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Exploring Enantioselective Recognition of dTMP-Co-bpe Coordination Polymer for Natural Amino Acids Using Molecular Simulations and Circular Dichroism

Supporting Information

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1. General Methods.

1.1. Materials.

Chemical reagents were used as purchased without further purification. Aladdin provided 1,2-di(4-pyridyl) ethene (bpe), while Alfa Aesar supplied $M(NO_3)_2.6H_2O$ ($M=Co^{2+}$) and 2'-Deoxythymidine-5'-monophosphate, disodium salt. *D*- histidine, *L*-histidine, *D*- phenylalanine, and *L*-phenylalanine were purchased from Macklin.

1.2. Instrumentation.

Elemental analysis of the C, H, and N components was performed using an elemental analyzer with plate number 1. KBr pellet FT-IR spectra were obtained in the 4000-400 cm^{-1} range using a Nicolet Nexus FT-IR spectrometer. A TU-1950 spectrophotometer was used to obtain UV-Vis

spectra. Powder diffraction X-ray studies were conducted using a Bruker D8 Advance X-ray diffractometer. Monochromatized graphite Mo Kα radiation with a number 1 was used to capture single crystal X-ray data using a Bruker APEX-II CCD and Rigaku Saturn724+ (2 x 2 bin mode). CD measurements were carried out using a JASCO J-810 spectropolarimeter under a constant nitrogen flow. Thermogravimetric analysis (TGA) was conducted using a DTG-60H thermal analyzer in an atmosphere of nitrogen with a heating rate of 5°C/min from room temperature to 400°C. The pH of the specimen solution was determined using a PHS-3C meter.

2. Synthesis and Structural Characterization.

The method of synthesis of the whole coordination polymer involves the addition of (4 mL) aqueous solution of 2'-Deoxythymidine 5'monophosphate disodium salt in (4 mL) Co $(NO_3)_2.6H_2O$ aqueous solution. Stirring the mixture for 15 minutes, then add the aqueous solution of auxiliary ligand (bpe). HNO_3 (1 M) is used to modify the suspension of acidity till the solution becomes transparent. The desired solution was filtered after stirring the solution around 30–40 min. At room temperature, slow evaporation helped us to obtain an appropriate investigation of single crystal X-ray diffraction. The X-ray powder diffraction pattern of polycrystalline specimens of its CP-1 and ligands was consistent with their theoretical patterns (Figure S7), confirming the bulk specimen phase purity. The CP-1's water content and thermal stability were determined by the analysis of thermo–gravimetric (Figure S12). The Metal Nucleotide's kinds of interactions have been identified by using FT–IR (Figure S11).

3. Crystal Structure Determination and Refinement.

The X-ray single crystal data collections for the CP-1 was performed on a diffractometer of Rigaku Saturn724+ (2x2 bin mode), and Bruker APEX-II CCD was used to acquire data of single crystal X-ray with M_O Kα radiation (λ =0.71073 Å) monochromatized graphite. The crystal size of the CP-1 is 0.32 × 0.21 × 0.18 mm^3 (1). The crystals were kept at 296(2) K during data collection. Utilizing Olex2, the structure was solved with the XT.3 Structure solution program using Intrinsic Phase formation, and refinement was performed using SHELXL4 and a refinement package that involved Least Squares minimization of whole non-hydrogen atoms in complexes. During refinement, the positions and thermal parameters of hydrogen atoms bound to atoms of carbon, nitrogen, and oxygen were fixed using geometrical calculations. In water molecules, hydrogen atoms are positioned geometrically. A summary of the crystallographic information and experimental data for structural analysis of the CP-1 is provided in Table 1, and a summary of certain angles and bond distances along its standard deviations is provided in Tables S2–S3. The summary of the CP-1 hydrogen bond is in Table S4.

4. Crystallographic Data and Structural Information.

4.1. Table S1: Crystallographic data for CP-1.

Parameters	CP-1
Empirical formula	$C_{22}H_{45}CoN_4O_{20}P$
Formula weight	775.52
Temperature/K	298.00

Crystal system	orthorhombic
Space group	$P2_12_12_1$
a/Å	13.6235(16)
b/Å	14.122(2)
c/Å	17.971(3)
α/°	90
β/°	90
γ/°	90
Volume/Å^3	3457.3(8)
Z	4
ρ_{calc}g/cm^3	1.490
μ/mm^{-1}	0.628
F(000)	1628.0
Crystal size/mm^3	0.32 × 0.21 × 0.18
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	4.732 to 49.472
Index ranges	-16 ≤ h ≤ 14, -16 ≤ k ≤ 16, -21 ≤ l ≤

	21
Reflections collected	25118
Independent reflections	5897 [R_{int} = 0.1004, R_{sigma} = 0.0829]
Data/restraints/parameters	5897/0/466
Goodness-of-fit on F^2	1.014
Final R indexes [I>=2σ (I)]	R_1 = 0.0432, wR_2 = 0.0830
Final R indexes [all data]	R_1 = 0.0754, wR_2 = 0.0946
Largest diff. peak/hole / e $Å^{-3}$	0.41/-0.37
Flack parameter	0.000(12)

4.2. Table S2: Bond length of CP-1.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
Co1	O1	2.061(4)	N2	C22	1.463(7)
Co1	O12	2.174(4)	N3	C8	1.341(7)
Co1	O14	2.137(4)	N3	C5	1.331(7)
Co1	N1	2.126(4)	C1	C12	1.461(7)
Co1	O20	2.119(4)	C1	C7	1.380(8)

Co1	N3[1]	2.150(4)	C1	C15	1.398(8)
P1	O1	1.531(4)	C6	C16	1.380(8)
P1	O8	1.505(4)	C6	C13	1.458(7)
P1	O10	1.522(4)	C6	C19	1.391(8)
P1	O5	1.596(4)	C8	C16	1.374(8)
O4	C14	1.450(7)	C10	C22	1.501(8)
O4	C22	1.415(7)	C10	C9	1.522(8)
O6	C4	1.220(6)	C12	C13	1.329(7)
O16	C9	1.408(7)	C14	C17	1.504(8)
O18	C2	1.243(7)	C14	C9	1.535(8)
N1	C18	1.351(7)	C18	C15	1.361(8)
N1	C11	1.330(7)	C20	C3	1.344(8)
O5	C17	1.432(7)	C11	C7	1.385(7)
N4	C4	1.365(8)	C3	C2	1.429(8)
N4	C2	1.383(9)	C3	C21	1.492(9)
N2	C4	1.379(8)	C19	C5	1.385(8)
N2	C20	1.373(8)			

