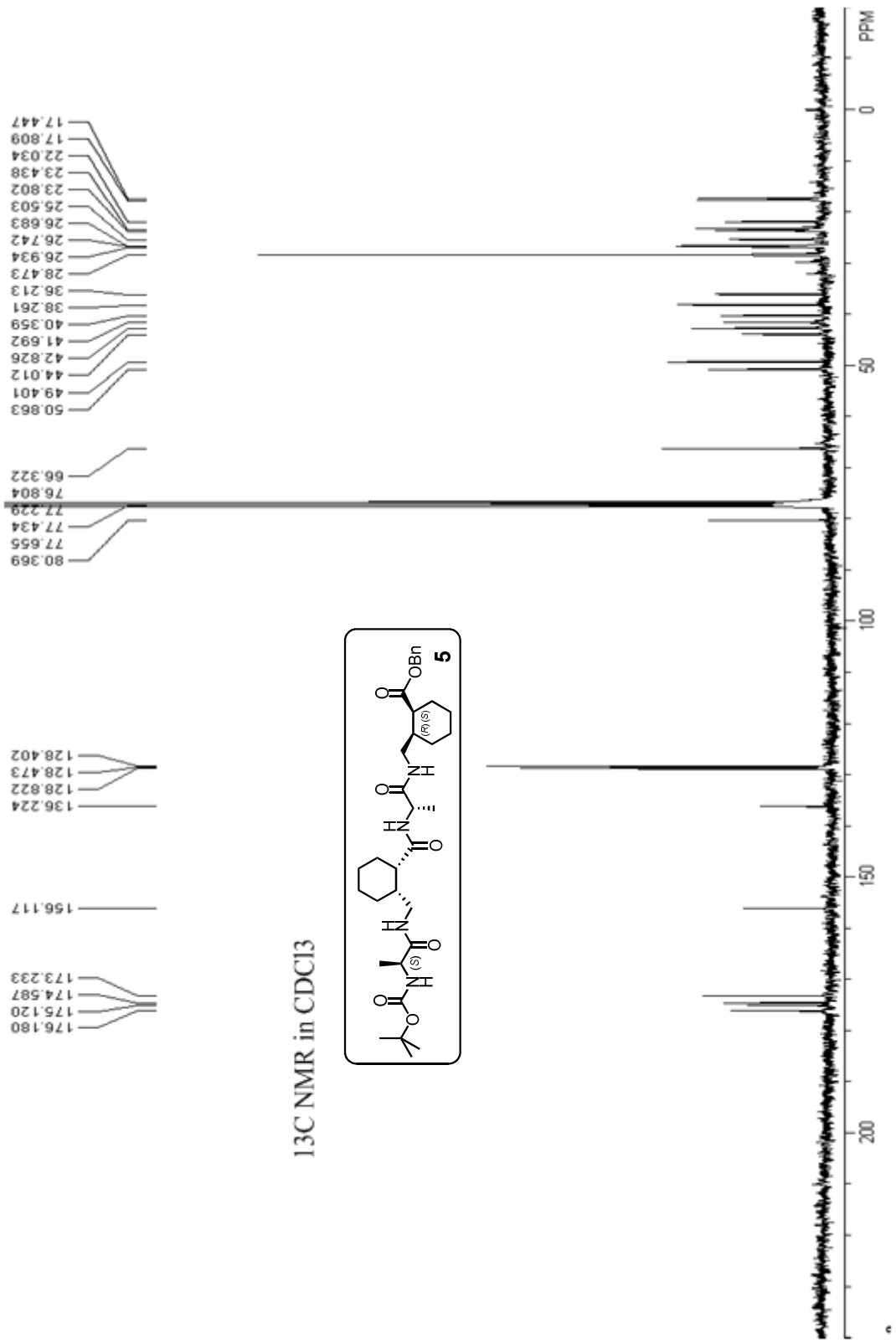
(S)
PPM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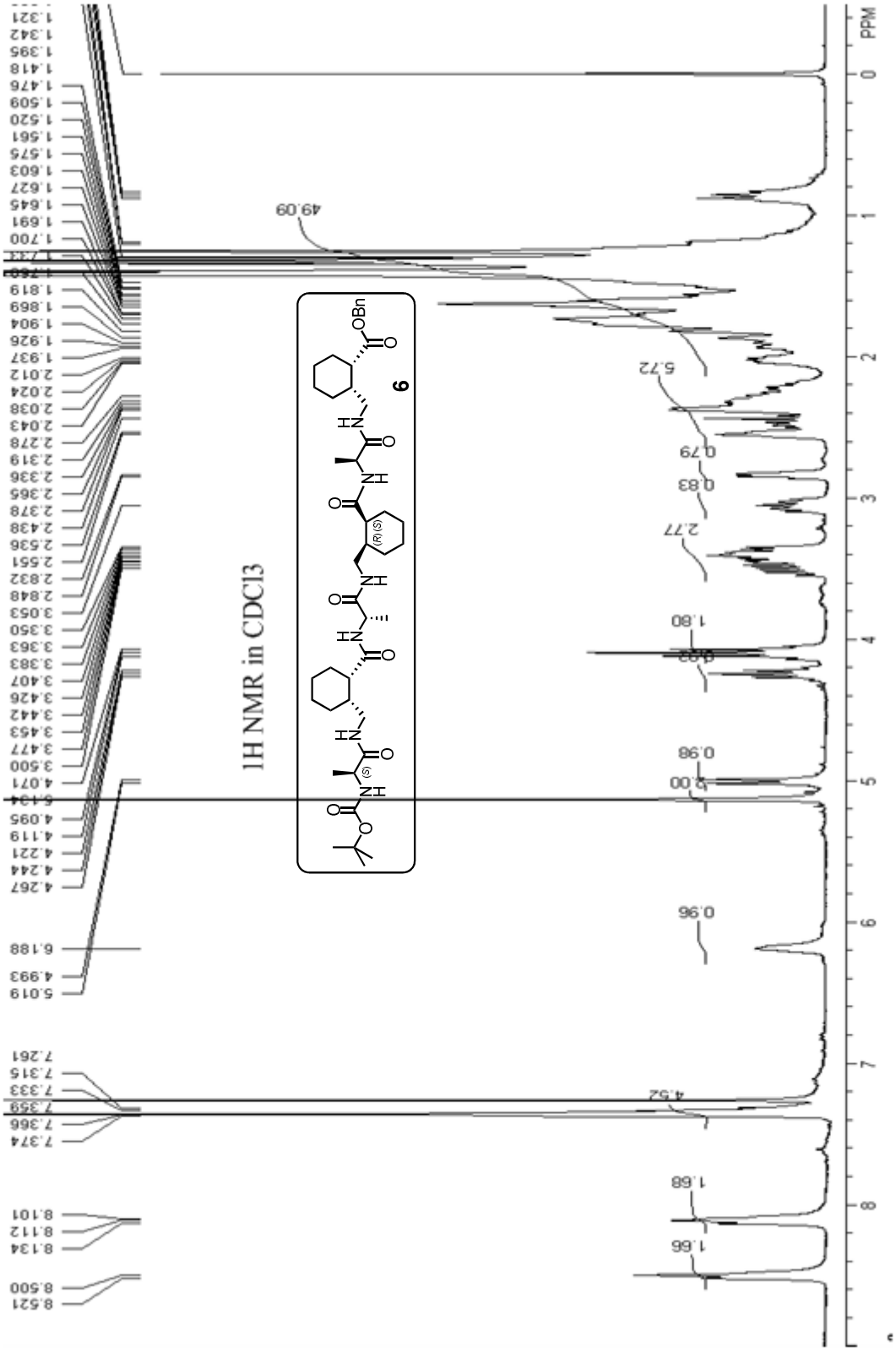
