Supplementary Information

Controlled packing of metal-peptide superhelices with β-peptide foldamers

Ingyu Han, [a] Ha-Jin Lee [b], and Soo Hyuk Choi *[a]

a I. Han, Prof. S. H. Choi
Department of chemistry
Yonsei University
50 Yonsei-ro, Seodaemun-gu, Seoul 03722, Republic of Korea
E-mail: sh-choi@yonsei.ac.kr

b Prof. H. Lee
Division of Chemistry and Bio-Environmental Sciences
Seoul Women's University
621 Hwarangro, Nowon-gu, Seoul 01797, Republic of Korea

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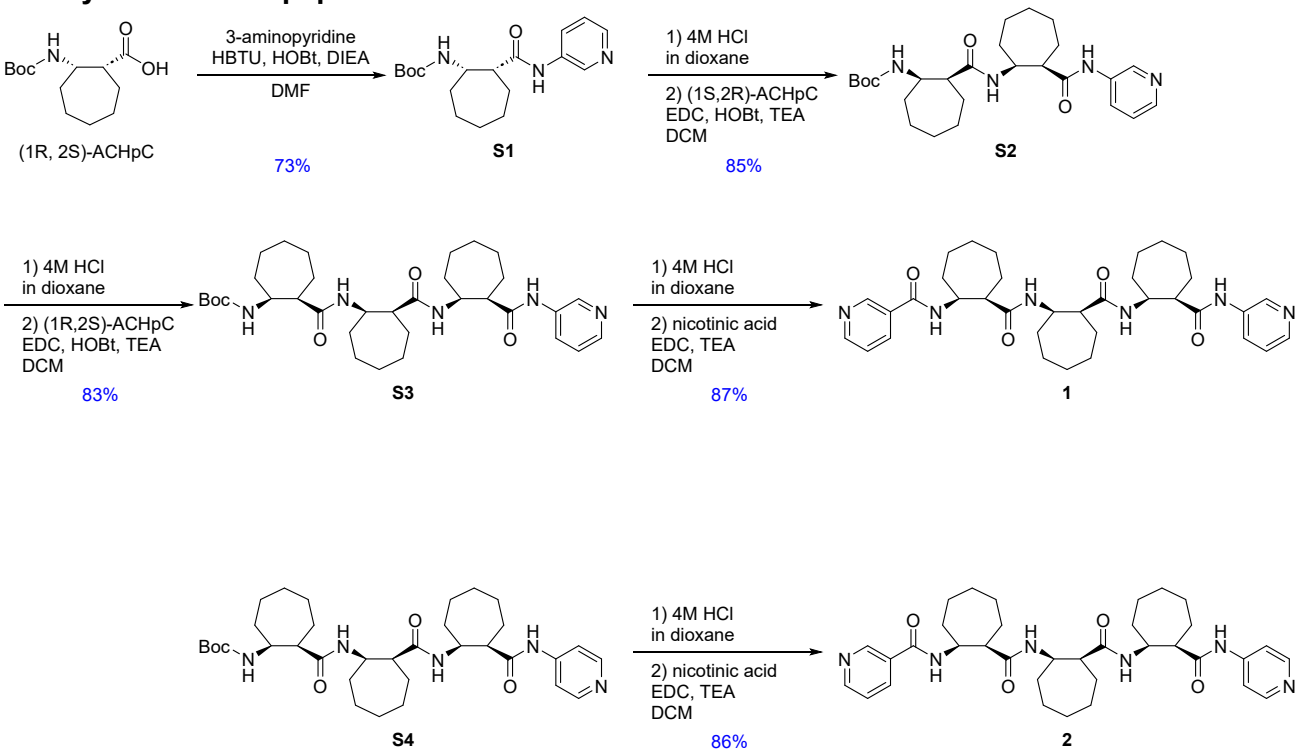
1. Experimental Data

1.1 General

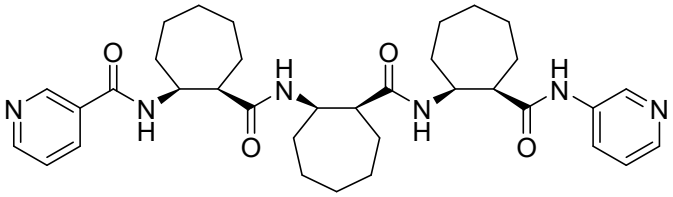
Boc-protected tripeptide **S3** and **S4** were prepared by following previously reported method in reference 13. β-peptides **1** and **2** were prepared by a solution-phase peptide synthesis with EDCI, HOBt, and TEA in DCM. EDCI was purchased from Aapptec. TEA was purchased from Samchun Chemical. Other reagents were purchased from Sigma-Aldrich, Alfa Aesar, and TCI. All the regents were used without any purification. Silica gel Si 60 (230~400 mesh, intertec) was used for flash column chromatography. High-resolution mass spectra (HRMS) were obtained in positive ion mode using a Bruker compact QTOF. NMR spectra were recorded on 400 MHz FT-NMR Spectrometer (Bruker Biospin AvanceIII HD 400).

1.2 Synthesis of Tripeptide



Scheme S1. Synthesis of β-tripeptides.

1.3 Characterization Data of Tripeptide 1



Synthetic Procedure The Boc-protected tripeptide precursor **S3** was prepared following the same experimental protocol described in reference 23 of the main article, except that 3-aminopyridine was used in place of 4-aminopyridine in the first step. **S3** (126 mg, 0.206 mmol) was treated with 4M HCl in 1,4-dioxane solution (2.0 mL) with stirring for the deprotection of Boc-group. The solvent was removed using a stream of nitrogen after 3 hours of deprotection. The Boc-deprotected **S3** was dissolved in dichloromethane and treated with nicotinic acid (33 mg, 0.268 mmol) and triethylamine (0.07 mL, 0.474 mmol). The mixture was stirred for 1 day at room temperature. Upon completion, the mixture was diluted with EtOAc, washed with 30% K_2CO_3 aqueous solution using separation funnel. The organic layer was concentrated in vacuo and the crude mixture was purified using flash column chromatography to afford white solid product **1** (110 mg, 0.178 mmol, 87%).