[1]-1+X,+Y,+Z

4.3. Table S3: Bond angle of CP-1.

Atom	Atom	Atom	Angle/˚	Atom	Atom	Atom	Angle/˚
O1	Co1	O12	89.95(16)	C15	C1	C12	122.8(5)
O1	Co1	O14	98.16(15)	O6	C4	N4	123.0(6)
O1	Co1	N1	89.72(16)	O6	C4	N2	122.8(6)
O1	Co1	O20	172.45(16)	N4	C4	N2	114.3(6)
O1	Co1	N3[1]	92.66(17)	C16	C6	C13	124.2(5)
O14	Co1	O12	171.70(16)	C16	C6	C19	116.9(5)
O14	Co1	N3[1]	87.55(17)	C19	C6	C13	118.9(5)
N1	Co1	O12	92.83(18)	N3	C8	C16	122.9(5)
N1	Co1	O14	88.94(17)	C22	C10	C9	102.9(5)
N1	Co1	N3[1]	176.0(2)	C13	C12	C1	124.3(5)
O20	Co1	O12	82.80(17)	O4	C14	C17	107.9(5)
O20	Co1	O14	89.15(16)	O4	C14	C9	106.6(4)
O20	Co1	N1	88.53(16)	C17	C14	C9	116.1(5)
O20	Co1	N3[1]	89.51(17)	C8	C16	C6	120.3(6)
N3[1]	Co1	O12	90.37(17)	N1	C18	C15	123.8(6)
O1	P1	O5	107.1(2)	C3	C20	N2	123.7(6)
O8	P1	O1	112.8(2)	O4	C22	N2	107.6(5)
O8	P1	O10	113.7(2)	O4	C22	C10	104.5(5)
O8	P1	O5	108.7(2)	N2	C22	C10	115.1(5)

O10	P1	O1	111.4(2)	N1	C11	C7	123.6(5)
O10	P1	O5	102.4(2)	C20	C3	C2	117.2(6)
P1	O1	Co1	135.4(2)	C20	C3	C21	122.3(6)
C22	O4	C14	108.8(4)	C2	C3	C21	120.5(6)
C18	N1	Co1	120.4(4)	C12	C13	C6	126.0(6)
C11	N1	Co1	123.4(4)	C1	C7	C11	119.9(5)
C11	N1	C18	116.2(5)	C18	C15	C1	119.9(5)
C17	O5	P1	120.4(3)	O18	C2	N4	119.3(6)
C4	N4	C2	126.8(6)	O18	C2	C3	124.3(6)
C4	N2	C22	119.1(5)	N4	C2	C3	116.4(6)
C20	N2	C4	121.6(5)	O5	C17	C14	107.1(5)
C20	N2	C22	119.2(5)	O16	C9	C10	112.8(5)
C8	N3	Co1[2]	120.7(4)	O16	C9	C14	107.8(5)
C5	N3	Co1[2]	122.1(4)	C10	C9	C14	102.7(5)
C5	N3	C8	117.2(4)	C5	C19	C6	119.4(6)
C7	C1	C12	120.6(5)	N3	C5	C19	123.3(6)
C7	C1	C15	116.6(5)				

[1]-1+X,+Y,+Z; [2]1+X,+Y,+Z

4.4. Table S4: Hydrogen Bonding of CP-1.

D-H	d(D-H)	d(H…A)	<DHA	d(D…A)	A	Symmetry
O12-H12A	0.85	1.76	159.2	2.577(5)	O10	

O12-H12B	0.86	2.08	141.0	2.801(7)	O13	**[1/2+x,1/2-y,1-z]**
O14-H14A	0.87	2.05	143.4	2.795(6)	O7	
O14-H14B	0.87	2.06	154.1	2.867(6)	O13	**[-1/2-x,1-y, -1/2+z.]**
O16-H16	0.82	1.84	173.2)	2.653(6)	O8	**[-1/2+x,3/2-y,1-z]**
O20-H20A	0.86	1.90	151.9	2.688(7)	O17	
O20-H20B	0.86	1.90	167.9	2.742(7)	O11	
O3-H3A	0.85	2.04	164.2	2.866(7)	O18	**[-x, -1/2+y,3/2-z]**
O3-H3B	0.85	1.91	159.4	2.724(7)	O10	
O13-H13D	0.85	1.93	158.6	2.744(10)	O19	
O7-H7A	0.85	2.04	166.3	2.872(7)	O6	**[1/2+x, 3/2-y,1-z]**
O7-H7B	0.85	2.03	160.9	2.843(8)	O3	
O15-H15B	0.85	1.95	170.1	2.796(7)	O8	
O2-H2A	0.85	2.06	136.0	2.740(7)	O10	**[3/2-x, -1/2+y,1-z]**
O17-H17C	0.85	2.19	138.2	2.880(13)	O9	
O17-H17D	0.85	1.99	158.4	2.801(8)	O16	**[-x,1/2+y,1/2-z]**
N4-H4	0.68(9)	2.12(9)	169(11)	2.793(8)	O2	**[-x,1/2+y,3/2-z]**

[1]1/2+x,1/2-y,1-z; [2]-1/2-x,1-y, -1/2+z; [3]-1/2+x,3/2-y,1-z; [4]-x, -1/2+y,3/2-z; [5]1/2+x,3/2-y,1-z; [6]-x,1/2+y,1/2-z; [7]-x,1/2+y,3/2-z

Amino Acid	L (ΔG)	D (ΔG)	(ΔΔG)
Alanine	-4.4551883	-4.6472797	0.1920914
Arginine	-9.791585	-9.9475193	0.1559343
Asparagine	-5.1172843	-7.3462014	2.2289171
Aspartate	-7.294735	-6.8797908	-0.4149442
Cysteine	-5.0861645	-6.1769829	1.0908184
Glutamate	-9.1023855	-9.2617321	0.1593466
Glutamine	-6.9063993	-9.1156626	2.2092633
Glycine	-4.1340561	-4.0230340	0.1110221
Histidine	-6.3831158	-9.2605658	2.87745
Isoleucine	-4.3050766	-6.5903096	2.285233
Leucine	-5.6766372	-5.806551	0.1299138
Lysine	-11.15537	-9.6076288	-1.5477412
Methionine	-6.8319883	-7.340785	0.5087967
Phenylalanine	-5.2889028	-9.1893711	3.9004683
Proline	-4.8883934	-5.6353655	0.7469721
Serine	-4.6347342	-5.5890551	0.9543209
Threonine	-5.3441644	-6.1785383	0.8343739
Tryptophan	-6.2097054	-7.9882946	1.7785892
Tyrosine	-7.4261208	-9.532464	2.1063432
Valine	-6.4103479	-6.445612	0.0352641

4.5. Table S5: Binding free energy differences of the D/L forms of different amino acids.

4.6. Table S6: CD-spectra of dTMP and coordination CP-1 in the solution phase.

Peak (nm)	λ_1	λ2	λ3	λ4
dTMP	200(+)	218(-)	233(-)	272(+)
CP-1	-	211(-)	231(-)	274 (+)

4.7. Table S7: The relative crystalline-state CD spectrum peaks.

Peak (nm)	λ_1	λ2
dTMP	212 (+)	242 (-)
CP-1	219 (-)	317 (+)