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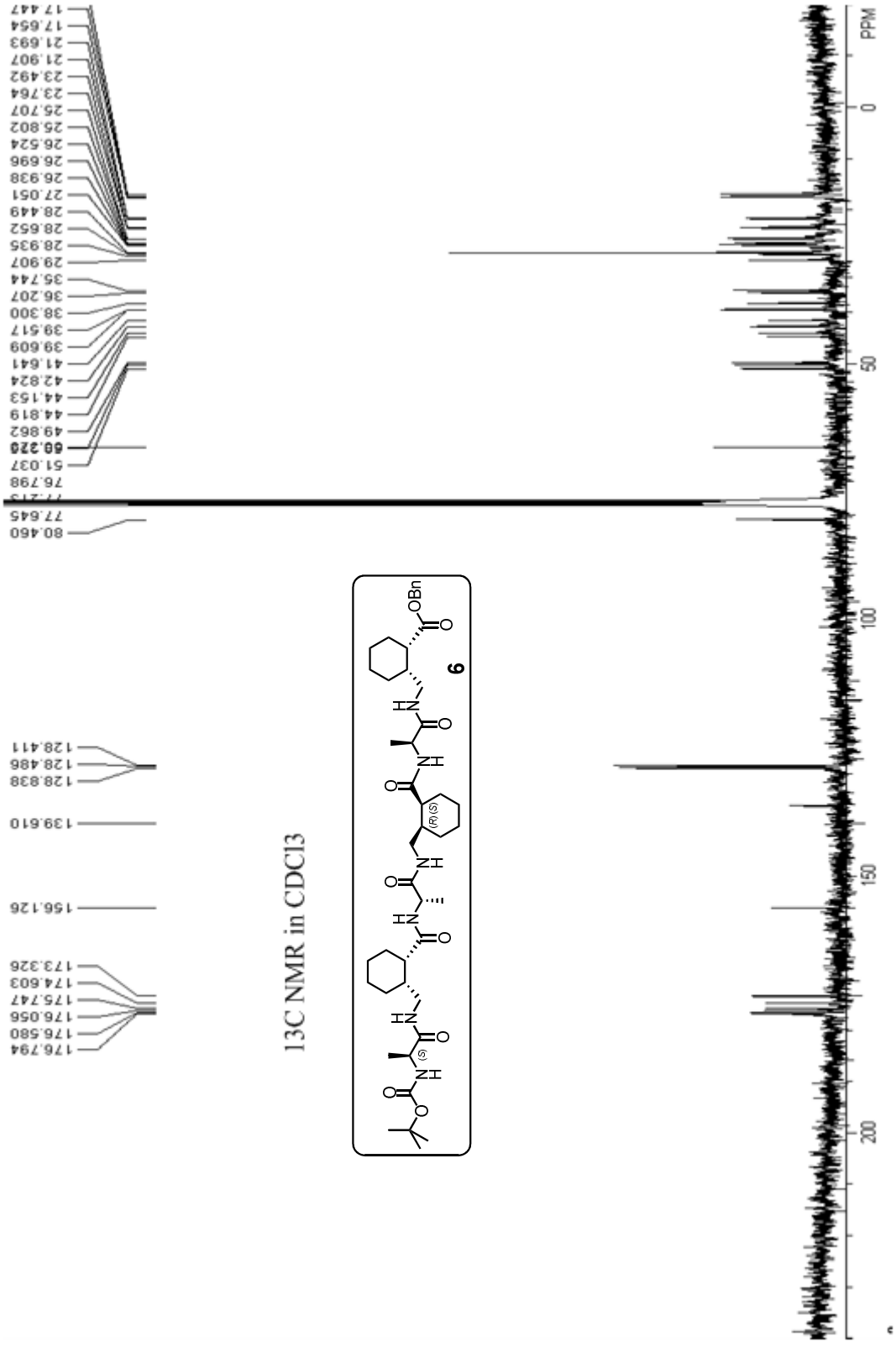
PPM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