^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ= 9.92 (s, 1H), 9.17 (s, 1H), 8.70 (d, *J* = 1.5 Hz, 1H), 8.67 (d, *J* = 4.6 Hz, 1H), 8.49 (d, *J* = 9.2 Hz, 1H), 8.30-8.24 (m, 2H), 8.20 (d, *J* = 8.3 Hz, 1H), 7.31 (m, 1H), 7.21 (dd, *J* = 13.0 Hz, *J* = 3.5 Hz, 1H), 6.31 (d, *J* = 9.0 Hz, 1H), 6.19 (d, *J* = 9.5 Hz, 1H), 4.62 (m, 1H), 4.32 (m, 2H), 3.01 (m, 1H), 2.84 (m, 1H), 2.19 (m, 2H), 2.07 (m, 1H), 2.00-1.74 (m, 12H), 1.69-1.39 (m, 14H), 1.38-1.25 (m, 2H);

^{13}C{H} NMR (100 MHz, $CDCl_3$, ppm) δ= 174.4, 173.7, 173.2, 164.8, 151.9, 149.1, 144.6, 141.3, 135.8, 135.5, 130.3, 126.7, 123.5, 123.1, 51.3, 50.7, 50.0, 49.8, 49.1, 48.9, 33.3, 31.5, 31.4, 29.1, 28.7, 28.4, 28.1, 26.4, 26.3, 25.87, 25.85, 25.5, 25.3, 23.2;

HRMS: m/z calcd for $C_{35}H_{49}N_6O_4^+$: 617.3810 $[M+H]^+$, found 617.3809; m/z calcd for $C_{35}H_{48}N_6O_4Na^+$: 639.3629 $[M+Na]^+$ found 639.3618

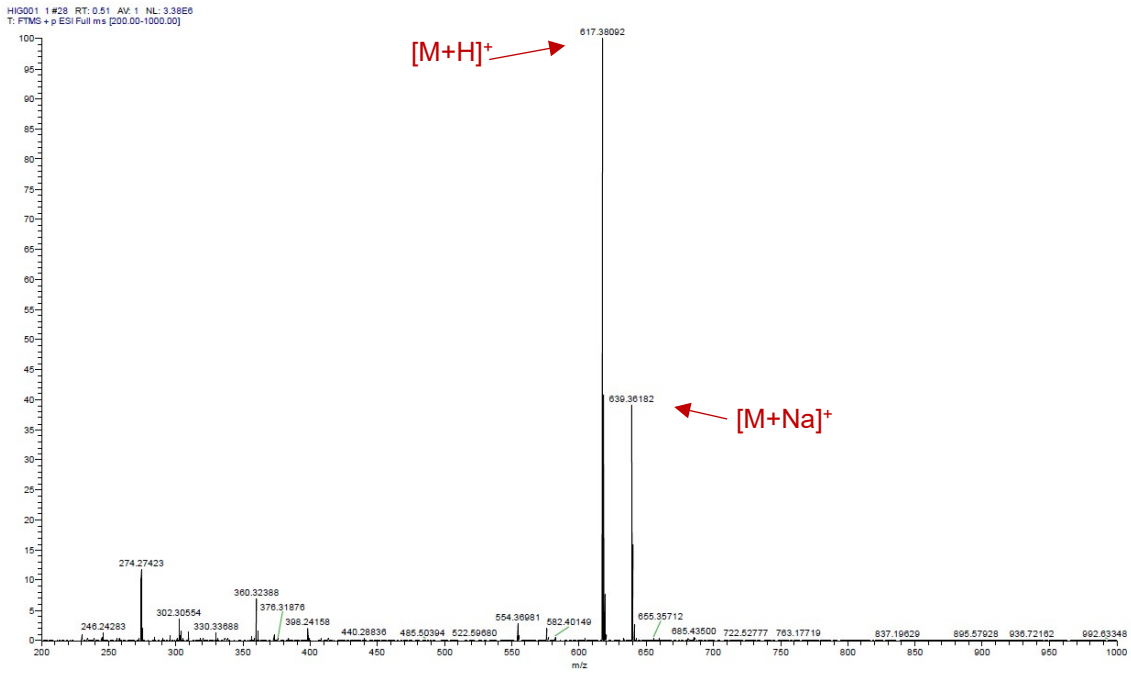


Figure S1. HRMS spectrum of **1**

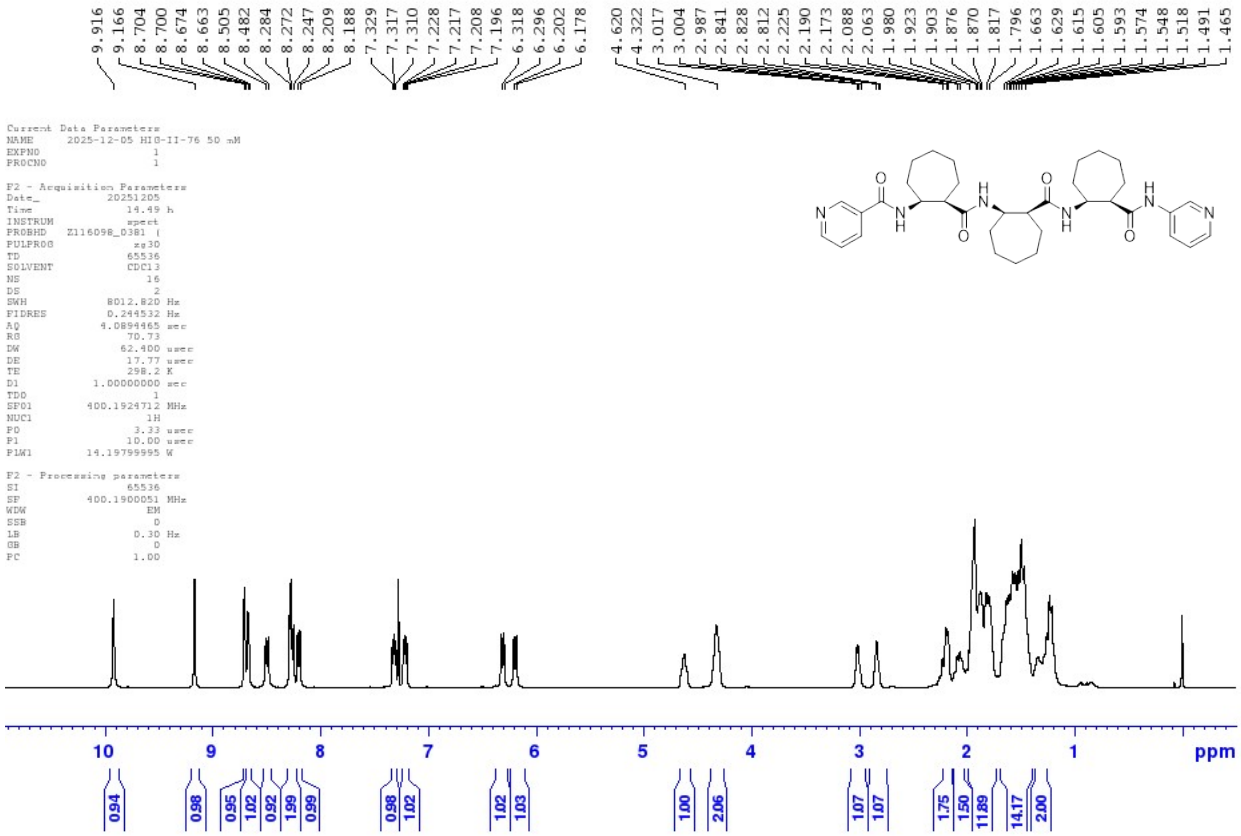


Figure S2. ^{1}H NMR spectrum of **1** (400 MHz, $CDCl_3$, 298 K)