5. Crystal structure.

5.1. Supporting information of CP-1

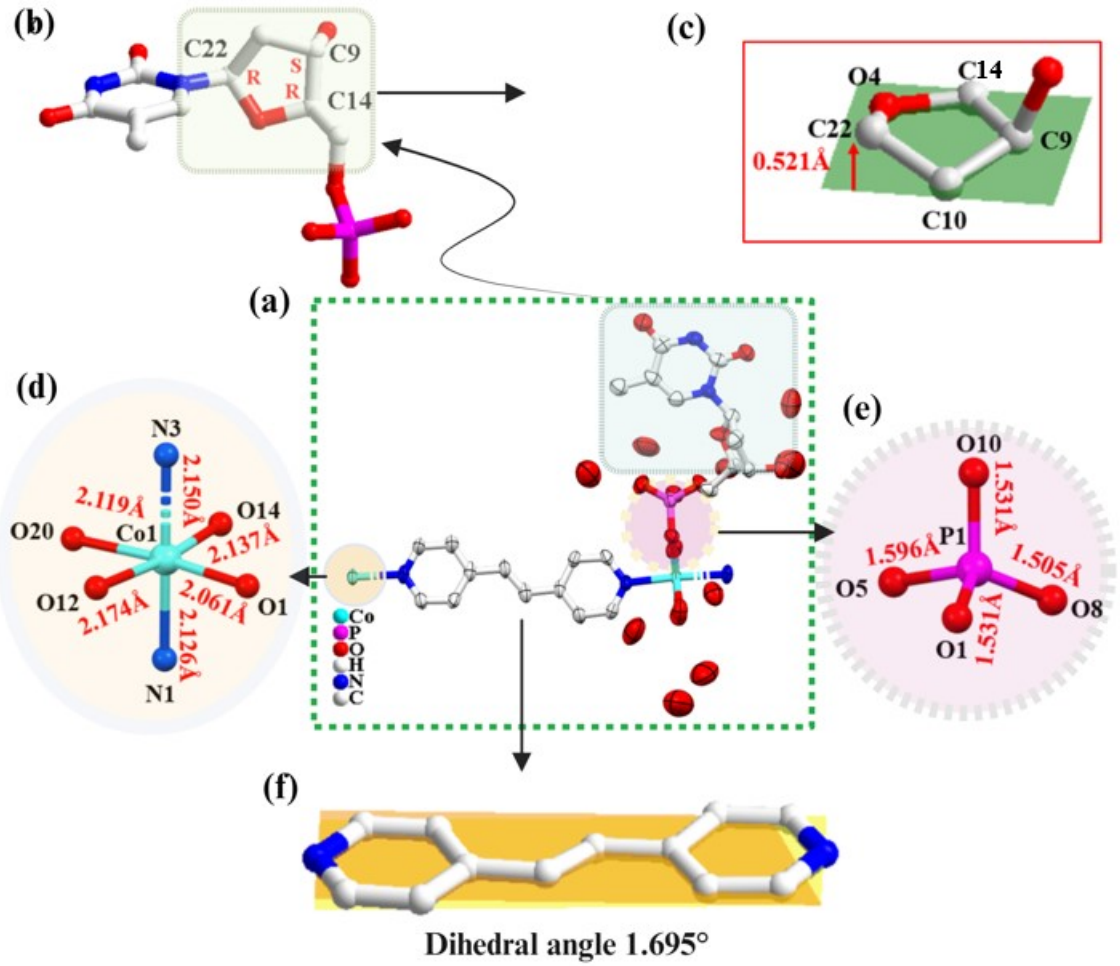

Figure S1: (a) CP-1, an asymmetric unit with guest water molecules. The hydrogen atoms are not shown for clarity. (b) dTMP ligands obtained new type configuration such as sugar motif shows the R, S, R configuration. (c) **C_3'-exo $_3$E** conformations of five-membered rings in 1. The green color indicates a perfect (C10−C9−C14−O4) plane while C22 out of the plane is 0.521Å. (d) Shows the distorted Octahedral geometry, one dTMP occupying the equatorial position and the two bpe on the axial position presenting trans-position. (e) The phosphate group revealed the distorted tetrahedral geometry. (f) Twisting of the bpe ligand presented by the dihedral angle 1.695º.

5.2. Supporting information of CP-1

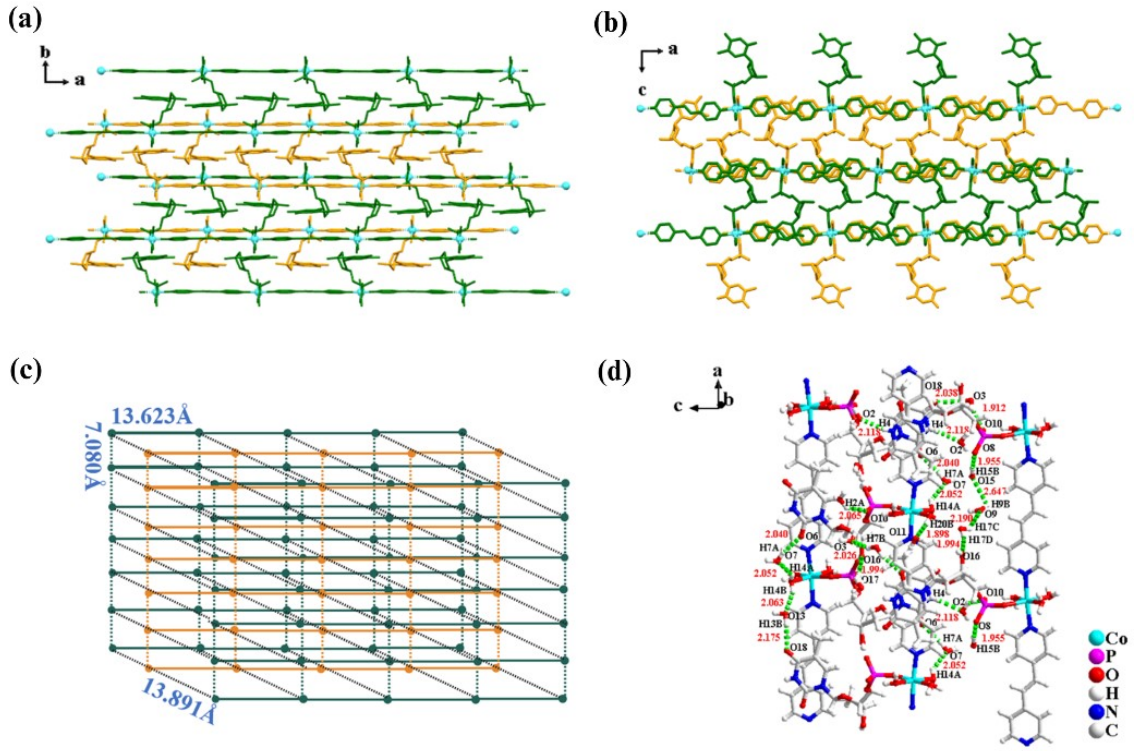

Figure S2: (a) Depicts the 2D structure of CP-1 formed by the interaction of nucleobase with bridging ligand along the c-axis. (b) In 3D structure, the green and orange layers are connected via supramolecular interactions between guest water molecules and the oxygen of phosphate and metal-coordinated water molecules. (c) The Topology illustrates Co(II) metal ions are arranged in a 2D manner with a distance of 13.623 Å between two Co metal ions separated by a bpe bridging ligand. The distance between Co atoms in two adjacent layers attached by pi-pi stacking is 7.080 Å. The distance between Co-1…Co-1 separated by bpe ligand in the 3D assembly is 13.891. (d) Hydrogen bonding via guest water molecules converts 2D supramolecular assembly into the 3D framework.

