SUPPORTING INFORMATION

Peptide Sequence Mediated Self-Assembly of Molybdenum Blue Nanowheel Superstructures

Shan She, Weimin Xuan, Nicola L. Bell, Robert Pow, Zoe Sinclair, Eduard Garrido Ribo, De-Liang Long* and Leroy Cronin*

School of Chemistry, University of Glasgow, University Avenue, Glasgow, G12 8QQ, United Kingdom

Table of Contents

1 Materials and instrumentation

Materials

The reagent-grade chemicals, including $Na_2MoO_4 \cdot 2H_2O$, $CeCl_3 \cdot 7H_2O$, $HClO_4$ and $[N_2H_4] \cdot 2HCl$, were obtained from Sigma-Aldrich. Solvents were purchased from several departmental suppliers, Honeywell, Fisher and Sigma-Aldrich. Fmoc-protected amino acids and coupling agents were purchased from Iris Biotech GmbH. The dipeptide and tripeptide were purchased from BACHEM.

Elemental Analysis

The content of carbon, nitrogen and hydrogen has been determined using EA 1110 CHNS CE-440 Elemental Analyzer, which belongs to the chemistry microanalysis services in the University of Glasgow. The contents of Mo, Ce and Na have been characterized using Leeman inductivity-coupled plasma (ICP) spectrometer.

FT-IR Spectroscopy

The FT-IR spectra were collected using a JASCO FT-IR 4100 spectrometer in the range of 400 - 4000 cm^{-1}. Wavenumbers are given in cm^{-1}. Intensities are demonstrated as s = strong, m = medium, w = weak, br = broad, sh = sharp.

Single Crystal X-ray Diffraction

The single crystals were quickly picked up from the mother liquid, wrapped with Fomblin oil and mounted onto a rubber loop. The data collection was performed on a Bruker Apex II Quasar CCD diffractometer (Mo Kα radiation, λ = 0.71073 Å) at 50 kV and 1.0 mA, using microfocus X-ray source at 150 K. Data collection, data reduction, cell refinement, and experimental absorption correction were performed with the Bruker Apex2 software package. Structures were solved by direct methods and refined against F^2 by full matrix least squares. Most non-hydrogen atoms, except disordered atoms, were refined anisotropically. Hydrogen atoms were generated geometrically. All calculations were performed using the SHELX program package with WinGX suite.[1] The X-ray crystallographic data in this manuscript have been deposited at the Crystallographic Data Centers. The data can be obtained free of charge from Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif with deposition number CCDC 2006398-2006402 and 2041759 , respectively.

Thermogravimetric Analysis (TGA)

Thermogravimetric analysis were performed on a TA Instruments Q 500 Thermogravimetric Analyzer under nitrogen flow, with heating rate 10 ℃ min^{-1}.

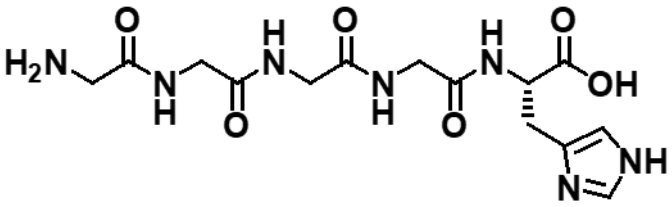
CD-Spectroscopy

CD Spectra were recorded in a JASCO J-810 spectropolarimeter in quartz cells using pathlengths 0.01 mm.

2 Peptide Synthesis

2.1 Synthesis and Characterization of H-GGGGH-OH (G_4H)

$C_{14}H_{21}N_7O_6$



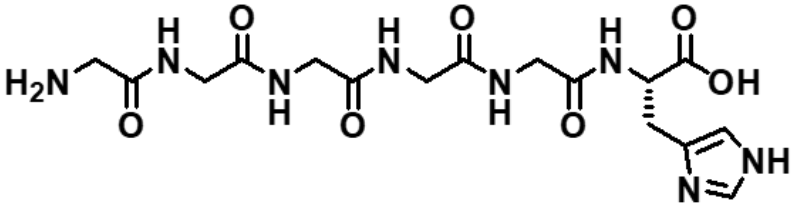
The pentapeptide was prepared via solid phase peptide synthesis (SPPS) on a Biotage Initiator + Alstra automated microwave peptide synthesizer. The synthesis was carried out on Fmoc-L-His(Trt)-Wang resin (0.70 mmol/g) on 0.5 mmol scale using a 30 mL reactor vial. Fmoc deprotections were performed at room temperature by using 20% piperidine DMF for 3 min, then repeated it for another 10 min. Peptide couplings were performed using 5 eq. of amino acid in DMF, 5.5 eq. of DIC in DMF and 5.5 eq. of HOBt in NMP. A coupling time of 10 minutes at 75 ℃ was employed. After the synthesis was completed, the resin was washed with DCM three times and thoroughly dried. Peptides were cleaved from the resin with TFA-H_2O-TES (95:3:2) cocktail for 3 hours. Then precipitated with cold diethyl ether.

Analysis of the peptide was performed by LCMS on a Bruker MaXis Impact instrument with Compass software coupled to an ESI-MS. The peptide was analyzed on an Agilent Poroshell 120 EC-C18 (4.6 x 150 mm, 2.7 µm) column.

Yield: 0.16 g, 0.42 mmol. **ESI-MS (m/z):** $[M+H]^+$ (calculated: 383.36), 384.16.

2.2 Synthesis and Characterization of H-GGGGGH-OH (G_5H)

$C_{16}H_{24}N_8O_7$



The hexapeptide was prepared via solid phase peptide synthesis (SPPS) on a Biotage Initiator + Alstra automated microwave peptide synthesizer. The synthesis was carried out on Fmoc-L-His(Trt)-Wang resin (0.70 mmol/g) on 0.5 mmol scale using a 30 mL reactor vial. Fmoc deprotections were performed at room temperature by using 20% piperidine DMF for 3 min, then repeated it for another 10 min. Peptide couplings were performed using 5 eq. of amino acid in DMF, 5.5 eq. of DIC in DMF and 5.5 eq. of HOBt in NMP. A coupling time of 10 minutes at 75 ℃ was employed. After the synthesis was completed, the resin was washed with DCM three times and thoroughly dried. Peptides were cleaved from the resin with TFA·H_2O·TES (95:3:2) cocktail for 3 hours. Then precipitated with cold diethyl ether.

Analysis of the peptide was performed by LCMS on a Bruker MaXis Impact instrument with Compass software coupled to an ESI-MS. The peptide was analyzed on an Agilent Poroshell 120 EC-C18 (4.6 x 150 mm, 2.7 µm) column.

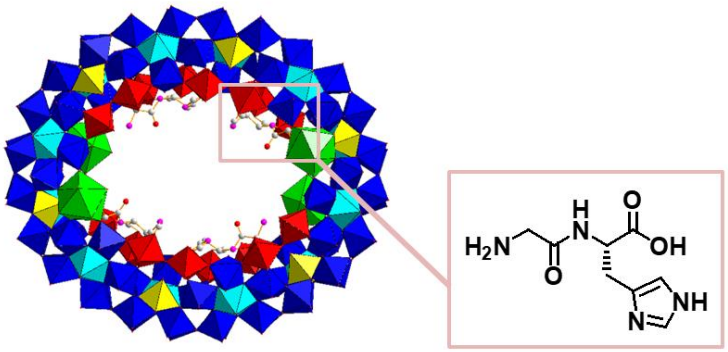
Yield: 0.17 g, 0.40 mmol. **ESI-MS (m/z):** $[M+H]^+$ (calculated: 441.41), 442.11.

3 Synthetic Procedure for bio-hybrid nanowheels

3.1 {Δ-$Mo_{124}Ce_4(GH)_4$}, $Mo_{124}Ce_4(GH)_4$

Formula: $Na_2(C_8H_{14}N_4O_3)[\Delta\text{-}Mo_{124}Ce_4O_{376}(H_2O)_{64}H_{12}(C_8H_{13}N_4O_3)_4]\cdot 155H_2O$

M.W.: 23543.72



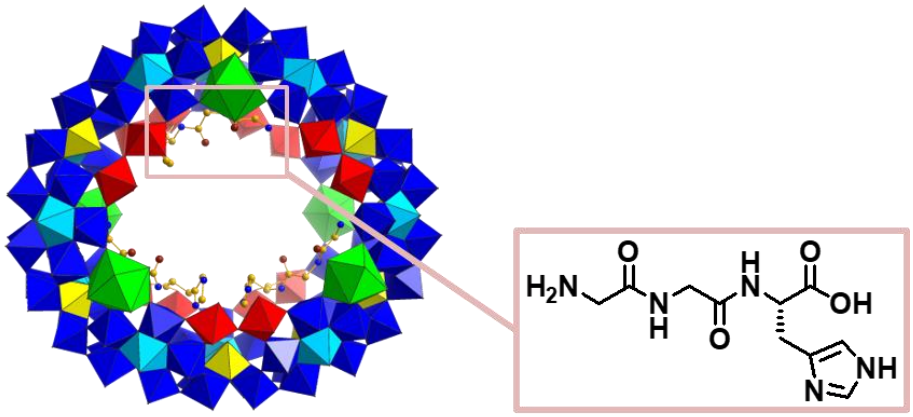
$CeCl_3$·$7H_2O$ (37.5 mg, 0.1 mmol) and H-Gly-L-His-OH (7.0 mg, 0.03 mmol) were added to a solution of Na_2MoO_4·$2H_2O$ (242.0 mg, 1.0 mmol) in water (50 mL). The solution was acidified to pH 1.1 by addition of 1 M $HClO_4$ (4.5 mL). Finally, an aqueous solution of 0.1 M $[N_2H_4]$·2HCl (0.8 mL) was added under stirring. The mixture was heated with medium stirring in a 100 mL Erlenmeyer flask (widenecked; covered with a watch glass) at 90 ℃ for 2 h. The resulting clear deep-blue solution was then cooled to room temperature and kept in an open 100 mL Erlenmeyer flask for 3 weeks. The resulting deep-blue block-like crystals were collected by filtration, washed with ice-cold H_2O, and dried under inert atmosphere over $CaCl_2$. Yield: 21 mg (11.1% based on Mo). Elemental analysis,

calc. (%): C, 2.04; H, 2.21; N, 1.19; Na, 0.19; Mo, 50.53; Ce, 2.38; found (%): C, 1.81; H, 1.70; N, 2.01; Na, 0.17; Mo, 50.25; Ce, 2.59. IR (KBr pellet, 4000-600 cm^{-1}): 3384(s, br), 3145(s, br), 2387(s), 2342(s), 2290(s), 1617(s), 1502(w), 1430(w), 973(s), 907(w), 866 (m), 803(sh), 739(s), 645(s).