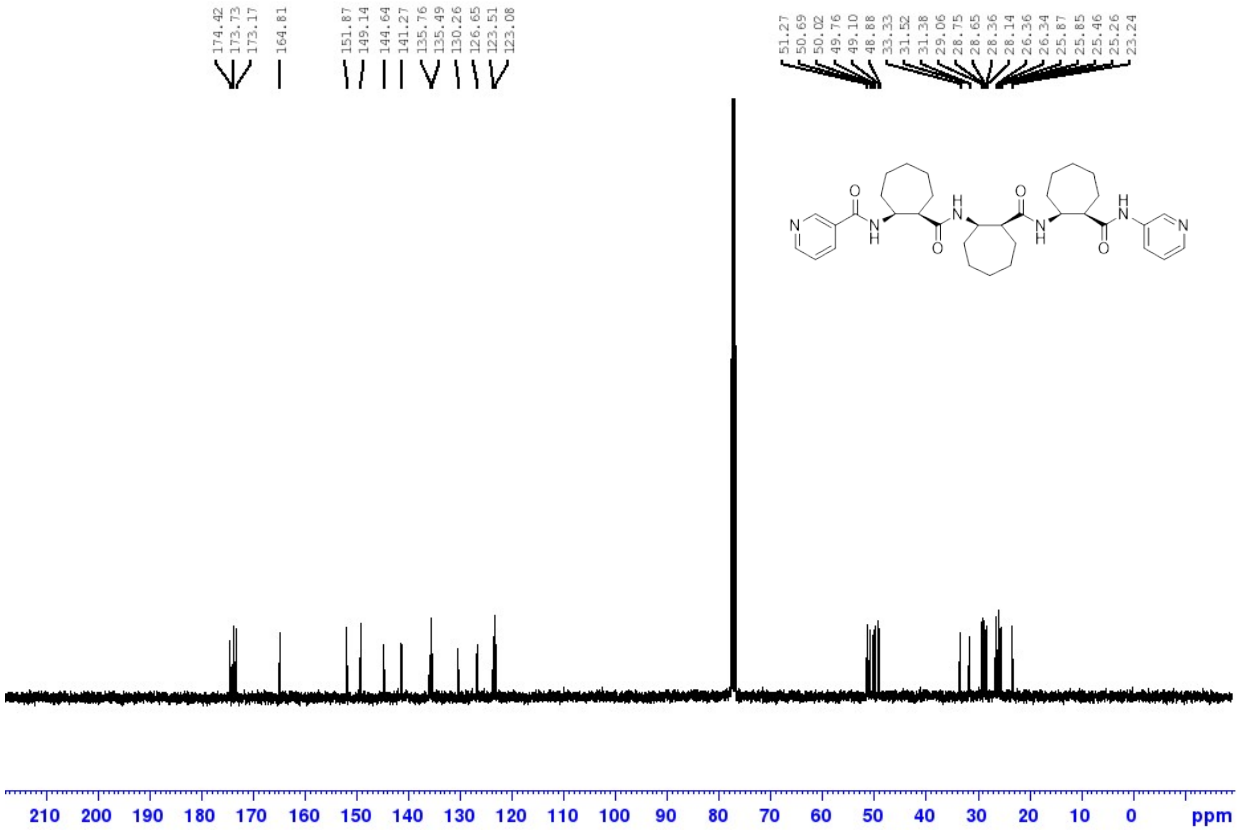
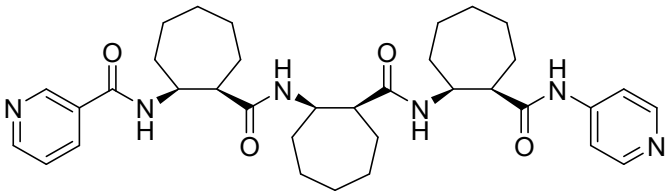


Figure S3. ^{13}C{H} NMR spectrum of **1** (100 MHz, $CDCl_3$, 298 K)

1.4 Characterization Data of Tripeptide 2



Synthetic Procedure The Boc-protected tripeptide precursor **S4** (206 mg, 0.337 mmol) was prepared following the same experimental protocol in reference 23 of the main article. Tripeptide **2** was synthesized following the same procedure with **1** (178 mg, 0.289 mmol, 87%).

^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ= 10.15 (s, 1H), 9.18 (s, 1H), 8.68 (d, *J* = 4.4 Hz, 1H), 8.57 (d, *J* = 9.2 Hz, 1H), 8.42 (d, *J* = 4.7 Hz, 2H), 8.27 (d, *J* = 7.9 Hz, 1H), 7.55 (d, *J* = 5.3 Hz, 2H), 7.33 (dd, *J* = 12.6 Hz, *J* = 2.9 Hz, 1H), 6.35 (d, *J* = 8.9 Hz, 1H), 6.15 (d, *J* = 9.6 Hz, 1H), 4.62 (m, 1H), 4.31 (m, 2H), 3.00 (m, 1H), 2.85 (m, 1H), 2.18 (m, 2H), 2.06 (m, 1H), 2.00-1.74 (m, 12H), 1.70-1.42 (m, 14H), 1.39-1.27 (m, 2H);

^{13}C{H} NMR (100 MHz, $CDCl_3$, ppm) δ= 175.0, 173.8, 173.2, 164.8, 151.9, 150.4, 149.2, 145.9, 135.5, 130.2, 123.1, 113.6, 51.3, 50.7, 50.0, 49.7, 49.12, 49.07, 33.4, 31.5, 31.2, 29.0, 28.8, 28.6, 28.3, 28.2, 26.4, 26.3, 25.9, 25.8, 25.3, 25.2, 23.1;

HRMS: m/z calcd for $C_{35}H_{49}N_6O_4^+$: 617.3810 $[M+H]^+$, found 617.3807; m/z calcd for $C_{35}H_{48}N_6O_4Na^+$: 639.3629 $[M+Na]^+$ found 639.3627