6. Molecular simulation for the chiral separation of amino acids.

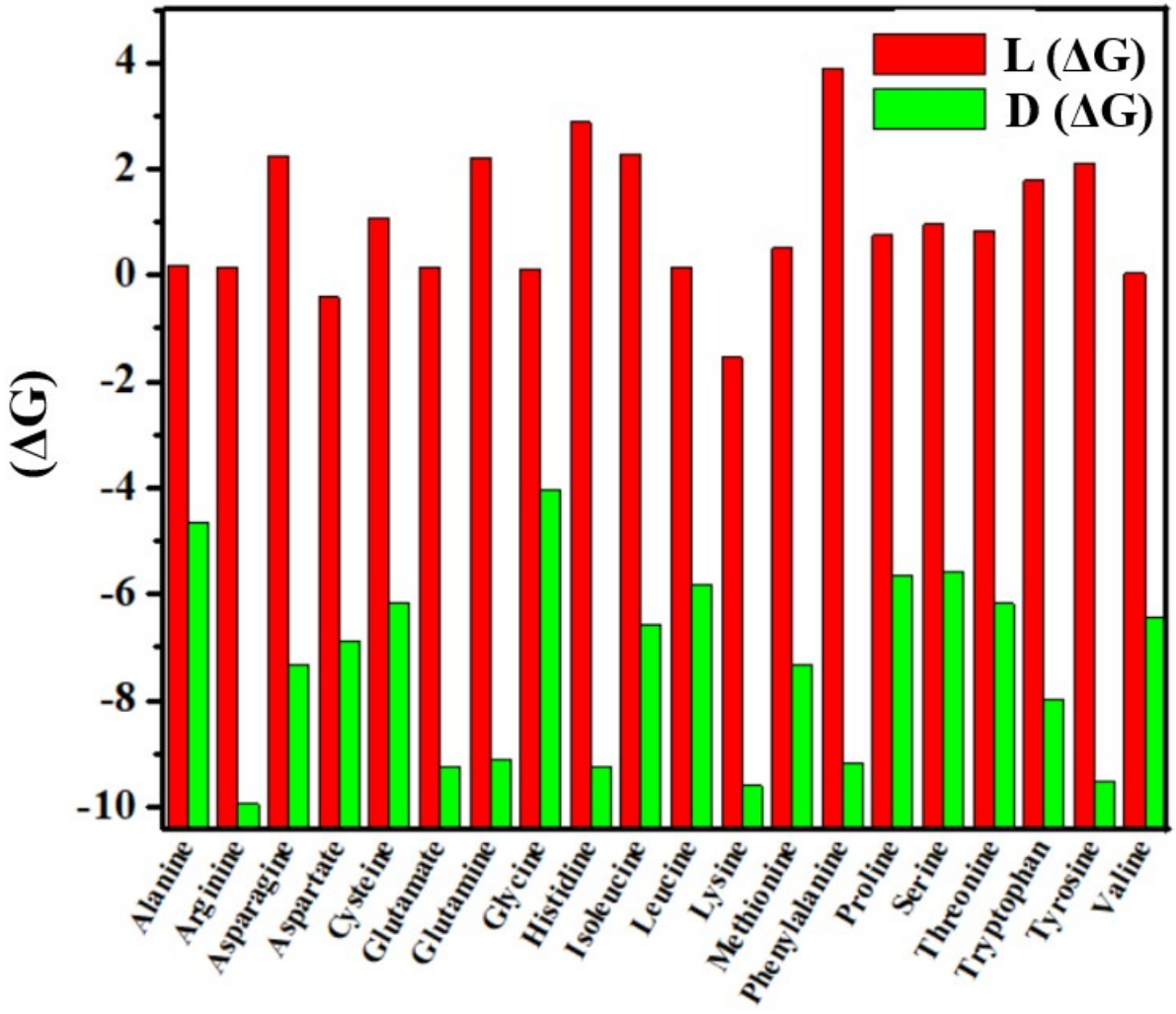

Figure S3: Binding free energy differences of the *D/L* forms of different amino acids.

6.1. Molecular Simulation-based Interactions of CP-1 with *D*-Phenylalanine *and* *L*-Phenylalanine.

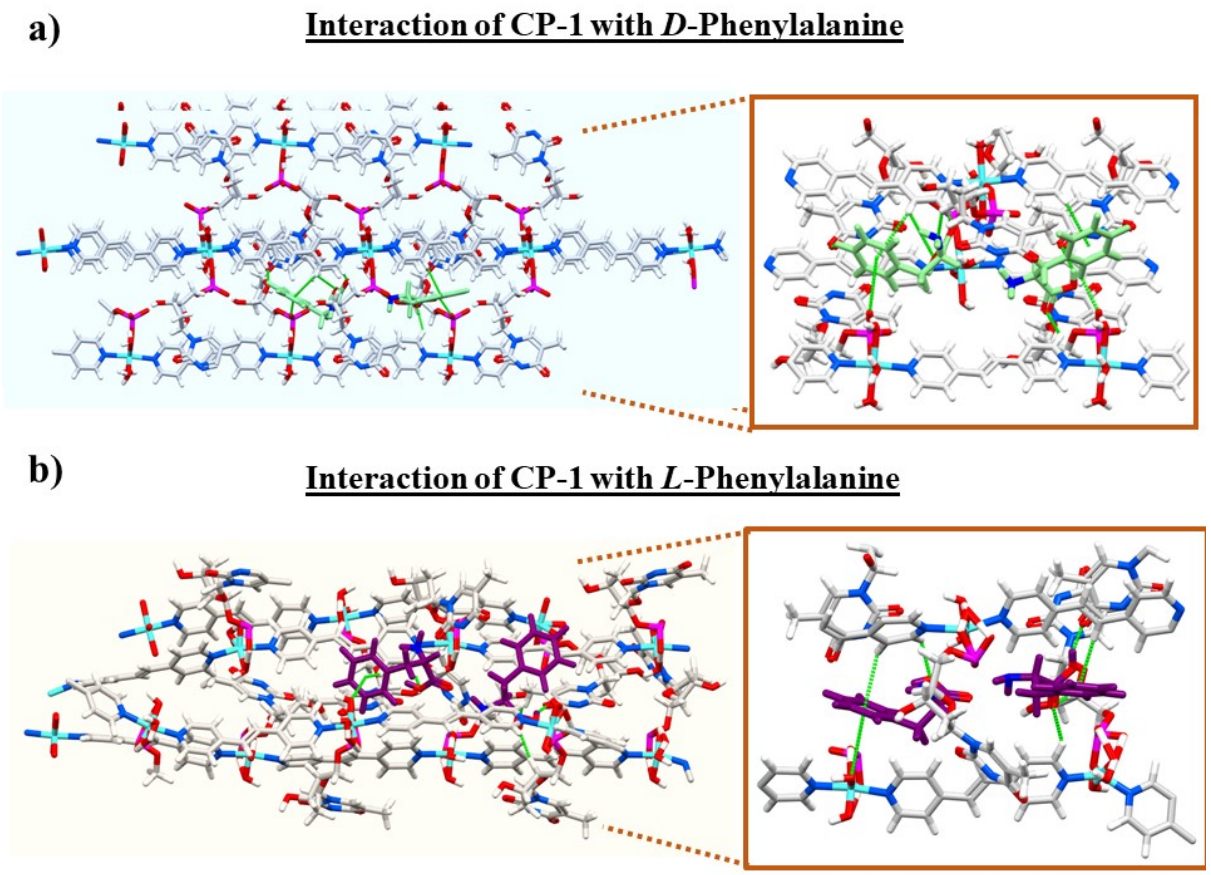

Figure S4: Molecular simulation-based CP-1 and *D/L*-amino acids interaction. (a) Interaction of CP-1 with *D*-Phenylalanine. (b) Interaction of CP-1 with *L*-Phenylalanine.