3.2 {$Mo_{122}Ce_5(G_2H)_3$}, $Mo_{122}Ce_5(GGH)_3$

Formula: $Na_2(C_{10}H_{17}N_5O_4)[Mo_{122}Ce_5O_{371}(H_2O)_{69}H_{12}(C_{10}H_{16}N_5O_4)_3]\cdot 160H_2O$

M.W.: 23607.11

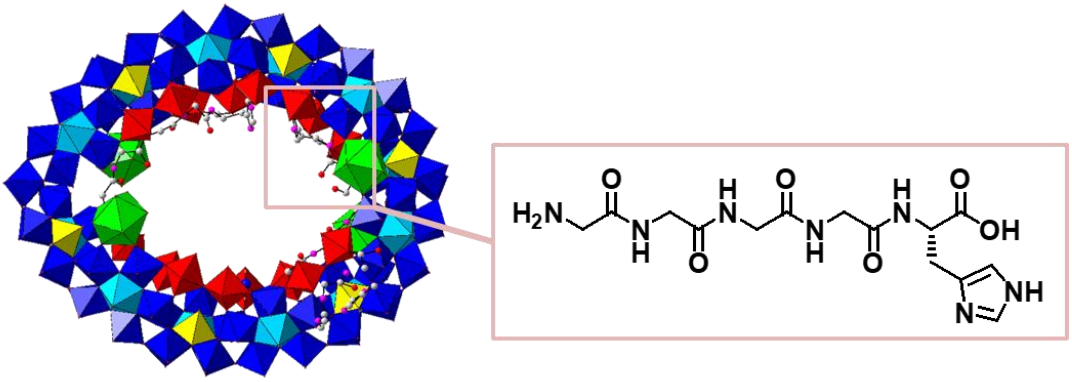


$CeCl_3$ $7H_2O$ (30.0 mg, 0.08 mmol) and H-Gly-Gly-L-His-OH (5.0 mg, 0.02 mmol) were added to a solution of Na_2MoO_4 $2H_2O$ (242.0 mg, 1.0 mmol) in water (50 mL). The solution was acidified to pH 1.1 by addition of 1 M $HClO_4$ (4.0 mL). Finally, an aqueous solution of 0.1 M $[N_2H_4]\cdot 2HCl$ (0.4 mL) was added under stirring. The mixture was heated with medium stirring in a 100 mL Erlenmeyer flask (wide necked; covered with a watch glass) at 90 ℃ for 1 h. The resulting clear deep-blue solution was then cooled to room temperature and kept in an open 100 mL Erlenmeyer flask for 2 weeks. The resulting deep-blue block-like crystals were collected by filtration, washed with ice-cold H_2O, and dried under inert atmosphere over $CaCl_2$. Yield: 40 mg (20.6% based on Mo). Elemental analysis, calc. (%): C, 2.04; H, 2.28; N, 1.18; Na, 0.20; Mo, 49.58; Ce, 2.96; found (%): C, 2.14; H, 1.82; N, 1.16; Na, 0.34; Mo, 46.69; Ce, 2.77. IR (KBr pellet, 4000-600 cm^{-1}): 3365(s, br), 3145(s, br), 2384(s), 2344(s), 2283(s), 1616(s), 1490(w), 1402(w), 1254(w), 1154(w), 1100 (w), 1079 (w), 970(s), 914(w), 870 (m), 796(s), 739(s), 634(s).

3.3 {$Mo_{126}Ce_4(G_4H)_3$}, $Mo_{126}Ce_4(GGGGH)_3$

Formula: $Na_4[Mo_{126}Ce_4O_{384}H_{17}(H_2O)_{71}(C_{14}H_{22}N_7O_6)_3]\cdot 150H_2O$

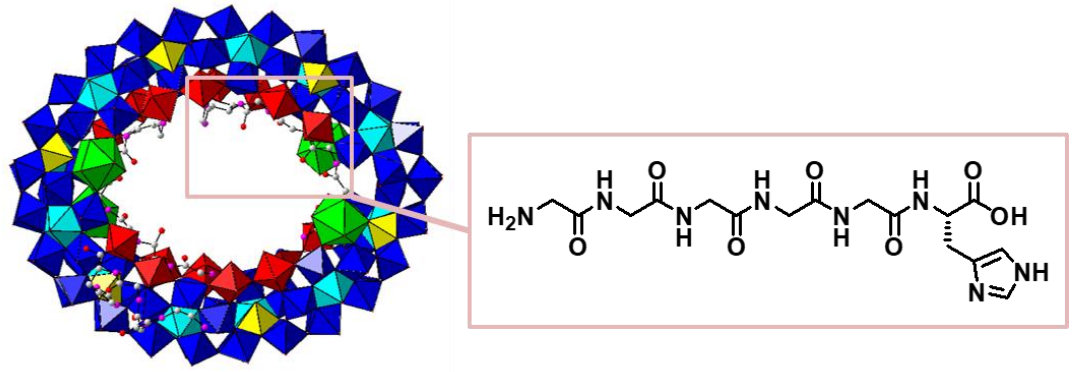
M.W.: 24036.68



$CeCl_3$ $7H_2O$ (30.0 mg, 0.08 mmol) and H-Gly-Gly-Gly-Gly-L-His-OH (7.5 mg, 0.03 mmol) were added to a solution of Na_2MoO_4 $2H_2O$ (242.0 mg, 1.0 mmol) in water (45 mL). The solution was acidified to pH 1.1 by addition of 1 M $HClO_4$ (4.5 mL). Finally, an aqueous solution of 0.1 M $[N_2H_4]\cdot 2HCl$ (0.5 mL) was added under stirring. The mixture was heated with medium stirring in a 100 mL Erlenmeyer flask (wide necked; covered with a watch glass) at 90 ℃ for 2 h. The resulting clear deep-blue solution was then cooled to room temperature and kept in an open 100 mL Erlenmeyer flask for 6 weeks. The resulting deep-blue block-like crystals were collected by filtration, washed with ice-cold H_2O, and dried under inert atmosphere over $CaCl_2$. Yield: 39 mg (20.4% based on Mo). Elemental analysis, calc. (%): C, 2.09; H, 2.20; N, 1.22; Na, 0.38; Mo, 50.29, Ce, 2.33; found (%): C, 2.05; H, 1.82; N, 2.05; Na, 0.35; Mo, 50.21; Ce, 2.50. IR (KBr pellet, 4000-600 cm^{-1}): 3374(s, br), 2384(s), 2340(s), 2283(s), 1616(s), 1397(w), 970(s), 909(w), 865 (m), 748(s), 634(s).

3.4 {$Mo_{126}Ce_4(G_5H)_3$}, $Mo_{126}Ce_4(GGGGGH)_3$

Formula: $Na_3[Mo_{126}Ce_4O_{384}H_{18}(H_2O)_{71}(C_{16}H_{25}N_8O_7)_3]\cdot 150H_2O$
M.W.: 24186.50

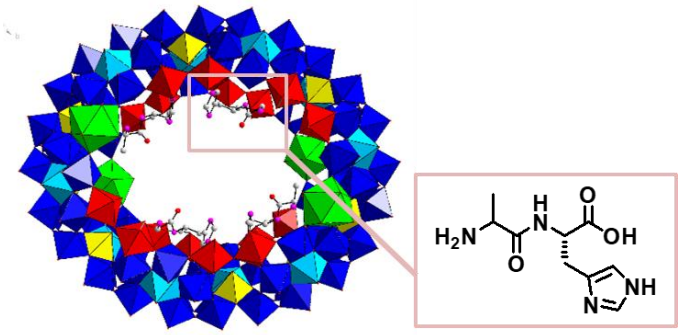


$CeCl_3 \cdot 7H_2O$ (30.0 mg, 0.08 mmol), H-Gly-Gly-Gly-Gly-Gly-L-His-OH (7.0 mg, 0.02 mmol) were added to a solution of $Na_2MoO_4 \cdot 2H_2O$ (242.0 mg, 1.0 mmol) in water (45 mL). The solution was acidified to pH 1.1 by addition of 1 M $HClO_4$ (4.5 mL). Finally, an aqueous solution of 0.1 M $[N_2H_4]\cdot 2HCl$ (0.5 mL) was added under stirring. The mixture was heated with medium stirring in a 100 mL Erlenmeyer flask (wide necked; covered with a watch glass) at 90 ℃ for 2 h. The resulting clear deep-blue solution was then cooled to room temperature and kept in an open 100-mL Erlenmeyer flask for 8 weeks. The deep-blue block-like crystals were collected by filtration, washed with ice-cold H_2O, and dried under inert atmosphere over $CaCl_2$, yield: 36 mg (18.7 % based on Mo). Elemental analysis, calc. (%): C, 2.38; H, 2.23; N, 1.40; Na, 0.28; Mo, 50.00; Ce, 2.32; found (%): C, 2.48; H, 1.85; N, 1.47; Na, 0.27; Mo, 54.72; Ce, 2.40. IR (KBr pellet, 4000-600 cm^{-1}): 3374(s, br), 2384(s), 2340(s), 2283(s), 1616(s), 1397(w), 970(s), 909(w), 865 (m), 748(s), 634(s).