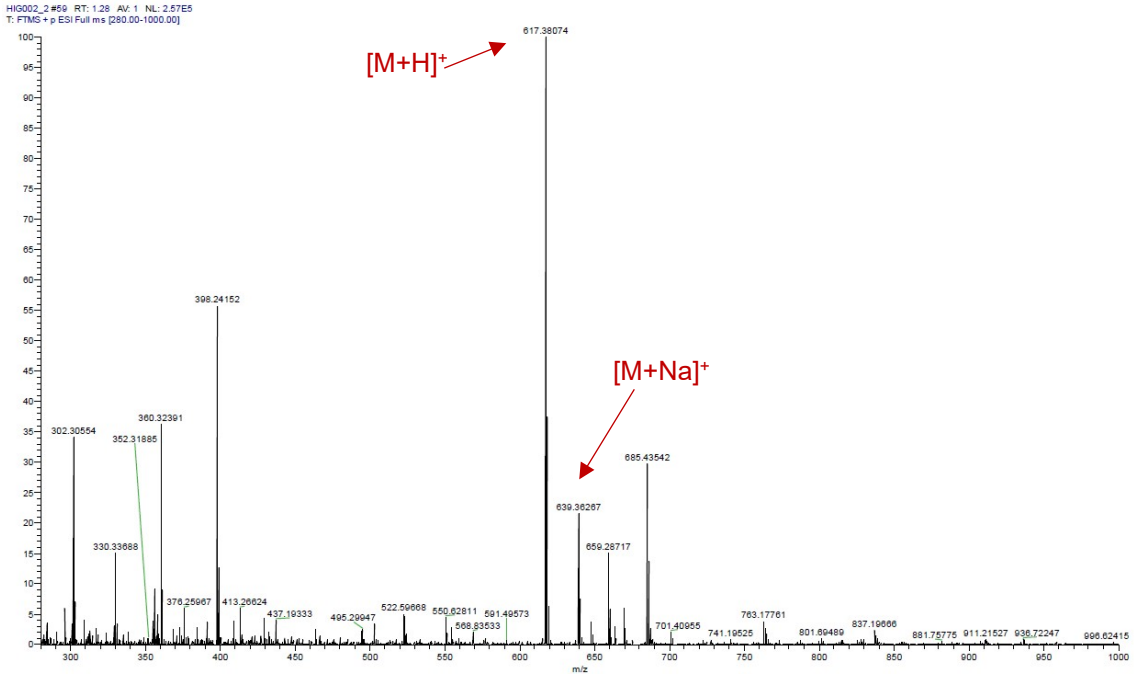


Figure S4. HRMS spectrum of **2**

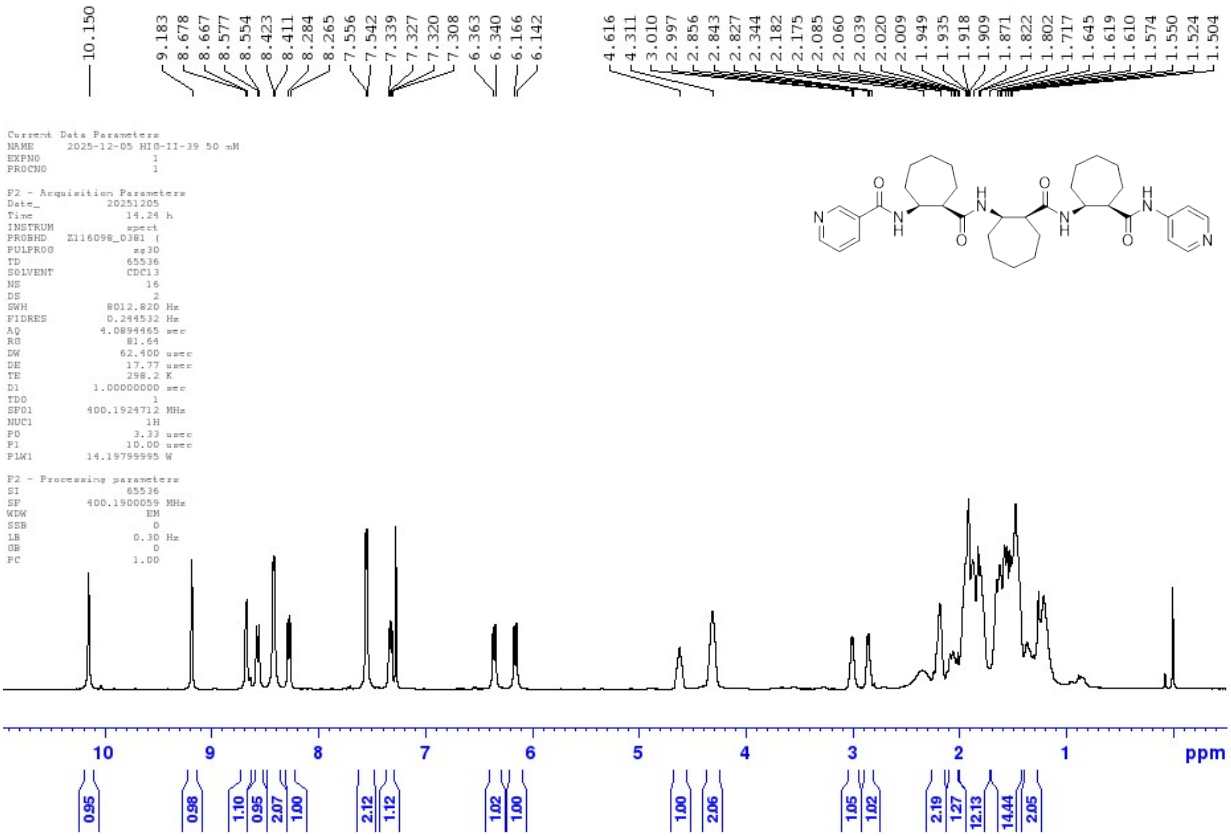


Figure S5. ^{1}H NMR spectrum of **2** (400 MHz, $CDCl_3$, 298 K)