6.2. Molecular Simulation-based Interactions of CP-1 with *D*-Histidine *and L*-Histidine.

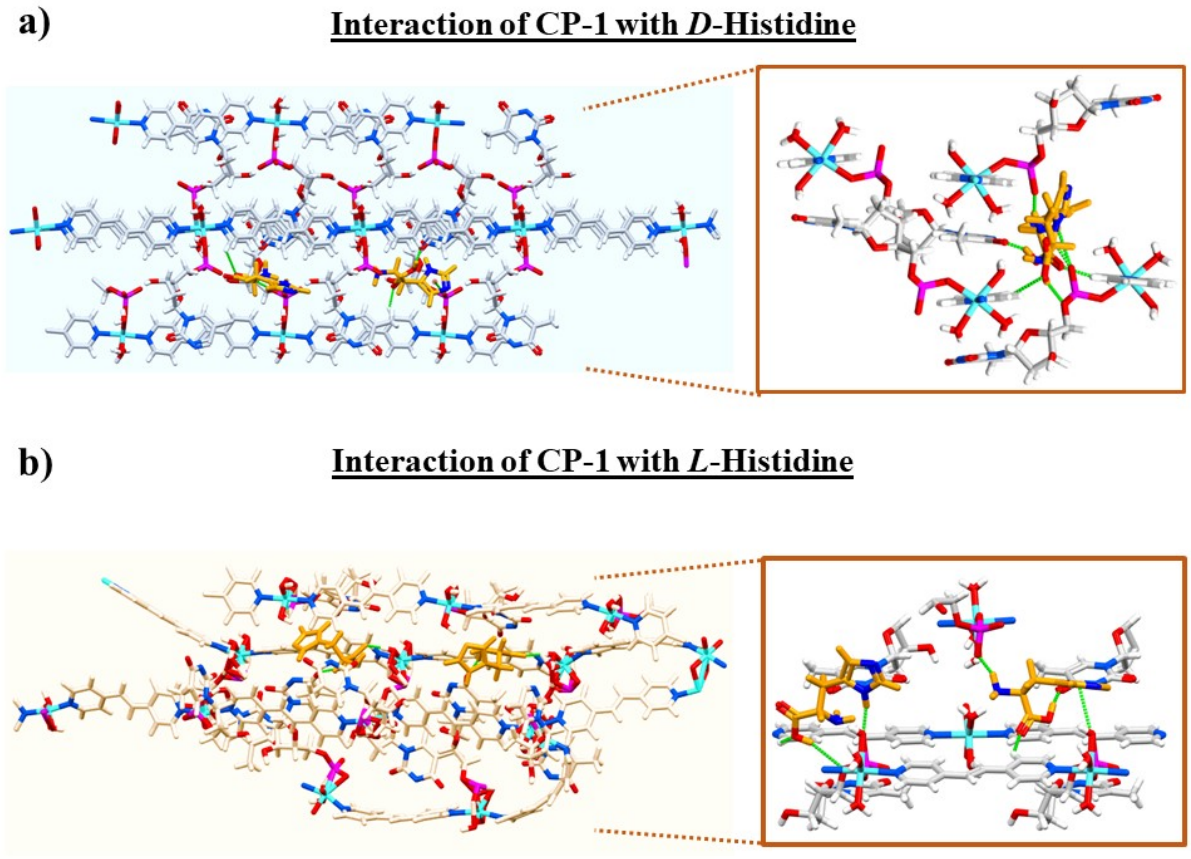

Figure S5: Molecular simulation-based CP-1 and *D/L*-amino acid interactions (a) Interaction of CP-1 with *D*-Histidine. (b) Interaction of CP-1 with *L*-Histidine.

6.3. The solution CD spectrum of CP-1 with Amino acids.

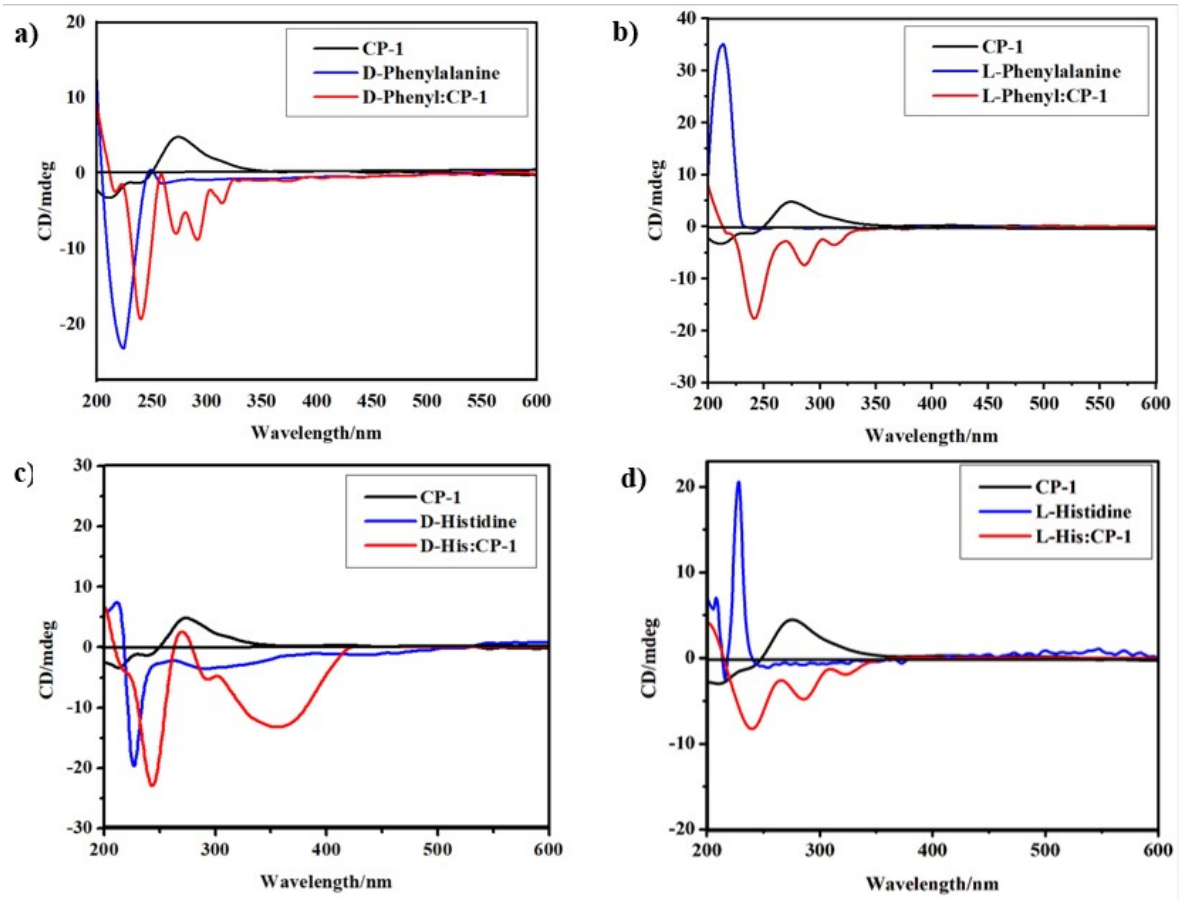

Figure S6: The solution CD spectrum of CP-1 (2.5×10^{-5} M; distilled water) with amino acids (2.5×10^{-5} M; distilled water). (a) CD results of *D*-Phenylalanine. (b) CD results of *L*-Phenylalanine. (c) CD results of *D*-Histidine. (d) CD results of *L*-Histidine.