3.5 {Λ-$Mo_{124}Ce_4(AH)_4$}, $Mo_{124}Ce_4(AH)_4$

Formula: $Na_3(C_9H_{16}N_4O_3)[\Lambda\text{-}Mo_{124}Ce_4O_{376}(H_2O)_{64}H_{12}(C_9H_{15}N_4O_3)_4]\cdot 165H_2O$

M.W.: 23589.75



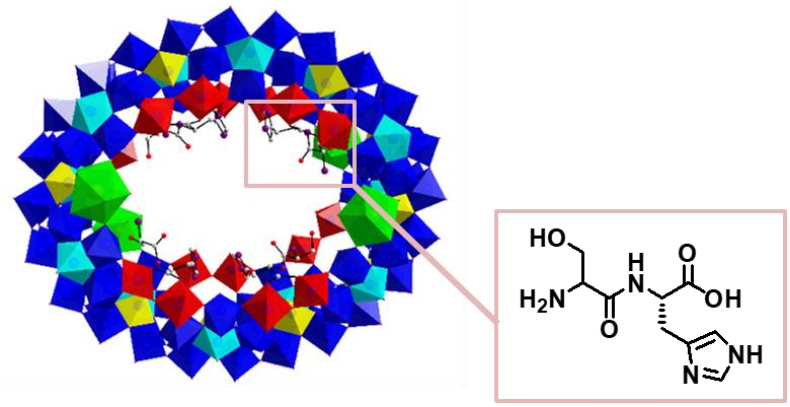
$CeCl_3 \cdot 7H_2O$ (30.0 mg, 0.08 mmol) and H-L-Ala-L-His-OH (5.5 mg, 0.02 mmol) were added to a solution of $Na_2MoO_4 \cdot 2H_2O$ (242.0 mg, 1.0 mmol) in water (40 mL). The solution was acidified to pH 1.1 by addition of 1 M $HClO_4$ (4.5 mL). Finally, an aqueous solution of 0.1 M $[N_2H_4]\cdot 2HCl$ (0.5 mL) was added under stirring. The mixture was heated with medium stirring in a 100 mL Erlenmeyer flask (wide necked; covered with a watch glass) at 90 ℃ for 1 h. The resulting clear deep-blue solution was then cooled to room temperature and kept in an open 100 mL Erlenmeyer flask for 8 weeks. The resulting deep-blue block-like crystals were collected by filtration, washed with ice-cold H_2O, and dried under inert atmosphere over $CaCl_2$. Yield: 18 mg (9.5% based on Mo). Elemental analysis, calc. (%): C, 1.83; H, 2.26; N, 0.95; Na, 0.29; Mo, 50.43; Ce, 2.38; found (%): C, 1.74; H, 1.65; N, 0.80; Na, 0.27; Mo, 46.73; Ce, 2.67. IR (KBr

pellet, 4000-600 cm^{-1}): 3356(s, br), 3145(s, br), 2387(s), 2340(s), 2290(s), 1611(s), 973(s), 907(w), 866 (m), 803(sh), 739(s), 645(s).

3.6 {Λ-$Mo_{124}Ce_4(SH)_4$}, $Mo_{124}Ce_4(SH)_4$

Formula: $Na_3(C_9H_{16}N_4O_4)[Λ\text{-}Mo_{124}Ce_4O_{376}(H_2O)_{64}H_{12}(C_9H_{15}N_4O_4)_4]\cdot 160H_2O$

M.W.: 23563.67



$CeCl_3 \cdot 7H_2O$ (30.0 mg, 0.08 mmol) and H-L-Ser-L-His-OH (5.0 mg, 0.02 mmol) were added to a solution of $Na_2MoO_4 \cdot 2H_2O$ (242.0 mg, 1.0 mmol) in water (40 mL). The solution was acidified to pH 1.1 by addition of 1 M $HClO_4$ (4.5 mL). Finally, an aqueous solution of 0.1 M $[N_2H_4]\cdot 2HCl$ (0.4 mL) was added under stirring. The mixture was heated with medium stirring in a 100 mL Erlenmeyer flask (wide necked; covered with a watch glass) at 90 ℃ for 2 h. The resulting clear deep-blue solution was then cooled to room temperature and kept in an open 100 mL Erlenmeyer flask for 2 weeks. The resulting deep-blue block-like crystals were collected by filtration, washed with ice-cold H_2O, and dried under inert atmosphere over $CaCl_2$. Yield: 51 mg (26.8% based on Mo). Elemental analysis, calc. (%): C, 1.83; H, 2.22; N, 0.95; Na, 0.29; Mo, 50.49; Ce, 2.38; found (%): C, 1.45; H, 1.65; N, 2.17; Na, 0.27; Mo, 50.03; Ce, 2.56. IR (KBr pellet, 4000-600 cm^{-1}): 3356(s, br), 3145(s, br), 2379(s), 2340(s), 2290(s), 1611(s), 970(s), 9011(w), 866 (m), 803(sh), 744(s), 630(s).

4 Structural Analysis for bio-hybrid nanowheels

Although the wheel-type molybdenum blue architectures are very complex, the general approach to the structural analysis and formula determination is well documented. The structural analysis requires the following lines of evidence/information to allow the assignment of formula and the structural details coupled with single crystal x-ray diffraction:

i. Redox titration to help determine the number of reduced Mo^{V} centres (UV-Vis spectroscopy also can help corroborate this data via the analysis of the extinction coefficient for the LMCT associated with the reduced Mo^{V} centres. Each centre should contribute ca. 5 - 6 x 10^3 L mol^{-1} cm^{-1} to ε).
ii. Elemental analysis of sodium, molybdenum, cerium and C, H, N analysis. (see Section 3 for details)
iii. Bond valence sum analysis to confirm the terminal oxo positions, reduced Mo^{V} centres and the positions of the hydroxide ligands.[2]
iv. TGA to estimate the number of ligand and solvent water molecules as well as coordinated amino acids.

Therefore, the analysis below both presents this data and demonstrates how the structural assignment is consistent with this data.

4.1 Redox Titrations and UV-Vis spectra

Because of the rather poor solubility of $\{Mo_{124}Ce_4(GH)_4\}$, $\{Mo_{124}Ce_4(AH)_4\}$, $\{Mo_{124}Ce_4(SH)_4\}$, $\{Mo_{122}Ce_5(G_2H)_3\}$, $\{Mo_{126}Ce_4(G_4H)_3\}$ and $\{Mo_{126}Ce_4(G_5H)_3\}$, it is impossible to perform redox titration to determine the number of reduced electrons within them.

Due to the rather poor solubility of $\{Mo_{124}Ce_4(GH)_4\}$, $\{Mo_{124}Ce_4(AH)_4\}$, $\{Mo_{124}Ce_4(SH)_4\}$, $\{Mo_{122}Ce_5(G_2H)_3\}$, $\{Mo_{126}Ce_4(G_4H)_3\}$ and $\{Mo_{126}Ce_4(G_5H)_3\}$, the UV-Vis spectra of them were recorded

in saturated aqueous solution and ε were not calculated. According to Figure S1, the above 6 compounds share the same characteristic peak of Mo Blue which is around 755 nm.

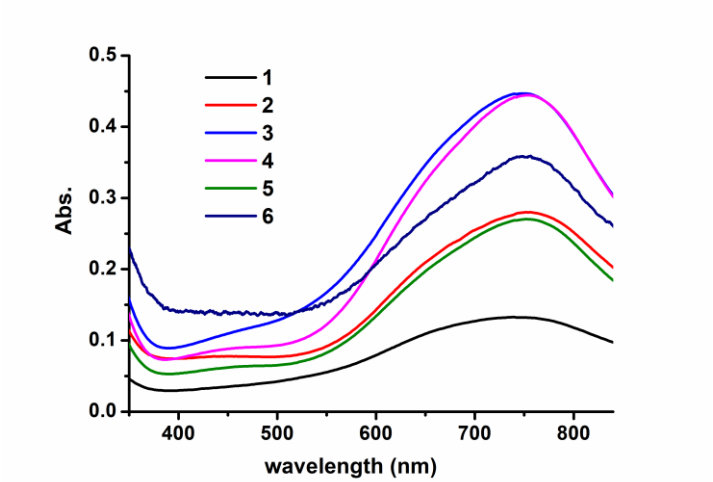


Figure S1. UV-Vis spectra: **1**, $\{Mo_{124}Ce_4(GH)_4\}$; **2**, $\{Mo_{122}Ce_5(G_2H)_3\}$; **3**, $\{Mo_{126}Ce_4(G_4H)_3\}$; **4**, $\{Mo_{124}Ce_4(AH)_4\}$; **5**, $\{Mo_{124}Ce_4(SH)_4\}$; **6**, $\{Mo_{126}Ce_4(G_5H)_3\}$.

4.2 Circular Dichroism

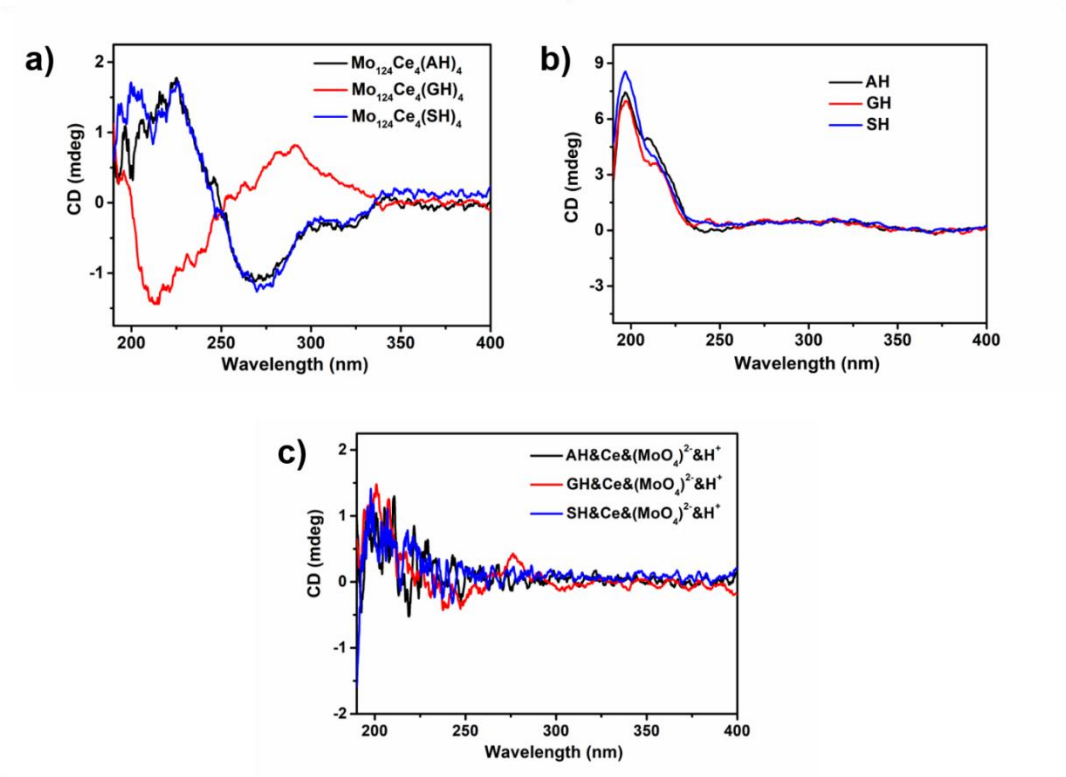


Figure S2. CD spectra of a) {Λ-$Mo_{124}Ce_4(AH)_4$}, {Δ-$Mo_{124}Ce_4(GH)_4$} and {Λ-$Mo_{124}Ce_4(SH)_4$} at 2 $mgmL^{-1}$ in water; b) L-Ala-L-His, Gly-L-His, and L-Ser-L-His at 2 $mgmL^{-1}$ in water; c) reaction mixture prepared in the same way as in Section 3 but without adding reductant hydrazine dihydrochloride. This is not expected to form the MB wheel but controls for any effect the metal ions may have on the dipeptides.