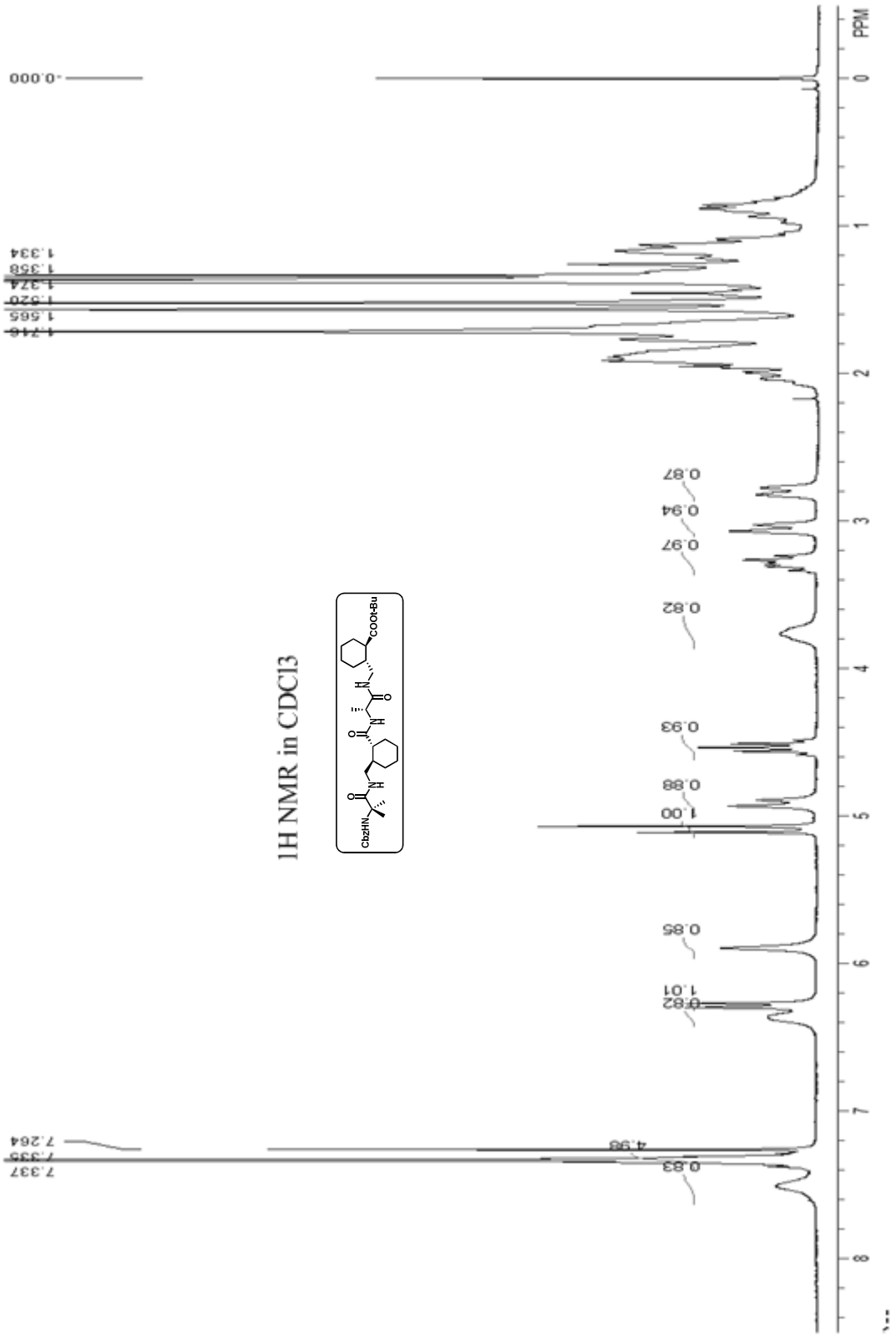
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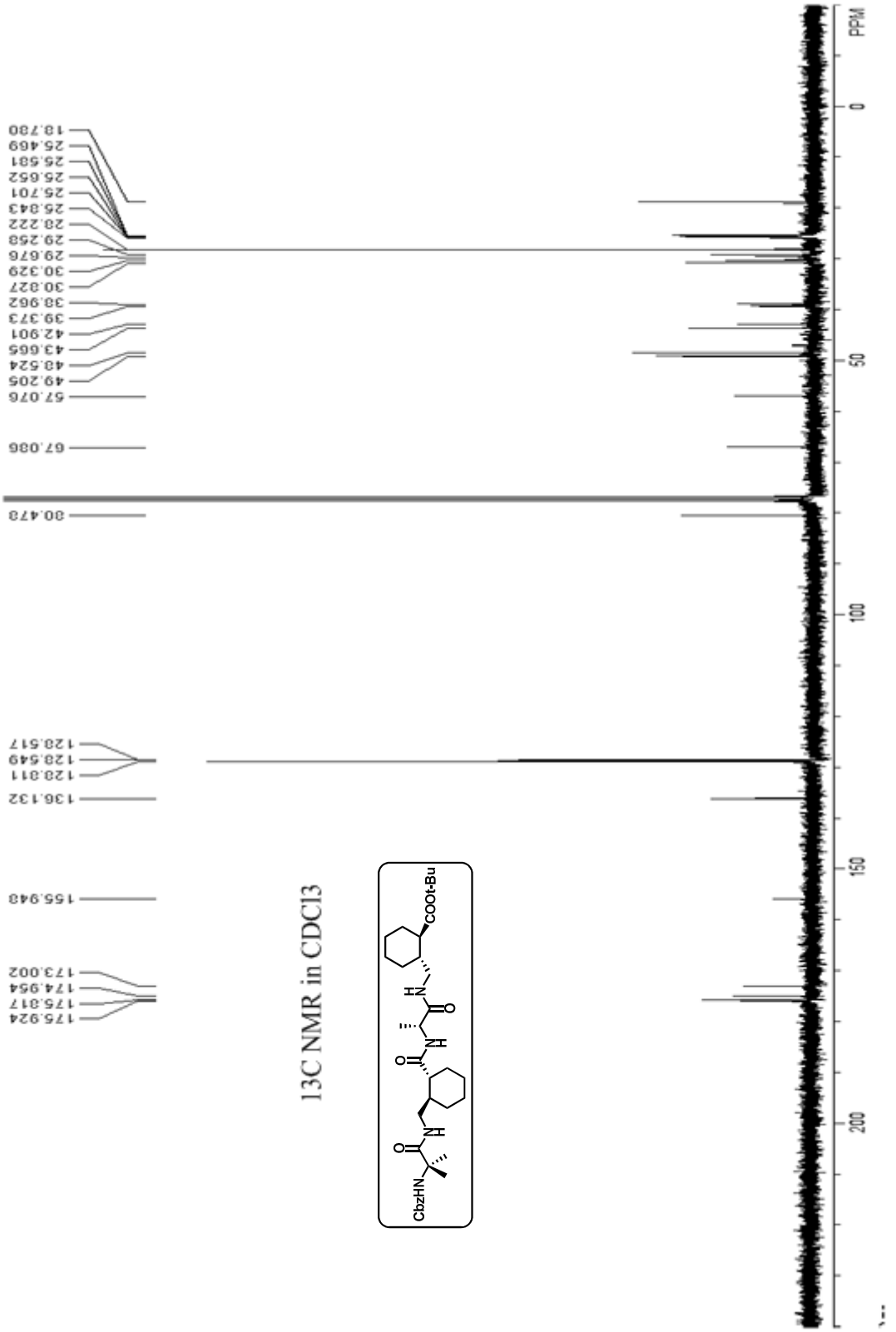