7. The PXRD patterns of the CP-1.

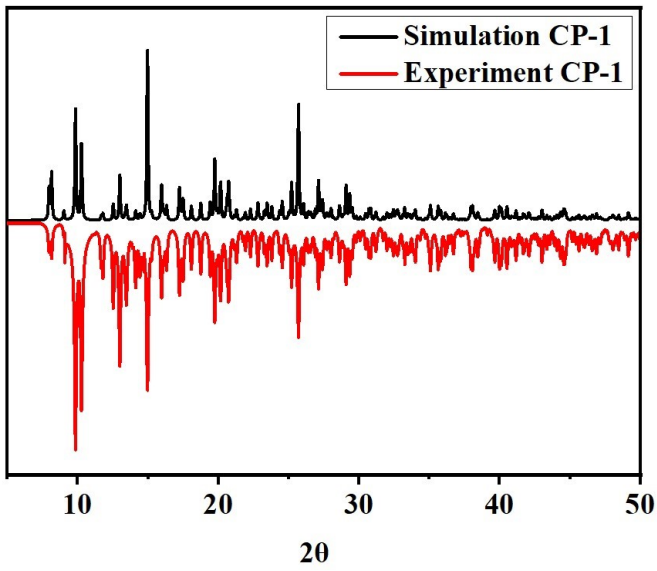

Figure S7: PXRD patterns compare the experimental and calculated values for CP-1.

8. The UV-Vis absorption spectrums of the ligand and CP-1.

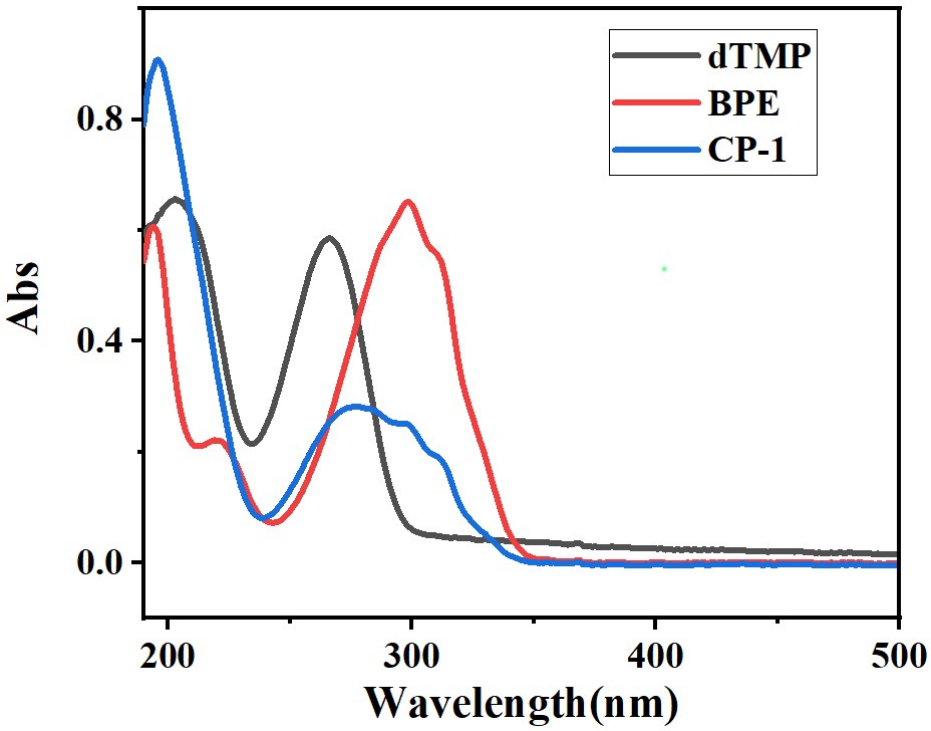

Figure S8: The solution–state UV-Vis absorption spectrum of dTMP.2Na, bpe, and CP-1 in aqueous solution at room temperature. The solution spectra were obtained by measuring 2.5×10^{-5} M solution in a 1 cm cell.

9. The CD spectra (Solid phase) of the ligand and CP-1.

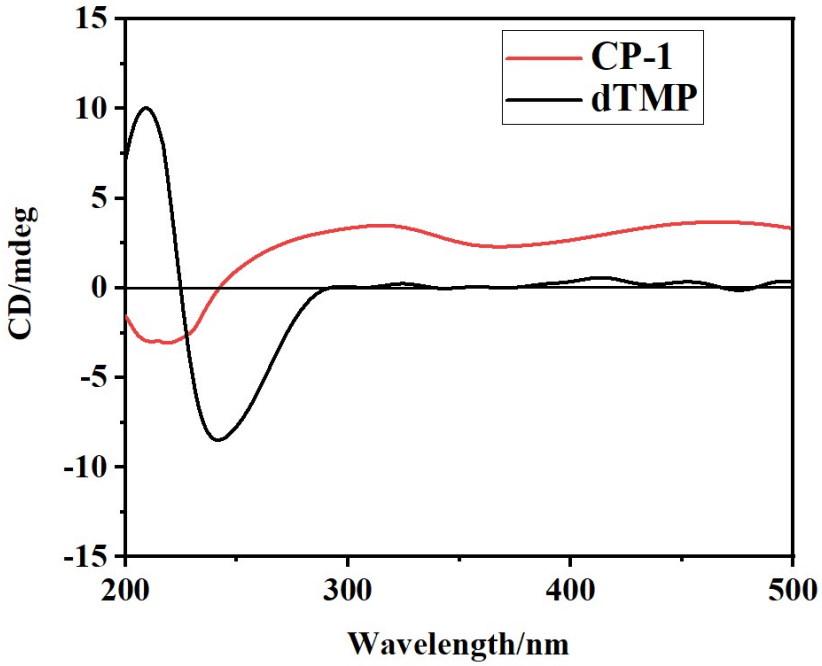

Figure S9: The solid-state CD spectrum of dTMP.2Na and its CP-1 measured in solid–state at room temperature. (KBr:[sample] = 200:1.

10. The CD spectra (Solution phase) of the ligand and CP-1.

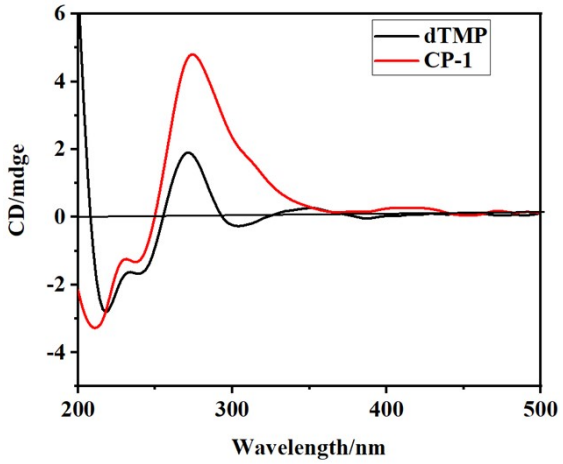

Figure S10: CD-spectra of dTMP.2Na and CP-1 in aqueous solution at room temperature; the solution spectra were obtained by measuring 2.5×10^{-5} M solution in a 1 cm cell.