For { Λ -$Mo_{124}Ce_4(AH)_4$} system, the mass concentration:

$$\mathrm{c}(Mo_{124}Ce_4(AH)_4) = 2\ \mathrm{mg}\, mL^{-1} = 2\ \mathrm{g}L^{-1}$$

There are 4 AH per {$Mo_{124}Ce_4(AH)_4$} molecule, and the MW for {$Mo_{124}Ce_4(AH)_4$} is 23,543 g/mol.

So the molar concentration of peptide AH in this system is:

$$\mathrm{c}(AH\ in\ \{Mo_{124}Ce_4(AH)_4\}) = 85\ \mu\mathrm{M}\ \times 4 = 0.34\ \mathrm{mM}$$

And the concentration of the pure peptide is:

$$c(AH) = 2\ \mathrm{mg}\, mL^{-1} =\ 8.85\ \mathrm{mM}$$

According to Beer's law absorbance is proportional to concentration,

$$\Delta\mathrm{A} = (\varepsilon_L - \varepsilon_R)cl$$

Therefore, one may expect a very low signal for the peptide in the MS Framework. Thus the fact that we see strong signal in the region 190-350 nm demonstrates that the MB framework significantly enhances the CD signal of the peptide.

Moreover, we also tried tetrapeptide (G_3H), but unfortunately, the crystals were tiny and thin, and not suitable for single crystal X-ray diffraction. Luckily, we were able to use them to test CD.

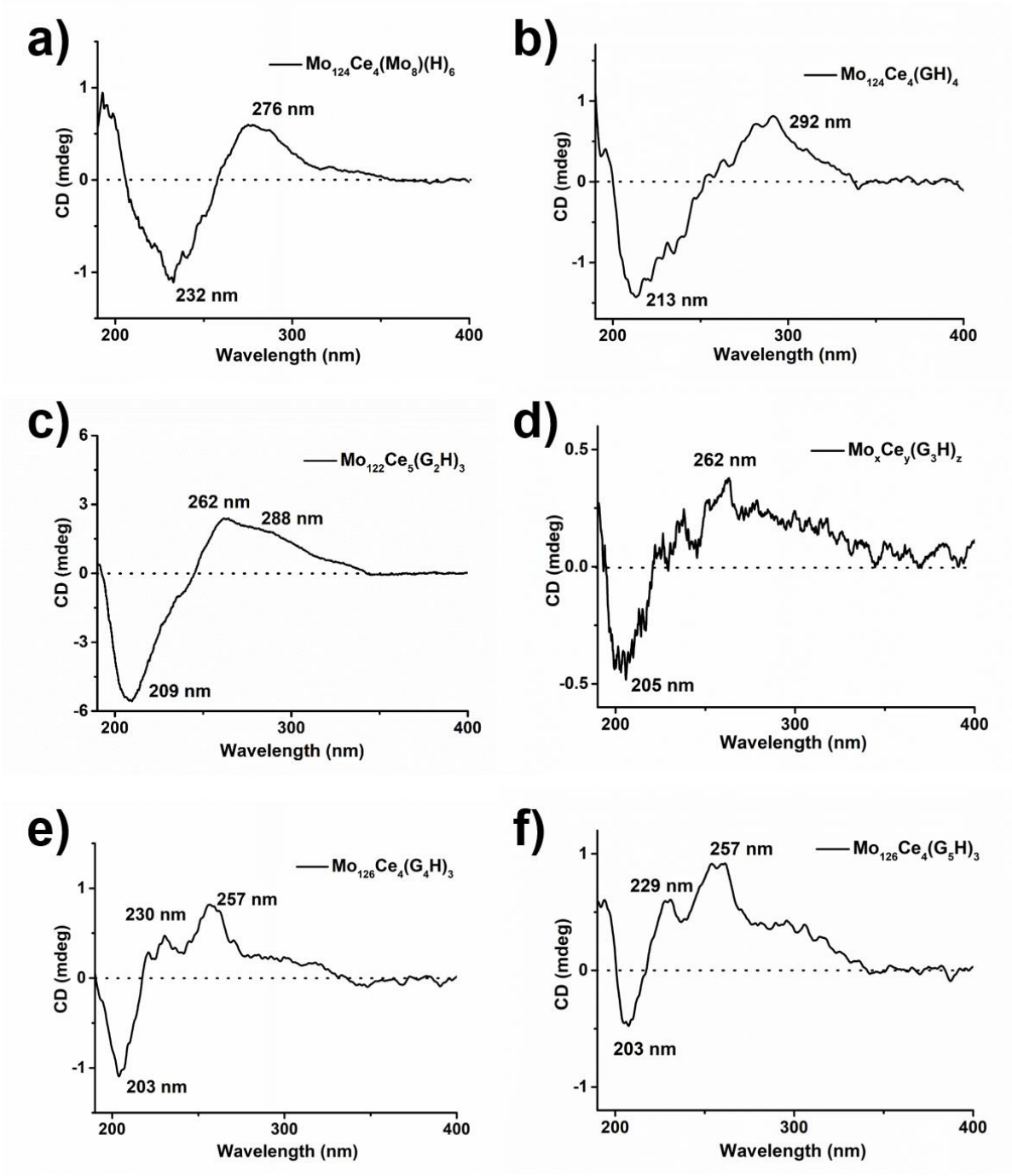


Figure S3. CD spectra of a) $\{Mo_{124}Ce_4(Mo_8)(H)_6\}$, b) $\{Mo_{124}Ce_4(GH)_4\}$, c) $\{Mo_{122}Ce_5(G_2H)_3\}$, d) $\{Mo_xCe_y(G_3H)_z\}$, e) $\{Mo_{126}Ce_4(G_4H)_3\}$, f) $\{Mo_{126}Ce_4(G_5H)_3\}$ at 2 $mgmL^{-1}$ in water.

Discussion: As shown in Figure S3, the CD signal tendency for $\{Mo_{124}Ce_4(Mo_8)(H)_6\}$, $\{Mo_{122}Ce_5(G_2H)_3\}$ and $\{Mo_{126}Ce_4(G_4H)_3\}$ are different towards each other, which is in consistant with they have different MB framework. However, the signal tendency for $\{Mo_{124}Ce_4(Mo_8)(H)_6\}$ and $\{Mo_{124}Ce_4(GH)_4\}$ are very similar to each other, which is in consistant that they share the same framework $\{Mo_{124}Ce_4\}$. The same situtation also happens on $\{Mo_{126}Ce_4(G_4H)_3\}$ and $\{Mo_{126}Ce_4(G_5H)_3\}$. It indicates that the MB framework may influence the peptide CD, and if two compounds share same framework, they may have similar CD signal.

4.3 Bond Valence Sum Analysis

Table S1. Average bond valence sum values for the Mo centres which span the incomplete $\{Mo_5O_6\}$-type double cubanes and the μ_3-O atoms of the $\{(\mu_3\text{-}O)_2O_2\}$-type compartments in compounds.

Compounds	BVS(Mo)	BVS (μ_3-O)
$\{Mo_{124}Ce_4(GH)_4\}$	5.77	1.26
$\{Mo_{122}Ce_5(G_2H)_3\}$	5.79	1.24
$\{Mo_{126}Ce_4(G_4H)_3\}$	5.79	1.27
$\{Mo_{126}Ce_4(G_5H)_3\}$	5.79	1.27
$\{Mo_{124}Ce_4(AH)_4\}$	5.74	1.25
$\{Mo_{124}Ce_4(SH)_4\}$	5.78	1.25

4.4 TGA Curves

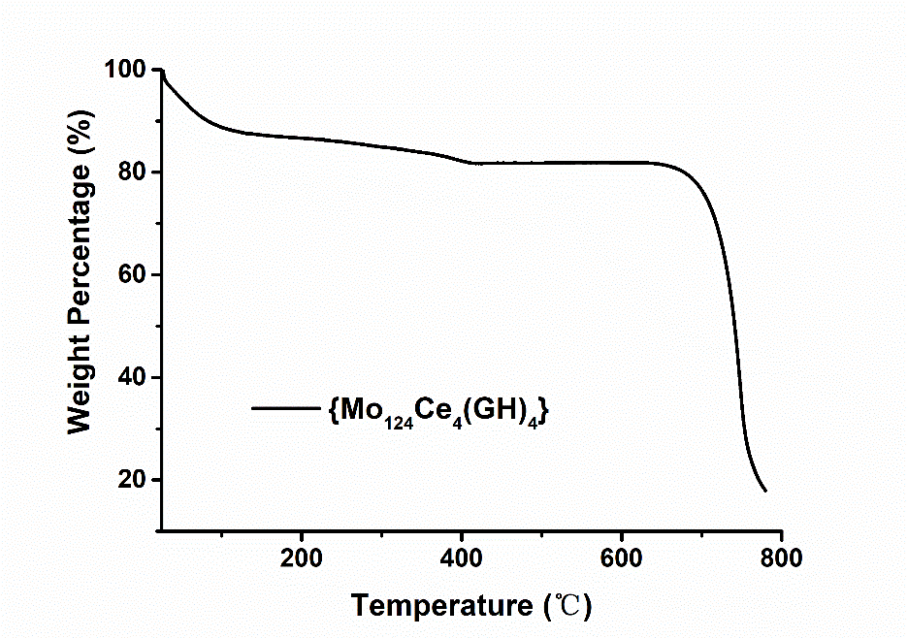


Figure S4. TGA curve of $\{Mo_{124}Ce_4(GH)_4\}$. 12.7% weight loss between r.t. to 150 ℃ corresponds to ~155 crystalline H_2O, further 5.4% weight loss between 200 to 450 ℃ corresponds to 5 H-Gly- L-His-OH ligands.

