Electronic Supplementary Material (ESI) for Inorganic Chemistry Frontiers.

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Carbon Based Drug Delivery System Derived from One-Dimensional Coordination Polymer, Doxorubicin Loading and Redox-Responsive Release

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Chemical and material

1-ethyl-3-[3-dimethylaminopropyl] carbodiimide hydrochloride (EDC), N-hydroxysuccinimide (NHS) and doxorubicin (DOX) were purchased from Sigma-Aldrich (St. Louis, USA). Ammonium persulfate (APS) and 2-(N-morpholino)-ethanesulfonic acid (MES) were products from Sinopharm Chemical Reagent Co. Ltd (Shanghai, China). 3-(4, 5-dimethylthiazol-2-yl)-2, 5-diphenyltetrazolium bromide (MTT) assay kit and DMEM (high glucose) were received from Nanjing KeyGEN Biotech (Nanjing, China). Other chemicals were obtained from Alfa-Aesar. All these reagents were at least of analytical-reagent grade and used without any further treatment.

X-Ray crystallography

Suitable single crystal of **CP** was carefully selected under an optical microscope and glued on a glass fiber. Structural measurement was performed on a Bruker AXS SMART APEX II CCD diffractometer at 293 K. The structure was solved with the direct method and refined by the full-matrix least-squares method on F^2 using the SHELXTL 97 crystallographic software package.[1] Anisotropic thermal parameters were used to refine all non-hydrogen atoms. Carbon-bound hydrogen atoms were placed in geometrically calculated positions. The X-ray structural analysis is given in Table S1. Selected bond lengths and angles are listed in Table S2. Further details of the crystal structure determination have been deposited to the Cambridge Crystallographic Data Centre as supporting information (CCDC 1542144).

Cell cytotoxicity assays

Human cervical cancer cell line (HeLa cells) was used to evaluate cytotoxicity of DOX and **Ag-SS-MC** by MTT assay. The HeLa cells are seeded in 96-well plates with a

density of 1000 cells per well in 100 mL of DMEM complete medium and cultured in 5 % CO_2 at 37 ˚C for 24 h. Then, the cells were washed with PBS, and the medium was changed to new DMEM solution containing DOX and **Ag-SS-MC**. After incubating for 20 h, 20 µL MTT solution (5.0 mg·mL^{-1}) was added and further incubated for 4 h. Then, the medium was removed and 200 µl of DMSO was added to dissolve the purple crystals. The absorbance of each well at 490 nm was measured. The viability ratio was calculated from the linear relationship between cell number and optical density.

To investigate the redox-response release of **DOX@Ag-SS-MC** in cells, the intracellular GSH concentration wa controlled by adding GSH with different concentrations as external enhancers.[2] The HeLa cells were seeded as described above and pretreated with GSH for 2 h. Then, the cells were washed with PBS to remove the loosely adsorbed GSH. Finally, **DOX@Ag-SS-MC** with concentration from 1 to 100 mg·mL^{-1} were added into the GSH pretreated HeLa cells for 24 h with untreated cells as a control. The cell cytotoxicity was evaluated with above mentioned MTT method.

Live-cell imaging

The imaging capacity of the delivery system was determined. The stock solutions of DOX, **Ag-SS-MC** and **DOX@Ag-SS-MC** were prepared in a PBS buffer, followed by dilution with DMEM. HeLa cells were seeded in a confocal dish and grown for 24 h and then we replaced the medium with fresh DMEM containing DOX, **Ag-SS-MC** and **DOX@Ag-SS-MC** respectively. After incubating for 3 h, the cells were washed with 10 mM PBS buffer at room temperature and immobilized by paraformaldehyde. The intracellular DOX release from **DOX@Ag-SS-MC** was visualized with a fluorescence

micro-imaging system.