11. Infrared Spectra.

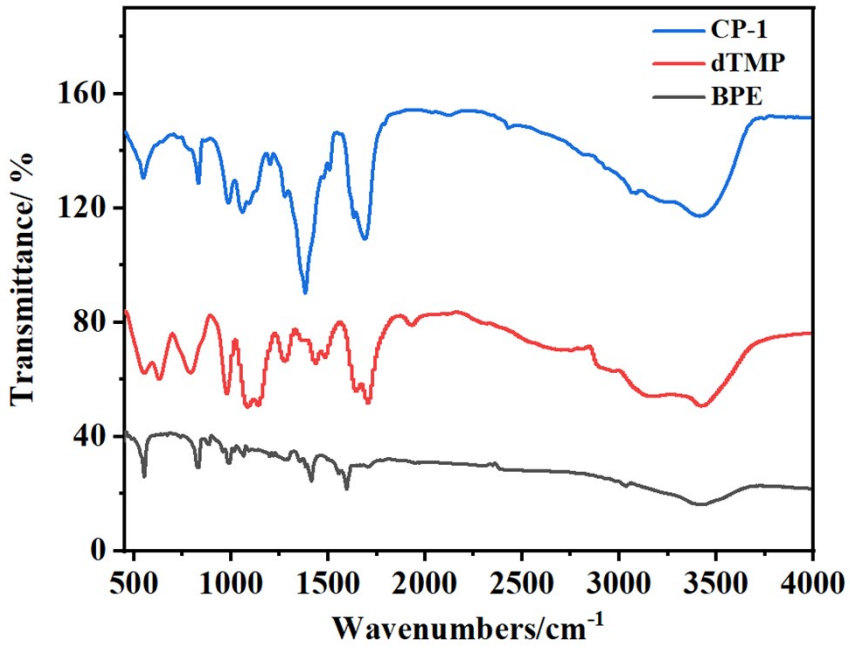

Figure S11: IR spectra of dTMP, bpe, CP-1. The infrared spectrum of the CP-1 includes not only the characteristic band of the dTMP.2Na ligand but also the characteristic band of the corresponding auxiliary ligand. Therefore, we infer that the CP-1 is a ternary complex.

12. Thermo–Gravimetric Analysis.

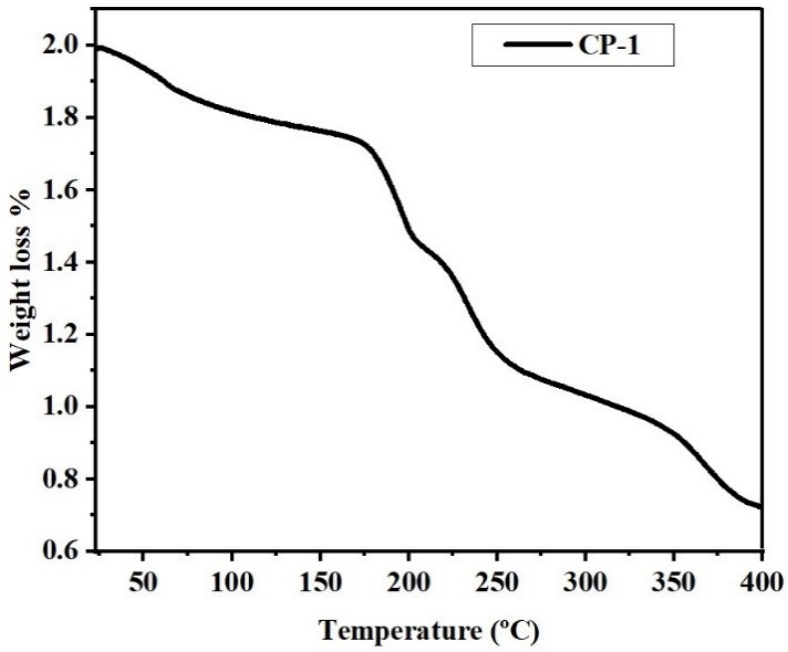

Figure S12: TG curves of CP-1.

13. The CD spectrum and UV-Vis titration of CP-1 with amino acids.

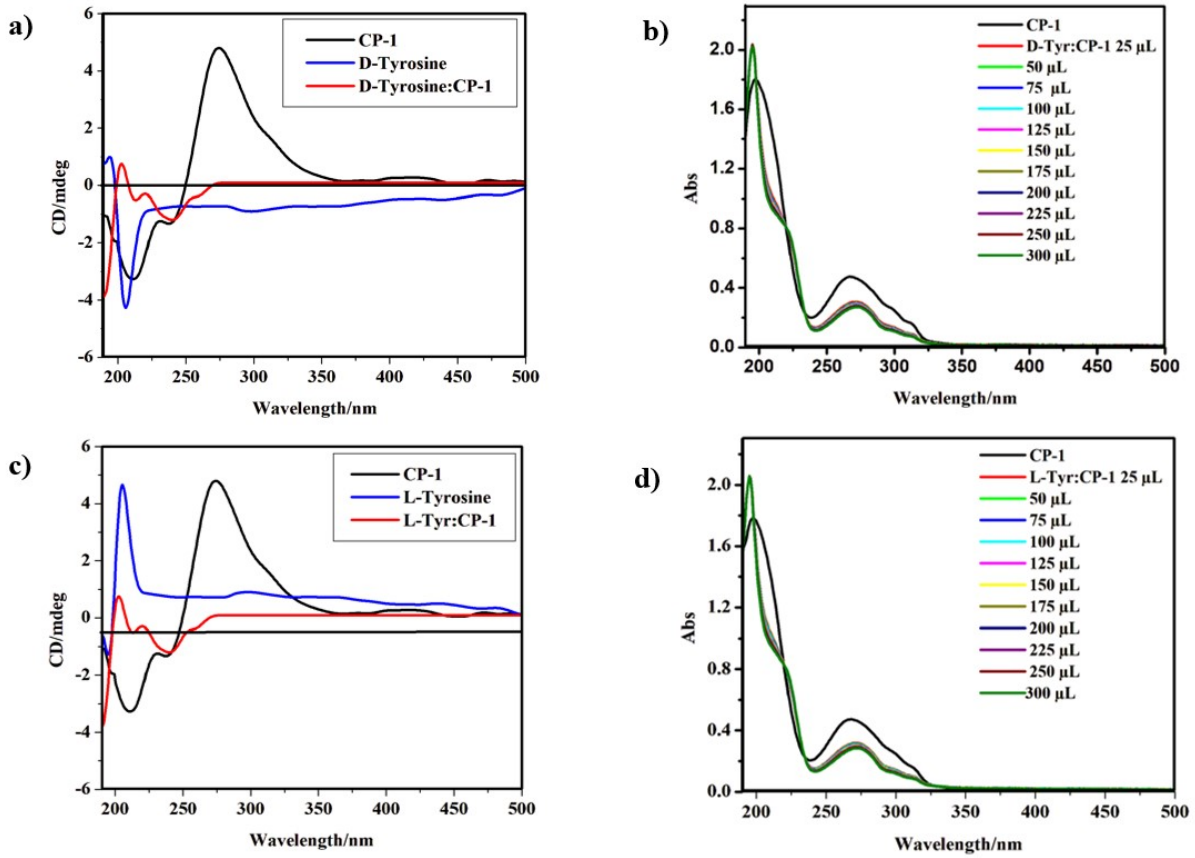

Figure S13: The solution CD spectrum and UV-visible titration of CP-1 (2.5×10^{-5} M; distilled water) with varying concentrations (25 µL-300 µL) of amino acids (2.5×10^{-5} M; distilled water). (a) CD results of *D*-Tyrosine. (b) Absorption spectra of *D*-Tyrosine. (c) CD results of *L*-Tyrosine. (d) Absorption spectra of *L*-Tyrosine.