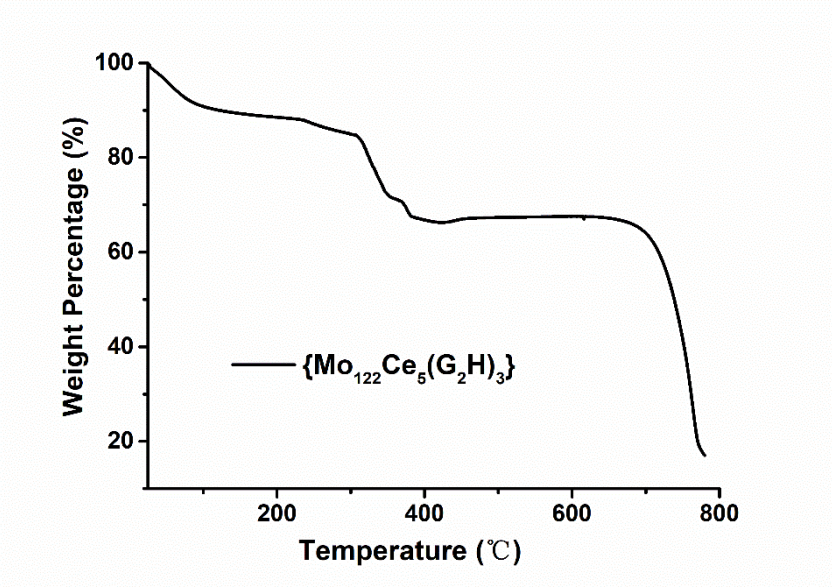


Figure S5. TGA curve of $\{Mo_{122}Ce_5(G_2H)_3\}$. 11.3% weight loss between r.t. to 150 ℃ corresponds to ~160 crystalline H_2O, further 5.4% weight loss between 350 to 450 ℃ corresponds to 4 H-Gly-Gly- L-His-OH ligands.

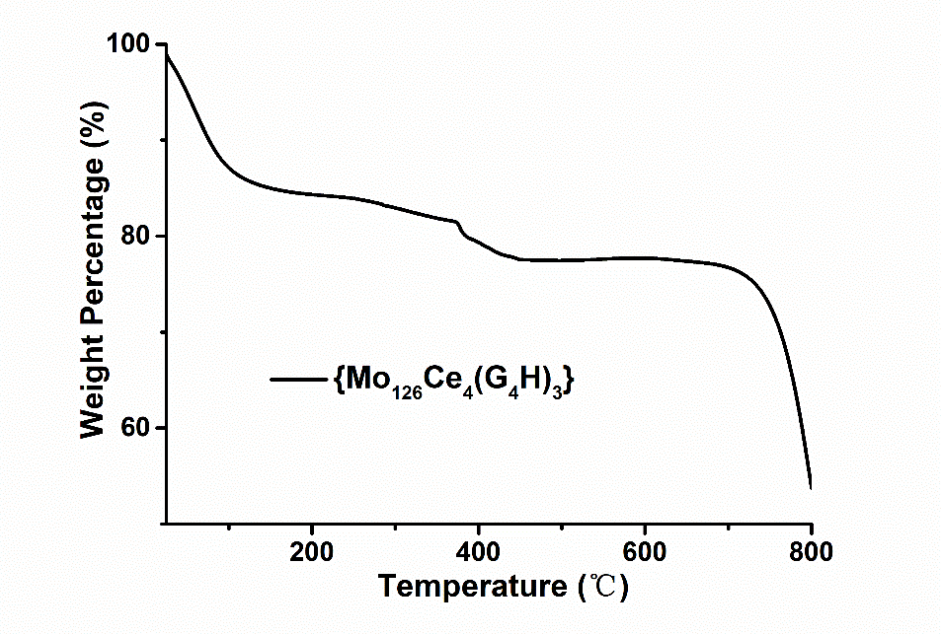


Figure S6. TGA curve of {$Mo_{126}Ce_4(G_4H)_3$}. 15% weight loss between r.t. to 150 ℃ corresponds to ~150 crystalline H_2O, further 8% weight loss between 200 to 450 ℃ corresponds to 3 H-Gly-Gly-Gly-Gly- L-His-OH ligands.

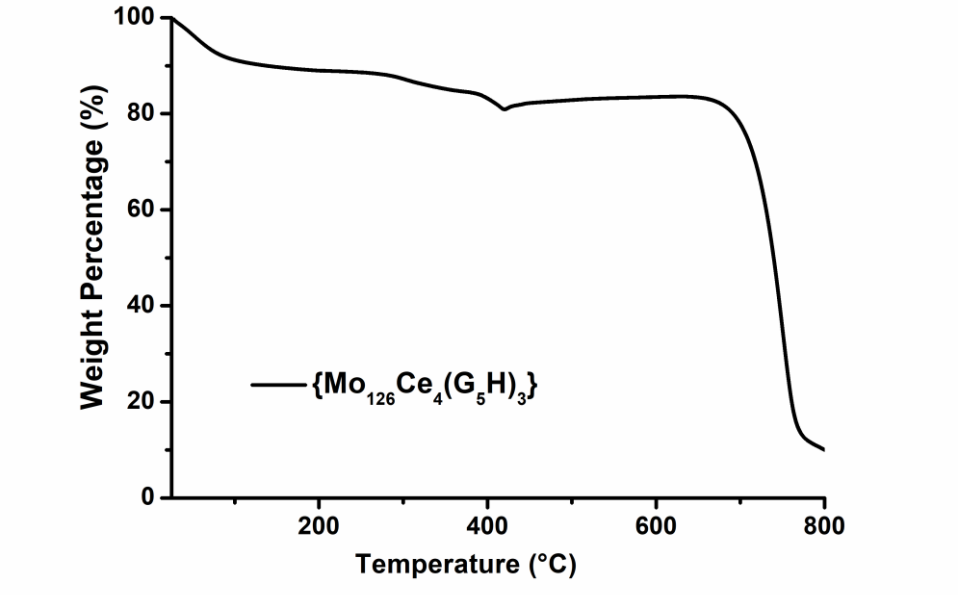


Figure S7. TGA curve of {$Mo_{126}Ce_4(G_5H)_3$}. 12% weight loss between r.t. to 150 ℃ corresponds to ~150 crystalline H_2O, further 9% weight loss between 200 to 450 ℃ corresponds to 3 H-Gly-Gly-Gly-Gly-Gly- L-His-OH ligands.

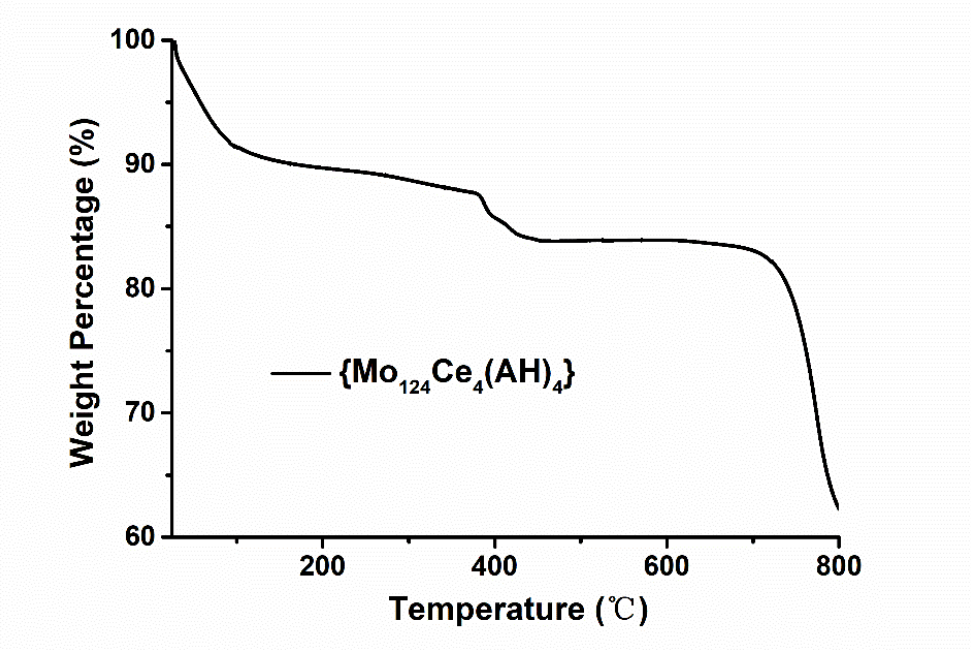


Figure S8. TGA curve of $\{Mo_{124}Ce_4(AH)_4\}$. 9.8% weight loss between r.t. to 150 ℃ corresponds to ~160 crystalline H_2O, further 6.0% weight loss between 200 to 450 ℃ corresponds to 5 H- L-Ala- L-His-OH ligands.

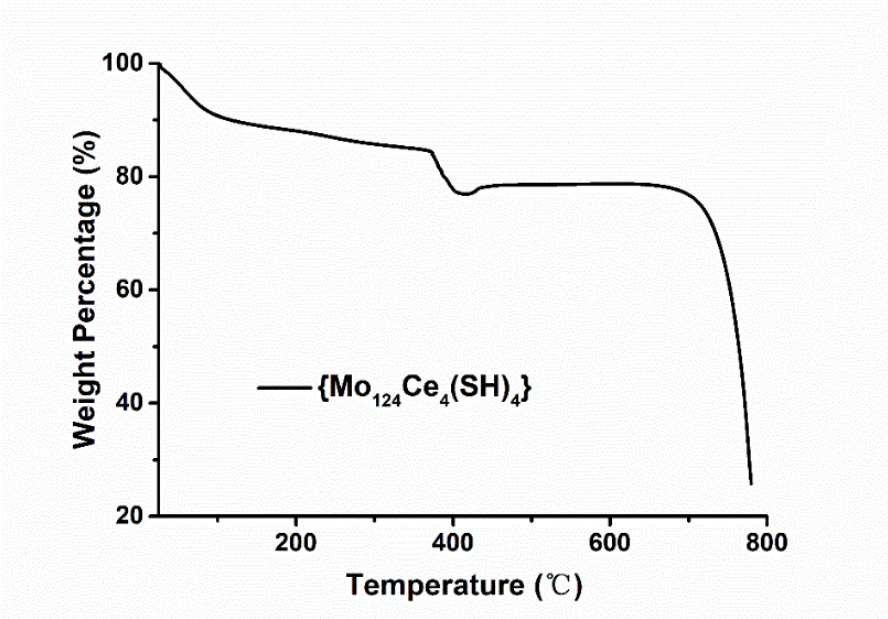


Figure S9. TGA curve of $\{Mo_{124}Ce_4(SH)_4\}$. 11.9 % weight loss between r.t. to 150 ℃ corresponds to ~160 crystalline H_2O, further 6.0 % weight loss between 200 to 450 ℃ corresponds to 5 H- L-Ser- L-His-OH ligands.