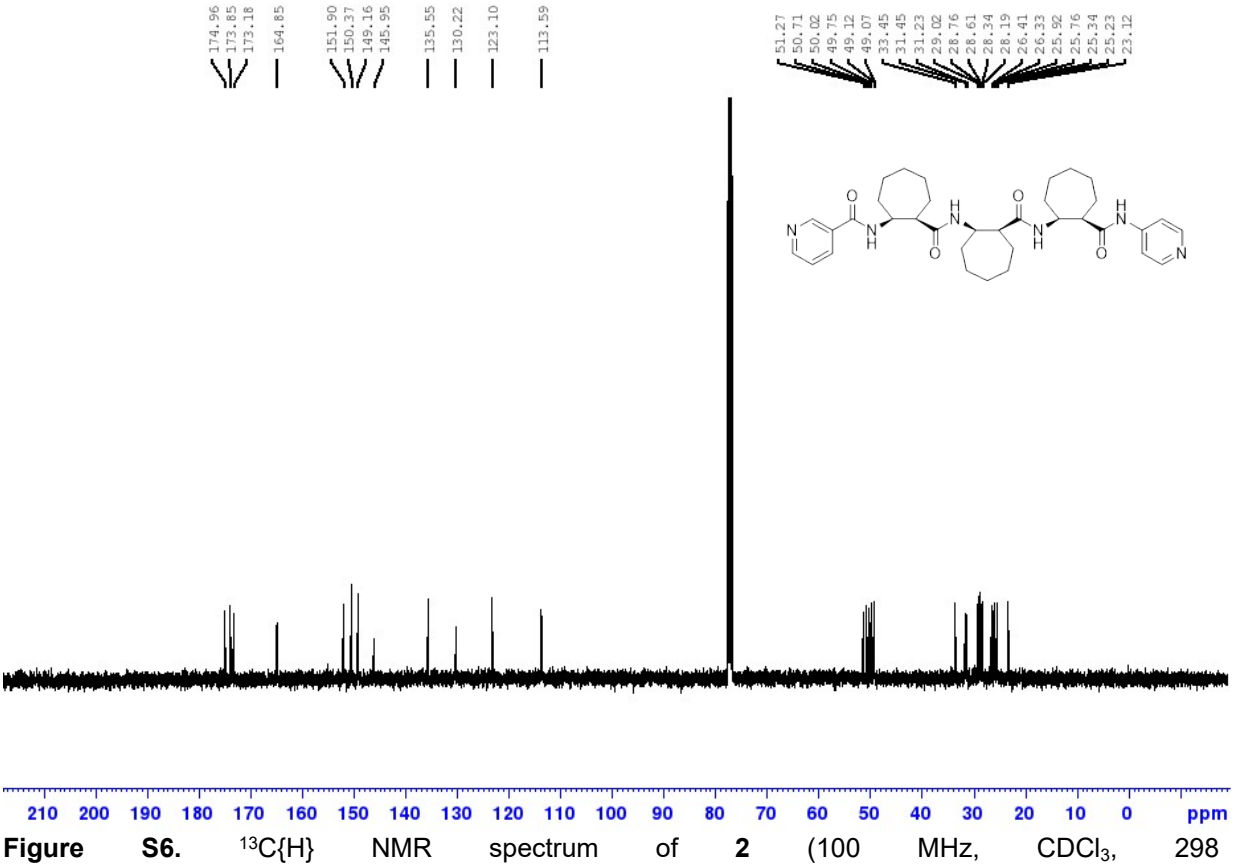


Figure S6. ^{13}C{H} NMR spectrum of **2** (100 MHz, $CDCl_3$, 298 K)

1.5 Circular Dichrosim Analysis

Circular dichroism (CD) measurements were carried out on a JASCO J-1500 spectropolarimeter at 293 K. Samples were prepared at a concentration of 0.3 mM, and measurements were performed in a 1 mm path length quartz cuvette Spectra were collected from 190 to 260 nm, with a 0.1 nm data interval and a bandwidth of 1.0 nm. Background spectra of the corresponding solvents were subtracted to provide baseline-corrected sample traces. The resulting CD profiles were then normalized according to sample concentration and cell path length. Each measurement was carried out in duplicate, and the averaged spectra were used for analysis.

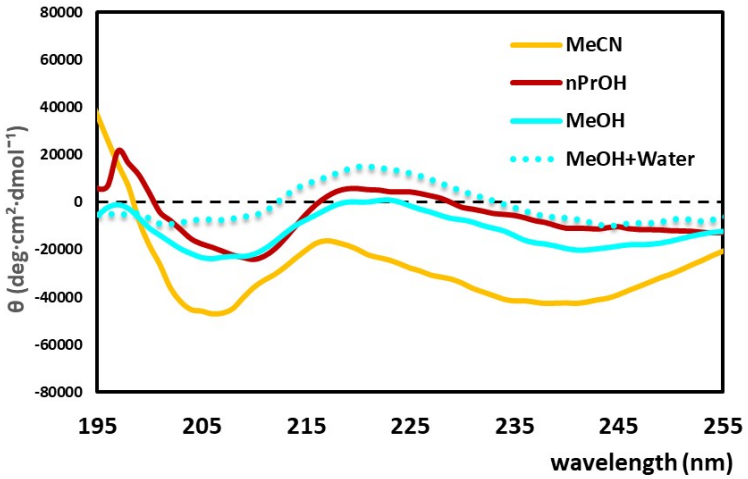


Figure S7. CD spectra of **1** measured under various solvent conditions

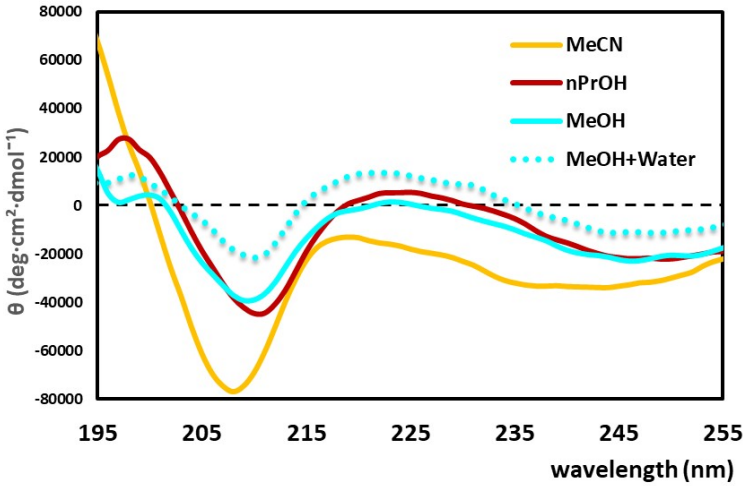


Figure S8. CD spectra of **2** measured under various solvent conditions

2. SC-XRD Data

2.1 Crystal Growth

2: Single crystals of **2** were recrystallized by layering the methanol solution of **2** over the water in a Φ5 mm microtube for 1 day.

Ag-1: Single crystals of **Ag-1** were recrystallized by triple layering technique. The ethanol solution of **1** (0.15 mL, 50 mM) a buffer solution (0.15 mL, EtOH:H_2O=1:1, v/v), and an aqueous solution of $AgBF_4$ (0.15 mL, 50 mM) were sequentially layered in a Φ5 mm microtube. After 10 days of crystallization, visible crystals formed at the interface of the bottom layer.

***iso*-Ag-1**: Single crystals of ***iso*-Ag-2** were recrystallized by triple layering technique. The methanol solution of **1** (0.10 mL, 50 mM) a buffer solution (0.10 mL, MeOH:CH_3NO_2=1:1, v/v), and an aqueous solution of $AgBF_4$ (0.10 mL, 50 mM) were sequentially layered in a Φ5 mm microtube. After 1 day of crystallization, visible crystals formed at the interface of the bottom layer.

Ag-2: Single crystals of **Ag-2** were recrystallized by triple layering technique. The ethanol solution of **2** (0.15 mL, 50 mM) a buffer solution (0.15 mL, EtOH:H_2O=1:1, v/v), and an aqueous solution of $AgBF_4$ (0.15 mL, 50 mM) were sequentially layered in a Φ5 mm microtube. After 6 days of crystallization, visible crystals formed at the interface of the bottom layer.