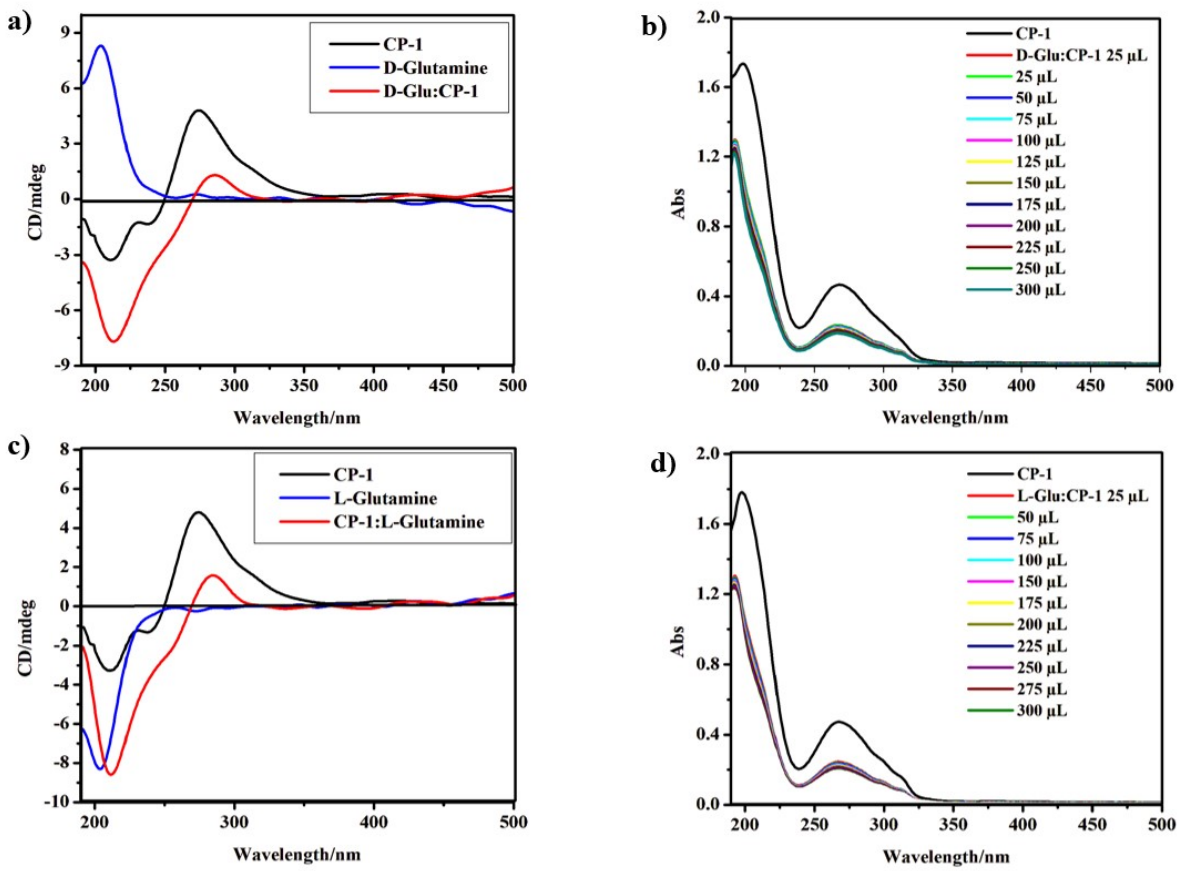

Figure S14: The solution CD spectrum and UV-visible titration of CP-1 (2.5×10^{-5} M; distilled water) with varying concentrations (25 µL-300 µL) of amino acids (2.5×10^{-5} M; distilled water). (a) CD results of *D*-Glutamine. (b) Absorption spectra of *D*-Glutamine. (c) CD results of *L*-Glutamine. (d) Absorption spectra of *L*-Glutamine.

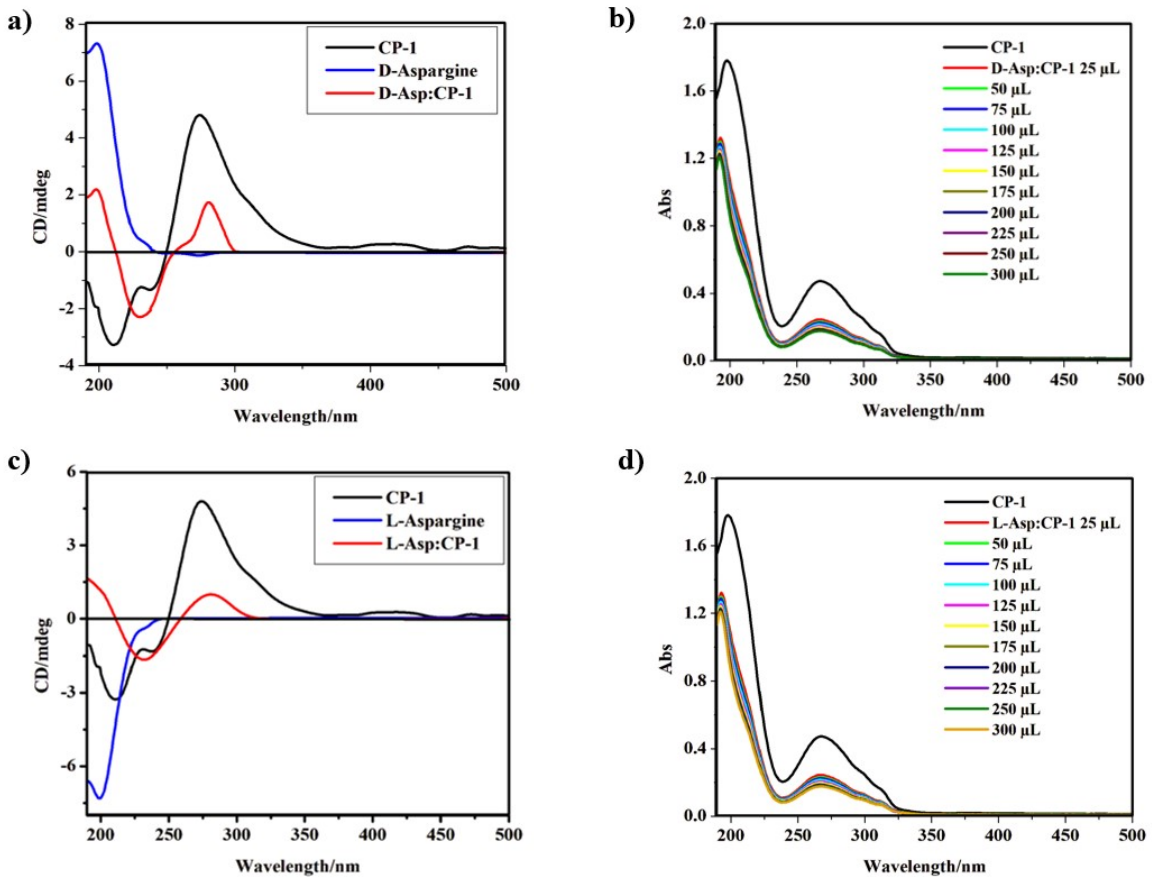

Figure S15: The solution CD spectrum and UV-visible titration of CP-1 (2.5×10^{-5} M; distilled water) with varying concentrations (25 µL-300 µL) of amino acids (2.5×10^{-5} M; distilled water). (a) CD results of *D*-Aspargine. (b) Absorption spectra of *D*-Aspargine. (c) CD results of *L*-Aspargine. (d) Absorption spectra of *L*-Aspargine.