5 Crystallographic data for bio-hybrid nanowheels

Table S2. Crystallographic Details for $\{Mo_{124}Ce_4(GH)_4\}$, $\{Mo_{122}Ce_5(G_2H)_3\}$, $\{Mo_{126}Ce_4(G_4H)_3\}$

Compound	**$\{Mo_{124}Ce_4(GH)_4\}$**	**$\{Mo_{122}Ce_5(G_2H)_3\}$**	**$\{Mo_{126}Ce_4(G_4H)_3\}$**
Empirical formula	$Mo_{124}Ce_4O_{610}N_{20}C_{40}H_{516}Na_2$	$Mo_{122}Ce_5O_{616}N_{20}C_{40}H_{535}Na_2$	$Mo_{126}Ce_4O_{623}N_{21}C_{42}H_{525}Na_4$
Formula weight	23543.72	23607.11	24036.68
Temperature (K)	150(2)	150(2)	150(2)
Crystal system	Orthorhombic	Orthorhombic	Triclinic
Space group	*P2₁2₁2*	*P2₁2₁2*	*P*-1
Unit Cell dimensions	a = 34.657(2) Å, α = 90 º	a = 38.106(2) Å, α = 90 º	a = 32.599(4) Å, α = 104.7(5) º
	b = 45.430(0) Å, β = 90 º	b = 38.268(5) Å, β = 90 º	b = 32.769(4) Å, β = 98.8(7) º
	c = 20.974(1) Å, γ = 90 º	c = 46.913(6) Å, γ = 90 º	c = 35.206(2) Å, γ = 104.9(3) º
Volume ($Å^3$)	33023(2)	68413(5)	34154 (3)
Z	2	4	2
Density (calculated) (Mg/m^3)	2.368	2.292	2.337
Absorption coefficient (mm^{-1})	2.650	2.590	2.602
F (000)	22476	45116	22952
Reflections collected / unique	365651 / 64861 [$R_{(int)}$ = 0.0591]	435271 / 108095 [$R_{(int)}$ = 0.0612]	74448 / 135327 [$R_{(int)}$ = 0.0632]
Data / restraints / parameters	64861 / 25 / 2849	108095 / 2886 / 5740	135327 / 3107 / 6262
Goodness-of-fit on F^2	1.022	1.086	1.014
Final R indices [I>2δ (I)]	R_1 = 0.0285, wR_2 = 0.0678	R_1 = 0.0766, wR_2 = 0.1927	R_1 = 0.1054, wR_2 = 0.2572
R indices (all data)	R_1 = 0.0336, wR_2 = 0.0715	R_1 = 0.1091, wR_2 = 0.2314	R_1 = 0.1896, wR_2 = 0.3389
Largest diff. peak and hole (e. $Å^{-3}$)	1.55 and -0.82	2.97 and -1.60	2.80 and -2.28

Table S3. Crystallographic Details for $\{Mo_{126}Ce_4(G_5H)_3\}$, $\{Mo_{124}Ce_4(AH)_4\}$ and $\{Mo_{124}Ce_4(SH)_4\}$

Compounds	**$\{Mo_{126}Ce_4(G_5H)_3\}$**	**$\{Mo_{124}Ce_4(AH)_4\}$**	**$\{Mo_{124}Ce_4(SH)_4\}$**
Empirical formula	$Mo_{126}Ce_4O_{626}N_{24}C_{48}H_{535}Na_3$	$Mo_{124}Ce_4O_{617}N_{16}C_{36}H_{531}Na_3$	$Mo_{124}Ce_4O_{616}N_{16}C_{36}H_{521}Na_3$
Formula weight	24185.86	23543.72	23563.67
Temperature (K)	150(2)	150(2)	150(2)
Crystal system	Triclinic	Orthorhombic	Orthorhombic
Space group	*P*-1	$P2_12_12$	$P2_12_12$
Unit Cell dimention	a = 32.444(3) Å, α = 104.7(6) º	a = 34.884(5) Å, α = 90 º	a = 34.853(1) Å, α = 90 º
	b = 32.749(4) Å, β = 98.8(6) º	b = 45.668(6) Å, β = 90 º	b = 45.172(2) Å, β = 90 º
	c = 35.233(4) Å, γ = 104.7(6) º	c = 20.929(3) Å, γ = 90 º	c = 20.924(3) Å, γ = 90 º
Volume ($Å^3$)	34063 (6)	33341(7)	32943(3)
Z	2	2	2
Density (calculated) (Mg/m^3)	2.358	2.350	2.376
Absorption coefficient (mm^{-1})	2.610	2.627	2.658
F (000)	23112	22536	22500
Reflections collected / unique	370145 / 99546 [$R_{(int)}$ = 0.0995]	230445 / 60898 [$R_{(int)}$ = 0.0650]	238145 / 62762 [$R_{(int)}$ = 0.0871]
Data / restraints / parameters	99546 / 261 / 6216	60898 / 1447 / 2916	62762 / 1532 / 3024
Goodness-of-fit on F^2	1.106	1.093	1.028
Final R indices [I>2δ (I)]	R_1 = 0.0887, wR_2 = 0.2247	R_1 = 0.0686, wR_2 = 0.1726	R_1 = 0.0593, wR_2 = 0.1424
R indices (all data)	R_1 = 0.1479, wR_2 = 0.2931	R_1 = 0.0959, wR_2 = 0.2051	R_1 = 0.0891, wR_2 = 0.1622
Largest diff. peak and hole (e. $Å^{-3}$)	3.29 and -2.61	3.13 and -1.52	2.36 and -1.44

6 X-ray Crystal Structures for bio-hybrid nanowheels

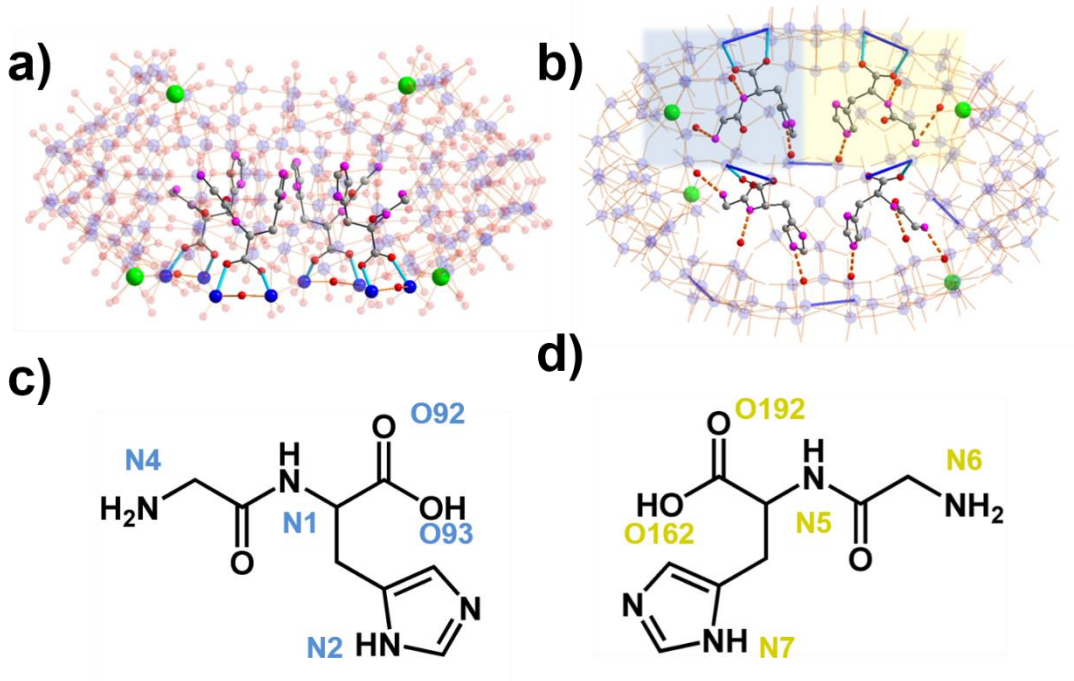


Figure S10. Molecular structure of $\{Mo_{124}Ce_4(GH)_4\}$. Color code: green, Ce; blue, Mo; red, O; pink, N; grey, C; navy line, $\{Mo_2\}$ units. a) side view, b) top view, coordination bonds (sky blue line) and hydrogen bond networks (orange dash) between four GH and MB framework are highlighted in the cavity, while the oxygen atoms on MB are omitted for clarity., c) the atom labels for the blue part GH peptide in Fig. S10b, d) the atom labels for the yellow part GH peptide in Fig. S10b.