2.2 Crystal Data Collection

Each crystals were mounted using inert oil and transferred to the cold gas stream of the diffractometer. Crystal data of **2**, **Ag-1**, **Ag-2** were collected at Western Seoul Center for Korea Basic Science Institute (KBSI) 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.. Crystal data of ***iso*-Ag-1** were collected using a synchrotron radiation at PLSII 11C Micro-MX beamline in a Pohang Accelerator Laboratory, Korea (PAL).

2.3 Crystallographic Details of 2

The crystal structures of **2** (CCDC: 2514356) were determined by standard crystallographic methods. A colorless block-shaped crystal (0.465 × 0.183 × 0.112 mm^3) was used for single-crystal X-ray diffraction. The data were collected at 253(2) K. Data collection and integration were performed with SMART APEX3 software package (SAINT+).[1] Absorption correction was performed by multi-scan method implemented in SADABS.[2] The structure was solved by direct methods and refined by full-matrix least-squares on F^2 using SHELXTL program package (version 6.14).[3] All the non-hydrogen atoms were refined anisotropically, and hydrogen atoms were added to their geometrically ideal positions.

Crystal Data for $C_{37}H_{56}N_6O_6$ (M =680.87 g/mol): monoclinic, space group $P2_1$ (no. 4), a = 9.339(5) Å, b = 18.620(9) Å, c = 10.873(5) Å, β = 93.783(12)°, V = 1886.5(16) $Å^3$, Z = 2, T = 253(2) K, μ(MoKα) = 0.082 mm^{-1}, *Dcalc* = 1.199 g/cm^3, 21080 reflections measured (4.346° ≤ 2Θ ≤ 57.938°), 9649 unique (R_{int} = 0.1007, R_{sigma} = 0.1710) which were used in all calculations. The final R_1 was 0.0988 (I > 2σ(I)) and wR_2 was 0.3155 (all data).

Table S1. Crystal data and structure refinement for **2**.

Empirical formula	C37 H56 N6 O6	
Formula weight	680.87	
Temperature	253(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	$P2_1$	
Unit cell dimensions	a = 9.339(5) Å	α= 90°.
	b = 18.620(9) Å	β= 93.783(12)°.
	c = 10.873(5) Å	γ = 90°.
Volume	1886.5(16) $Å^3$	
Z	2	
Density (calculated)	1.199 Mg/m^3	
Absorption coefficient	0.082 mm^{-1}	
F(000)	736	
Crystal size	0.465 x 0.183 x 0.112 mm^3	
Theta range for data collection	2.173 to 28.969°.	
Index ranges	-12<=h<=9, -24<=k<=25, -14<=l<=14	
Reflections collected	21080	
Independent reflections	9649 [R(int) = 0.1007]	
Completeness to theta = 25.242°	99.9 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7457 and 0.5373	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	9649 / 44 / 446	
Goodness-of-fit on F^2	0.968	
Final R indices [I>2sigma(I)]	R1 = 0.0988, wR2 = 0.2449	
R indices (all data)	R1 = 0.2273, wR2 = 0.3155	
Absolute structure parameter	0.0(10)	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.793 and -0.340 $e.Å^{-3}$	

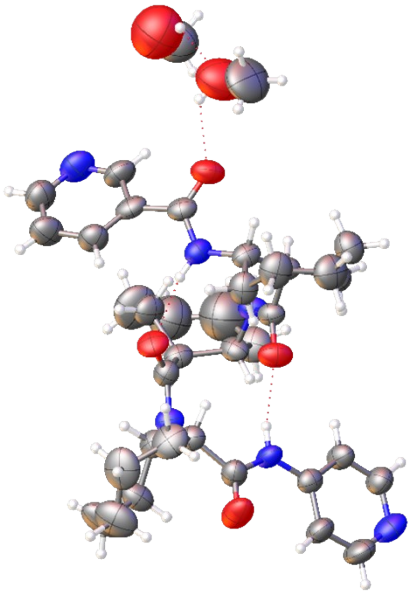


Figure S9. Molecular conformation of **2** (CCDC: 2514356) shown with 50% probability ellipsoids (grey: carbon, white: hydrogen, red: oxygen, blue: nitrogen).

2.4 Crystallographic Details of Ag-1

The crystal structures of **Ag-1** (CCDC: 2514358) were determined by standard crystallographic methods. A colorless block-shaped crystal (0.466 × 0.090 × 0.057 mm^3) was used for single-crystal X-ray diffraction. The data were collected at 243(2) K. Data collection and integration were performed with SMART APEX3 software package (SAINT+).[1] Absorption correction was performed by multi-scan method implemented in SADABS.[2] The structure was solved by direct methods and refined by full-matrix least-squares on F^2 using SHELXTL program package (version 6.14).[3] All the non-hydrogen atoms were refined anisotropically, and hydrogen atoms were added to their geometrically ideal positions. The disordered solvent molecules were treated using the SQUEEZE program [4] for better structure refinement.

Crystal Data for $C_{35}H_{48}AgBF_4N_6O_4$ (M =811.47 g/mol): orthorhombic, space group $P2_12_12_1$ (no. 19), a = 9.5779(18) Å, b = 16.535(3) Å, c = 25.143(5) Å, V = 3981.9(13) $Å^3$, Z = 4, T = 243(2) K, μ(MoKα) = 0.568 mm^{-1}, *Dcalc* = 1.354 g/cm^3, 104049 reflections measured (4.07° ≤ 2Θ ≤ 56.602°), 9872 unique (R_{int} = 0.1035, R_{sigma} = 0.0511) which were used in all calculations. The final R_1 was 0.0555 (I > 2σ(I)) and wR_2 was 0.1698 (all data).

Table S2. Crystal data and structure refinement for **Ag-1**.