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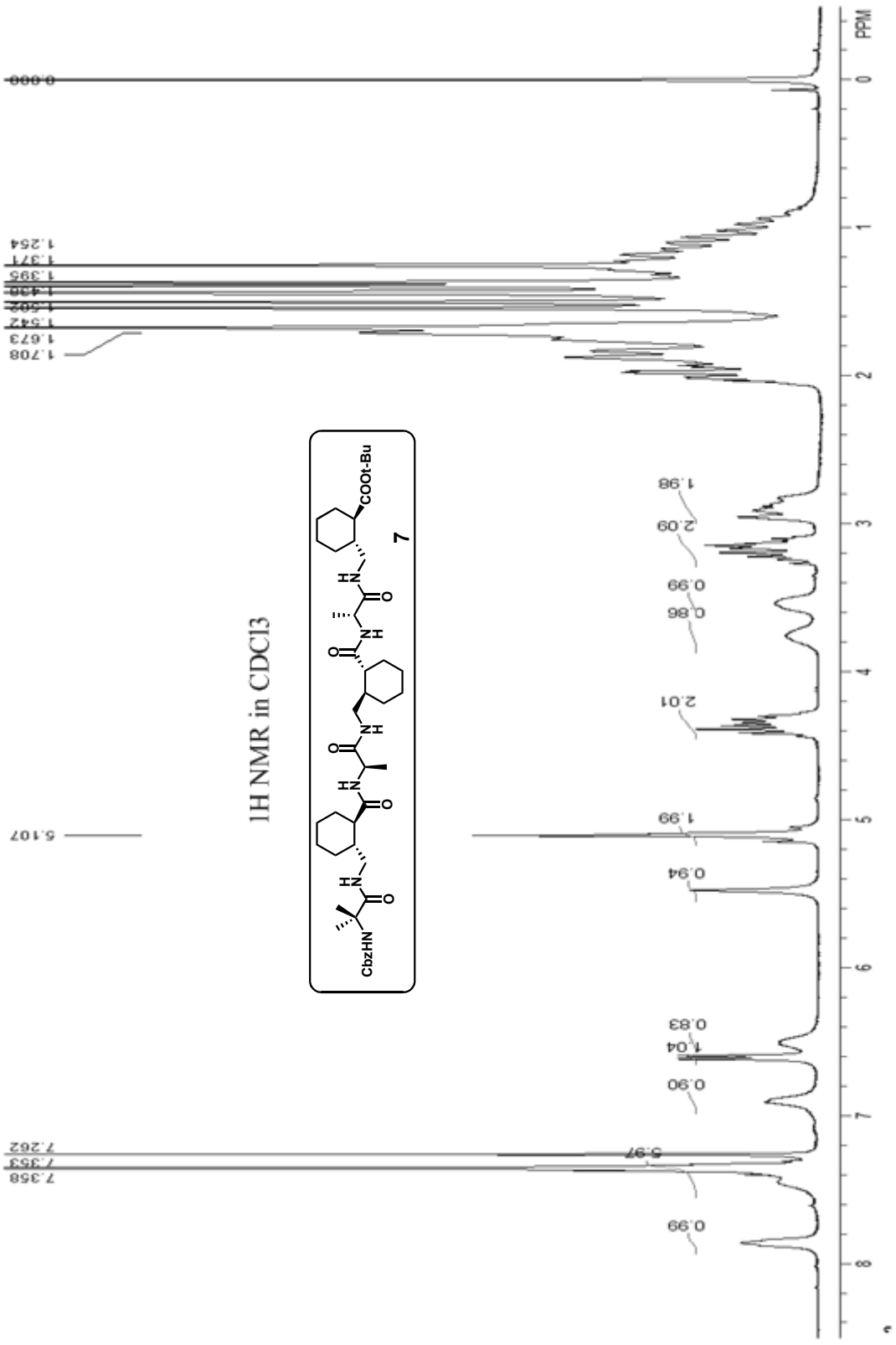
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COOt-Bu
PPM

PPM
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1.25
0.92
1.218
1.229
1.241
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1.253
1.268
1.277
1.416
1.431
1.591
1.757
1.776
3.624
3.671
4.296
4.323
4.335
4.363
4.714
4.733
4.758
4.775
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