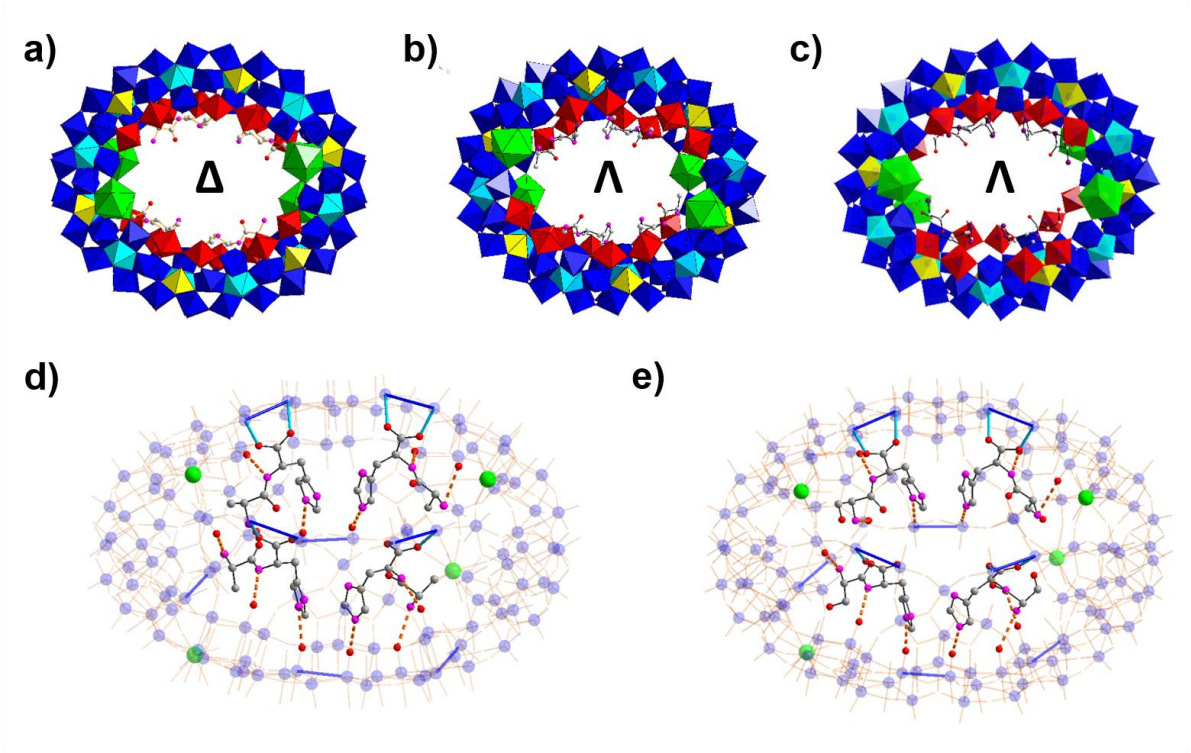


Figure S11. Polyhedron structure of a) {Δ-$Mo_{124}Ce_4(GH)_4$}, b) {Λ-$Mo_{124}Ce_4(AH)_4$} and c) {Λ-$Mo_{124}Ce_4(SH)_4$}. {Mo_1}, yellow polyhedron; {Mo_2}, red polyhedron; {Mo_8}, blue polyhedron with central pentagonal units in cyan polyhedron; {Ce}, green polyhedron; O, red; C, gray; N, pink. Ball and stick structure of d) {Λ-$Mo_{124}Ce_4(AH)_4$} and e) {Λ-$Mo_{124}Ce_4(SH)_4$}. Color code is identical to Figure 1.

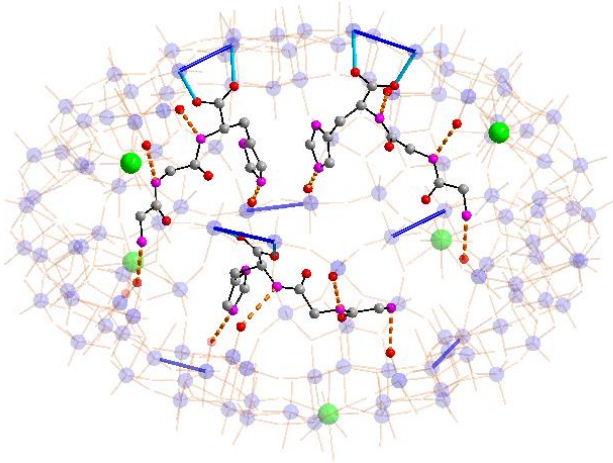


Figure S12. Molecular structure of {$Mo_{122}Ce_5(G_2H)_3$}. Colour code is identical to Figure 1.

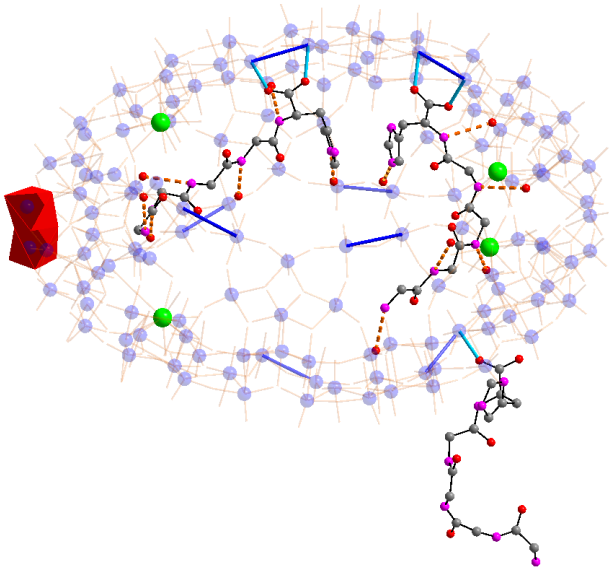


Figure S13. Molecular structure of {$Mo_{126}Ce_4(G_4H)_3$}. Colour code is identical to Figure 1.

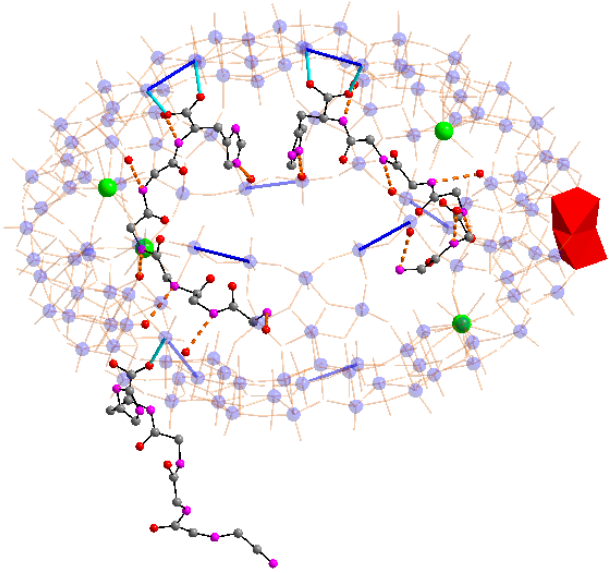


Figure S14. Molecular structure of {$Mo_{126}Ce_4(G_5H)_3$}. Colour code is identical to Figure 1.

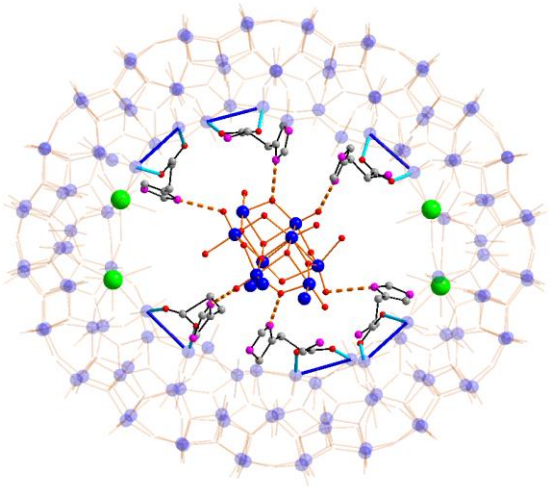


Figure S15. Molecular structure of $\{Mo_{124}Ce_4(H)_6(Mo_8)\}$. Colour code is identical to Figure 1.