Empirical formula	C35 H48 Ag B F4 N6 O4	
Formula weight	811.47	
Temperature	243(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	$P2_12_12_1$	
Unit cell dimensions	a = 9.5779(18) Å	α= 90°.
	b = 16.535(3) Å	β= 90°.
	c = 25.143(5) Å	γ = 90°.
Volume	3981.9(13) $Å^3$	
Z	4	
Density (calculated)	1.354 Mg/m^3	
Absorption coefficient	0.568 mm^{-1}	
F(000)	1680	
Crystal size	0.466 x 0.090 x 0.057 mm^3	
Theta range for data collection	2.035 to 28.301°.	
Index ranges	-12<=h<=12, -22<=k<=22, -33<=l<=33	
Reflections collected	104049	
Independent reflections	9872 [R(int) = 0.1035]	
Completeness to theta = 25.242°	99.9 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7366 and 0.6370	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	9872 / 51 / 461	
Goodness-of-fit on F^2	1.020	
Final R indices [I>2sigma(I)]	R1 = 0.0555, wR2 = 0.1420	
R indices (all data)	R1 = 0.0974, wR2 = 0.1698	
Absolute structure parameter	0.00(4)	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.603 and -0.516 $e.Å^{-3}$	

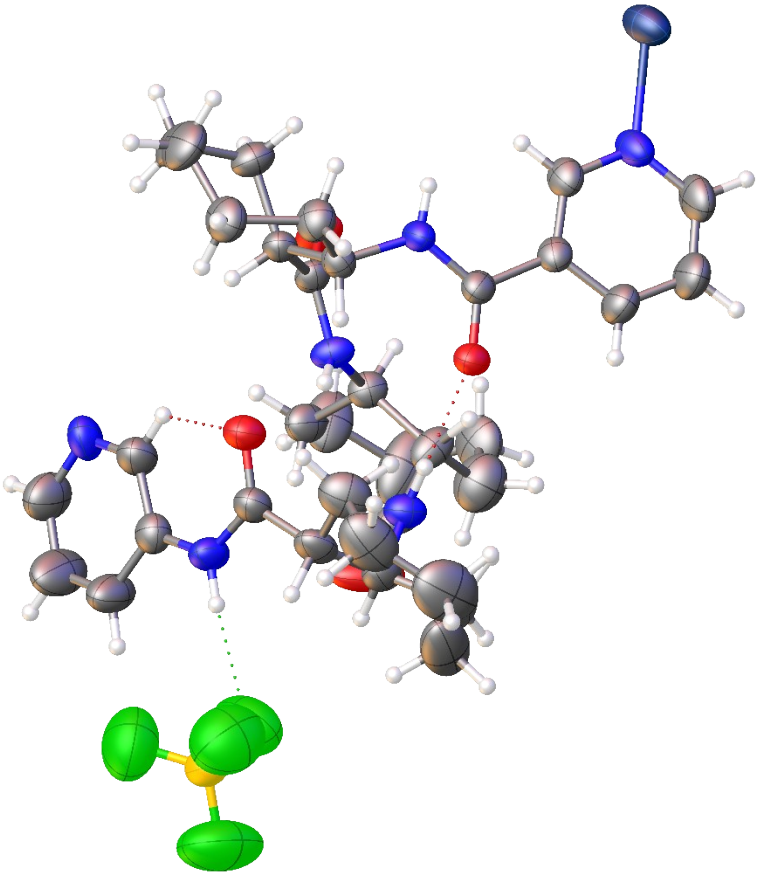


Figure S10. Molecular conformation of **Ag-1** (CCDC: 2514358) shown with 50% probability ellipsoids (grey: carbon, white: hydrogen, red: oxygen, blue: nitrogen green: fluorine, yellow: boron, deep blue: silver).

2.5 Crystallographic Details of *iso*-Ag-1

The crystal structures of ***iso*-Ag-1** (CCDC: 2514359) were determined by standard crystallographic methods.The data collection was performed at 100K with a radiation wavelength of λ = 0.700000 Å, detector distance of 150 mm, omega scan with ∆ω = 1º, and the exposure time was 1.0 sec per frame. The data were collected at 100 K using an ADSC Quantum 210 CCD diffractometer with synchrotron radiation (λ = 0.70000 Å) at Pohang Accelerator Laboratory (PAL). The diffraction images were collected using a PILATUS3 6M detector and raw data were processed and scaled using the program HKL3000.[5] The crystal structures were solved by the intrinsic phasing method using SHELXT (Ver.2018/2).[3] Since the data was collected at a wavelength of 0.7 Å using a synchrotron radiation source dispersion and absorption correction values have been provided using the DISP command line.

Crystal Data for $C_{35.5}H_{50.5}N_{6.5}O_5AgBF_4$ (*M* =843.00 g/mol): monoclinic, space group $P2_1$ (no. 4), *a* = 13.461(3) Å, *b* = 9.6300(19) Å, *c* = 15.925(3) Å, *β* = 109.83(3)°, *V* = 1941.9(8) Å^3, *Z* = 2, *T* = 100(2) K, μ(synchrotron) = 0.556 mm^{-1}, *Dcalc* = 1.442 g/cm^3, 26398 reflections measured (3.168° ≤ 2Θ ≤ 55.598°), 9084 unique (R_{int} = 0.1324, R_{sigma} = 0.1106) which were used in all calculations. The final R_1 was 0.0855 (I > 2σ(I)) and wR_2 was 0.2601 (all data).

Table S3. Crystal data and structure refinement for ***iso*-Ag-1**.

Empirical formula	C35.50 H50.50 Ag B F4 N6.50 O5	
Formula weight	843.00	
Temperature	100(2) K	
Wavelength	0.700 Å	
Crystal system	Monoclinic	
Space group	$P2_1$	
Unit cell dimensions	a = 13.461(3) Å	α = 90°
	b = 9.6300(19) Å	β = 109.83(3)°
	c = 15.925(3) Å	γ = 90°
Volume	1941.9(8) Å^3	
Z	2	
Density (calculated)	1.442 Mg/m^3	
Absorption coefficient	0.556 mm^{-1}	
F(000)	874	
Crystal size	0.030 x 0.020 x 0.015 mm^3	
Theta range for data collection	1.584 to 27.799°.	
Index ranges	-17<=h<=17, -12<=k<=12, -21<=l<=21	
Reflections collected	26398	
Independent reflections	9084 [R(int) = 0.1324]	
Completeness to theta = 24.835°	97.7 %	
Absorption correction	Empirical	
Max. and min. transmission	1.000 and 0.481	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	9084 / 13 / 516	
Goodness-of-fit on F^2	0.964	
Final R indices [I>2sigma(I)]	R1 = 0.0855, wR2 = 0.2310	
R indices (all data)	R1 = 0.1407, wR2 = 0.2601	
Absolute structure parameter	0.10(4)	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.673 and -0.548 e·Å^{-3}	

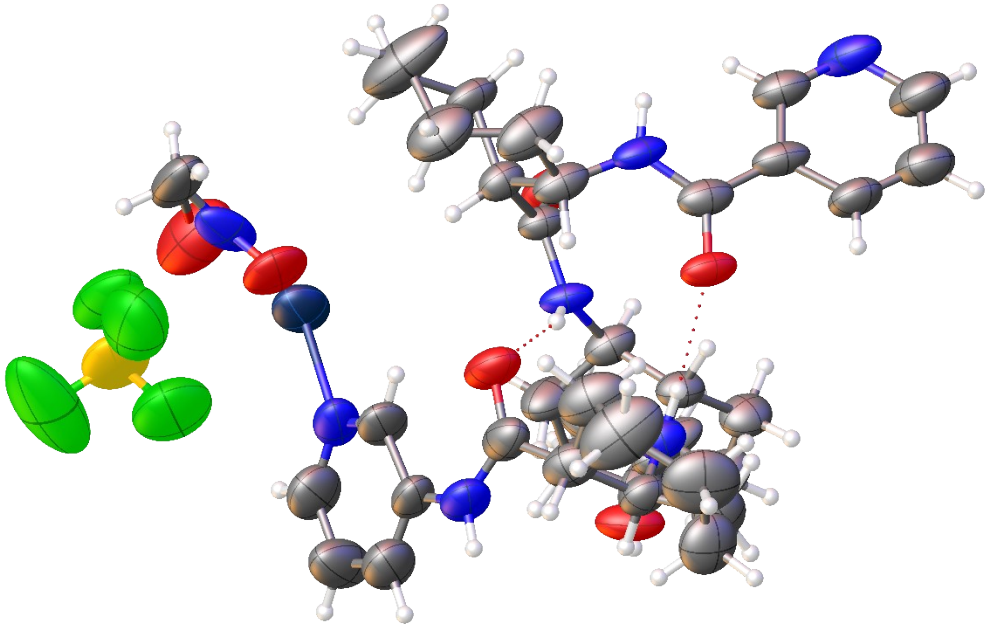


Figure S11. Molecular conformation of ***iso*-Ag-1** (CCDC: 2514359) shown with 50% probability ellipsoids (grey: carbon, white: hydrogen, red: oxygen, blue: nitrogen, green: fluorine, yellow: boron, deep blue: silver).

2.6 Crystallographic Details of Ag-2

The crystal structures of **Ag-2** (CCDC: 2514357) were determined by standard crystallographic methods. A colorless block-shaped crystal (0.352 × 0.267 × 0.153 mm^3) was used for single-crystal X-ray diffraction. The data were collected at 243(2) K. Data collection and integration were performed with SMART APEX3 software package (SAINT+).[1] Absorption correction was performed by multi-scan method implemented in SADABS.[2] The structure was solved by direct methods and refined by full-matrix least-squares on F^2 using SHELXTL program package (version 6.14).[3] All the non-hydrogen atoms were refined anisotropically, and hydrogen atoms were added to their geometrically ideal positions. The disordered solvent molecules and tetrafluoroborate counterions were treated using the SQUEEZE program [4] for better structure refinement.

Crystal Data for $C_{70}H_{96}Ag_2N_{12}O_9$ (M =1465.32 g/mol): triclinic, space group $P\bar{1}$ (no. 1), a = 11.114(9) Å, b = 18.316(16) Å, c = 23.20(2) Å, α = 68.48(3)°, β = 89.72(3)°, γ = 82.79(3)°, V = 4353(6) $Å^3$, Z = 2, T = 243(2) K, μ(MoKα) = 0.501 mm^{-1}, *Dcalc* = 1.118 g/cm^3, 115234 reflections measured (4.138° ≤ 2Θ ≤ 56.562°), 42367 unique (R_{int} = 0.1051, R_{sigma} = 0.1244) which were used in all calculations. The final R_1 was 0.0674 (I > 2σ(I)) and wR_2 was 0.1889 (all data).

Table S4. Crystal data and structure refinement for **Ag-2**.

Empirical formula	C70 H96 Ag2 N12 O9	
Formula weight	1465.32	
Temperature	243(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	$P\bar{1}$	
Unit cell dimensions	a = 11.114(9) Å	α= 68.48(3)°.
	b = 18.316(16) Å	β= 89.72(3)°.
	c = 23.20(2) Å	γ = 82.79(3)°.
Volume	4353(6) $Å^3$	
Z	2	
Density (calculated)	1.118 Mg/m^3	
Absorption coefficient	0.501 mm^{-1}	
F(000)	1532	
Crystal size	0.352 x 0.267 x 0.153 mm^3	
Theta range for data collection	2.069 to 28.281°.	
Index ranges	-14<=h<=14, -24<=k<=24, -30<=l<=30	
Reflections collected	115234	
Independent reflections	42367 [R(int) = 0.1051]	
Completeness to theta = 25.242°	99.9 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.6452 and 0.5592	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	42367 / 47 / 1686	
Goodness-of-fit on F^2	0.978	
Final R indices [I>2sigma(I)]	R1 = 0.0674, wR2 = 0.1638	
R indices (all data)	R1 = 0.1105, wR2 = 0.1889	
Absolute structure parameter	0.13(2)	
Extinction coefficient	n/a	
Largest diff. peak and hole	1.056 and -0.734 $e.Å^{-3}$	

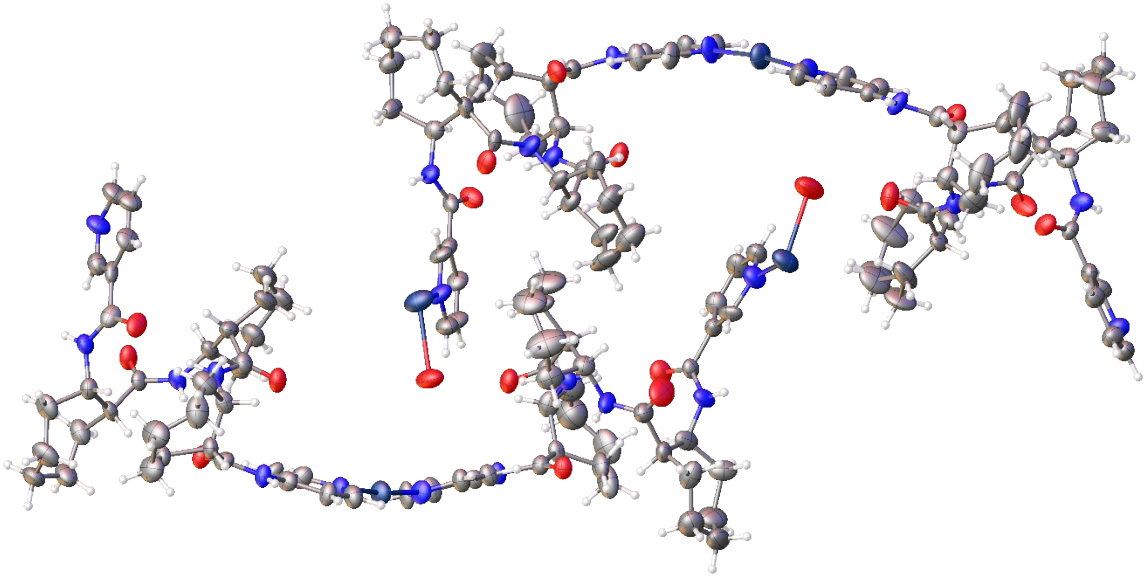


Figure S12. Molecular conformation of **Ag-2** (CCDC: 2514357) shown with 50% probability ellipsoids (grey: carbon, white: hydrogen, red: oxygen, blue: nitrogen, deep blue: silver).

3. References

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