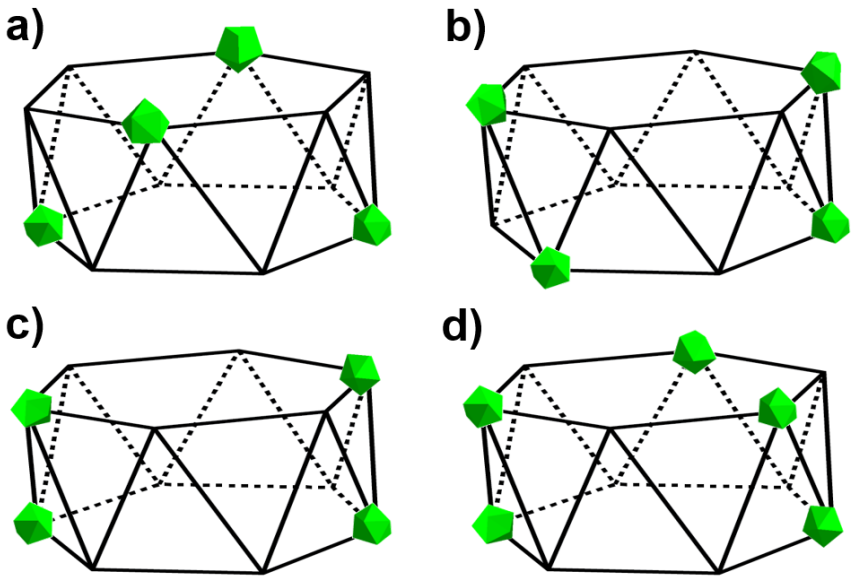
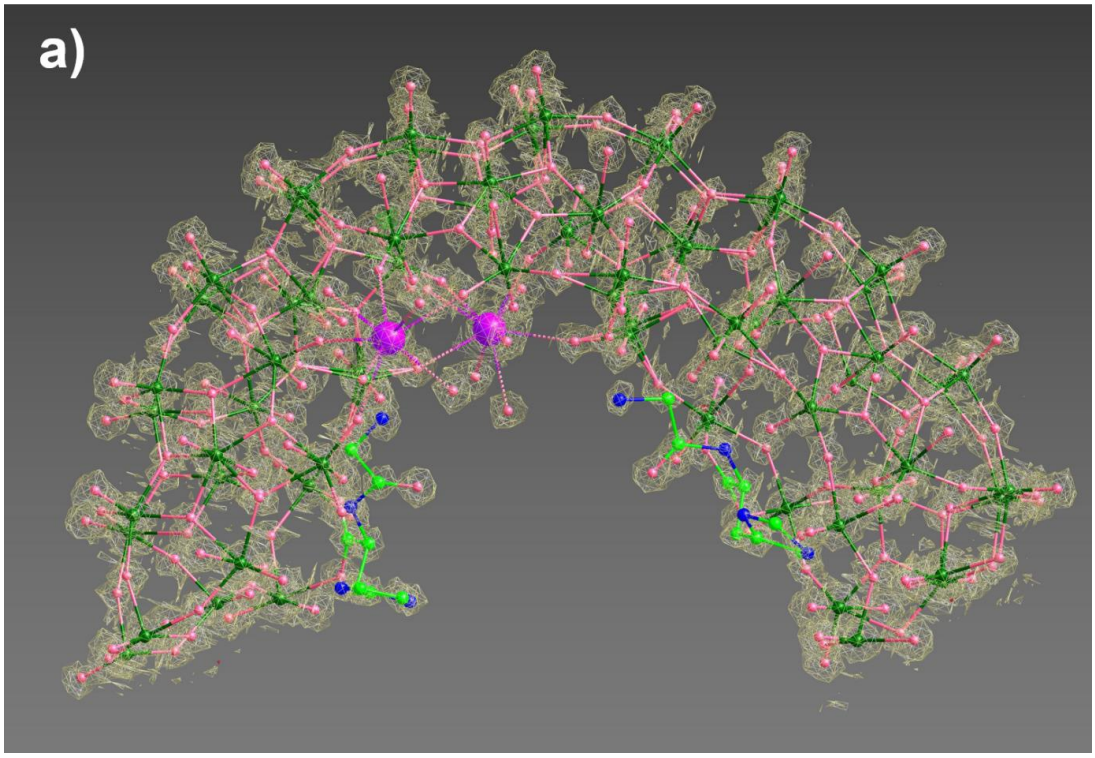
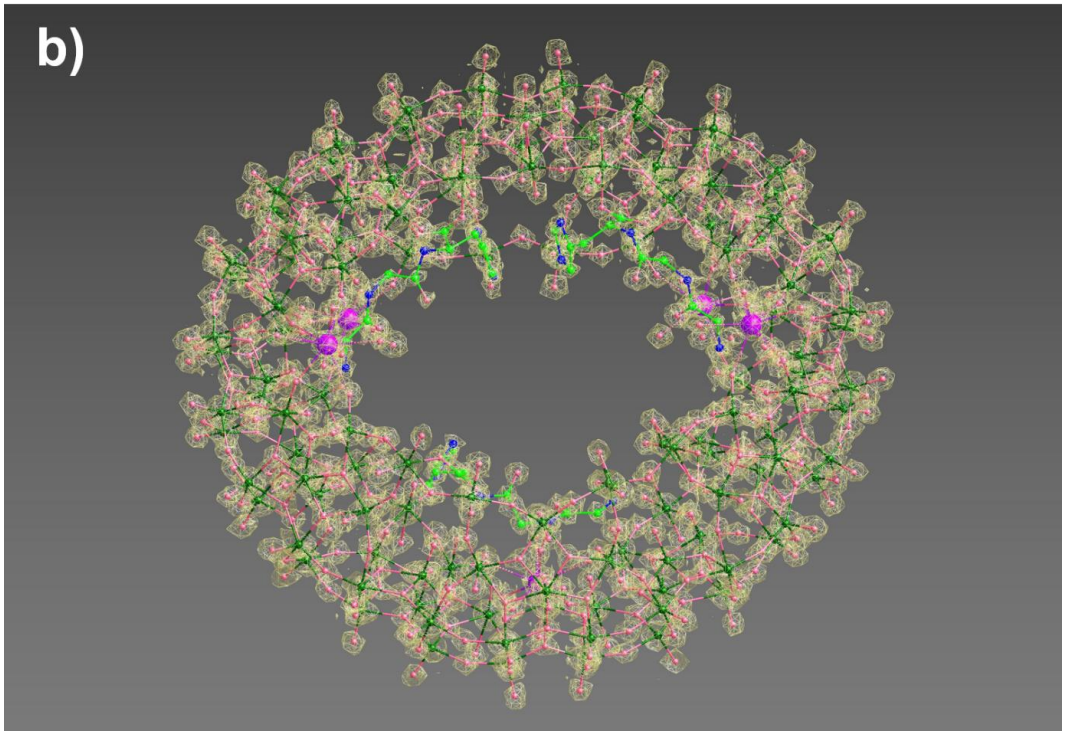
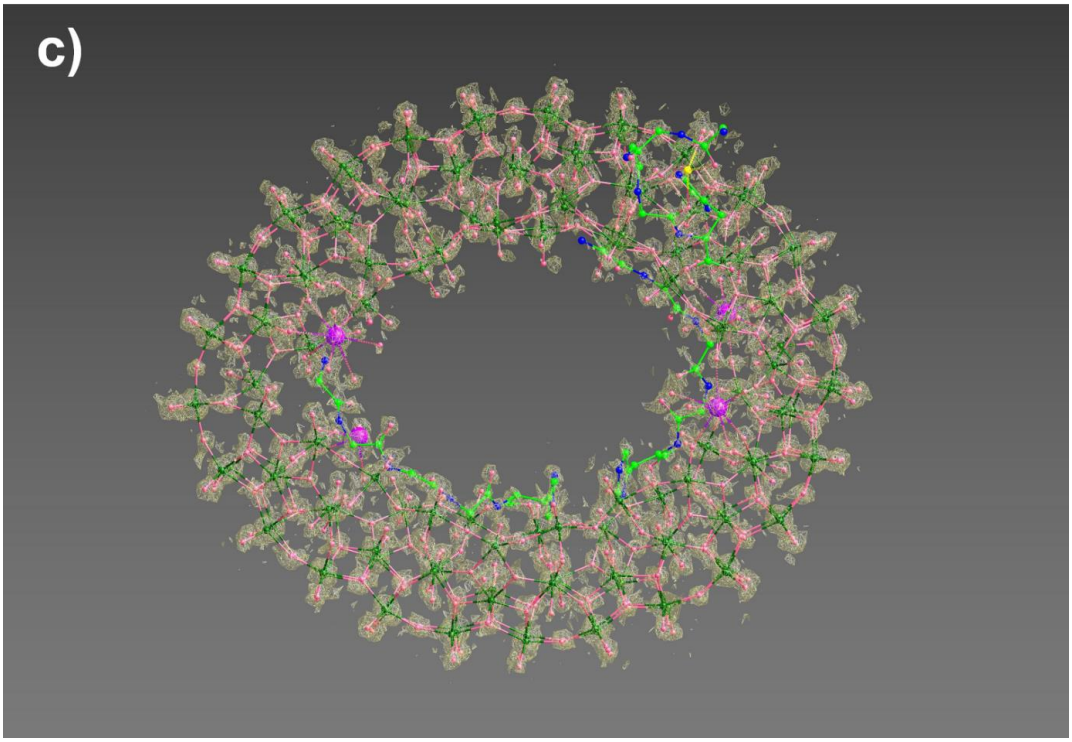


Figure S16. The distribution of Ce atoms (green polyhedron) in MB framework, each other corner represents a $\{Mo_2\}$ unit. a) $\{Mo_{124}Ce_4(PMo_{12})\}^3$, b) $\{Mo_{124}Ce_4(Mo_8)\}$ [4], c) $\{Mo_{124}Ce_4(GH)_4\}$, and d) $\{Mo_{122}Ce_5(G_2H)_3\}$.

7 Electron Density Plots for bio-hybrid nanowheels






c)

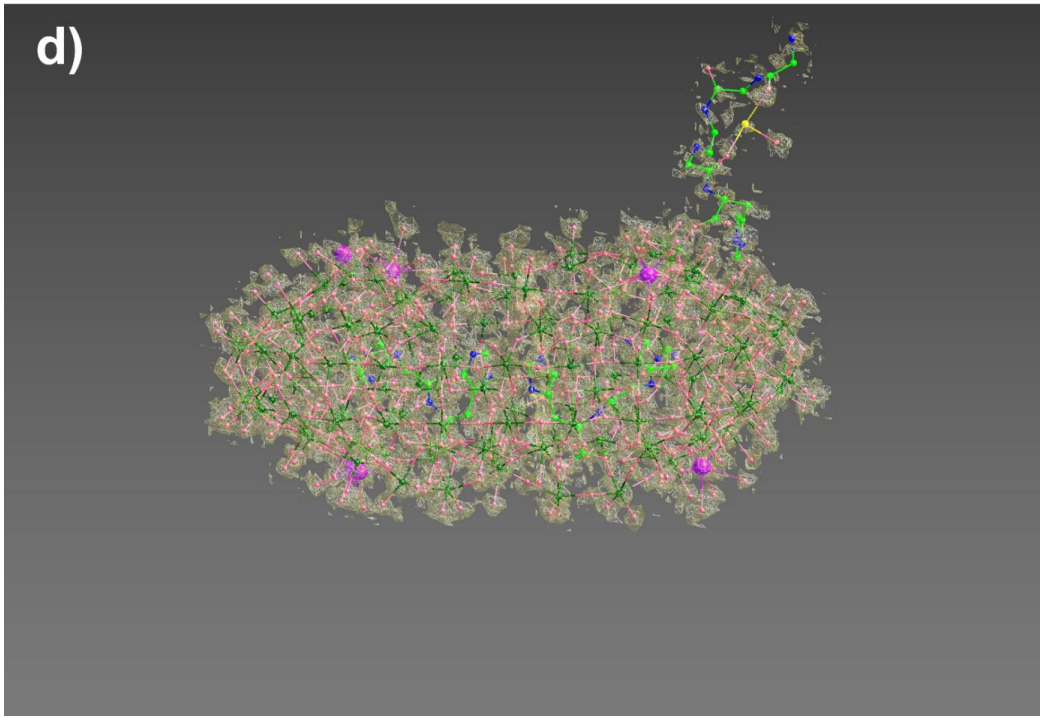

d)

Figure S17. The electron density map[5] F_{obs} of a) $\{Mo_{124}Ce_4(GH)_4\}$, resolution 2.7eÅ^3 ($\sigma = 4.1$); b) $\{Mo_{122}Ce_5(G_2H)_3\}$, resolution 2.7eÅ^3 ($\sigma = 3.6$); c) $\{Mo_{126}Ce_4(G_4H)_3\}$ (top view), resolution 1.9eÅ^3 ($\sigma = 1.5$); and d) $\{Mo_{126}Ce_4(G_4H)_3\}$ (side view), resolution 1.5eÅ^3 ($\sigma = 1.5$). The F_{obs} maps are superimposed with the structures of the wheels in color scheme of atoms Mo (green), Ce (pink), O (purple), C (bright green) and N (blue). These data further corroborate the locations and orientations of the peptides in these superstructures.

References

1. L. Farrugia, *J. Appl. Crystallogr.*, 1999, **32**, 837-838.
2. O. C. Gagne and F. C. Hawthorne, *Acta Crystallographica Section B*, 2015, **71**, 562-578.
3. H. N. Miras, C. Mathis, W. Xuan, D.-L. Long, R. Pow and L. Cronin, *Proc. Natl. Acad. Sci. U.S.A*, 2020, **117**, 10699-10705.
4. W. Xuan, R. Pow, Q. Zheng, N. Watfa, D.-L. Long and L. Cronin, *Angew. Chem. Int. Ed.*, 2019, **58**, 10867-10872.
5. C. B. Hubschle, G. M. Sheldrick and B. Dittrich, *J. Appl. Crystallogr.*, 2011, **44**, 1281-1284.