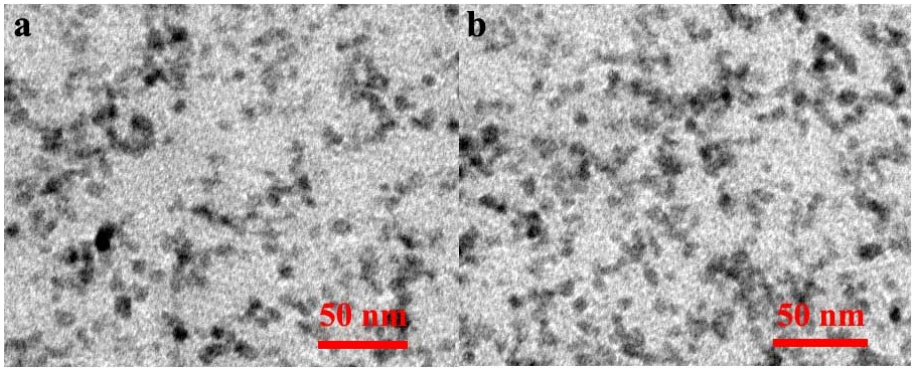

Fig. S1 (a) the TEM image of Ag nanoparticle with the size about 10 nm, (b) the TEM image of Ag nanoparticle with the size about 15 nm.

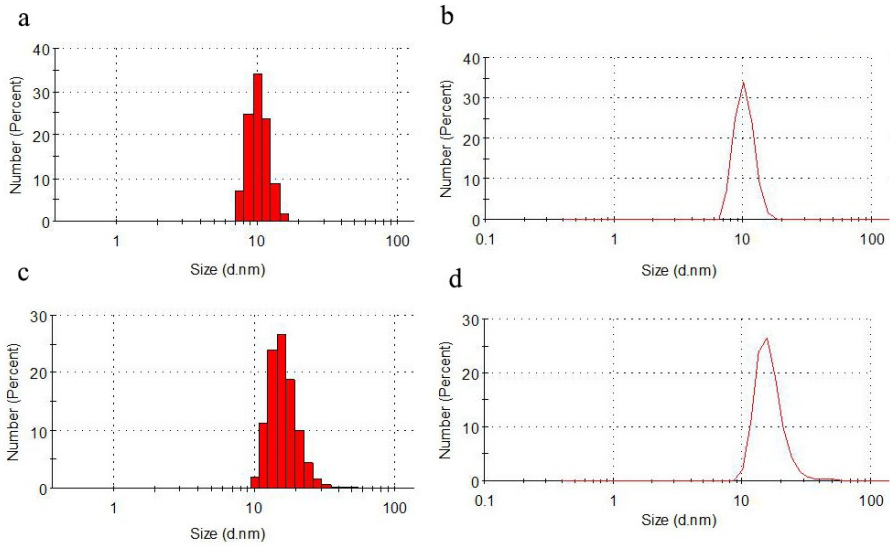

Fig. S2 the size distribution of Ag particle (a) Ag nanoparticle with the size about 10 nm; (b) Ag nanoparticle with the size about 15 nm.

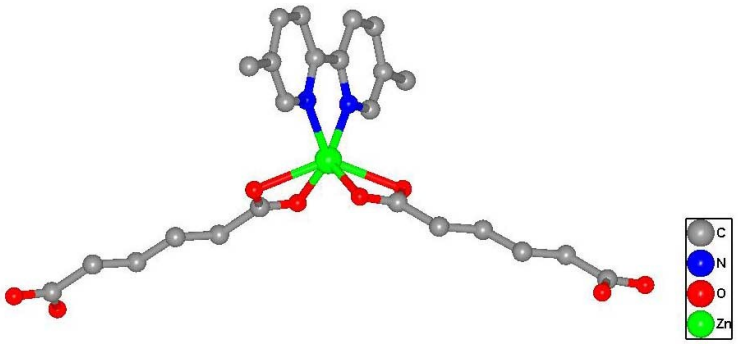

Fig. S3 the fundamental unit of **CP**.

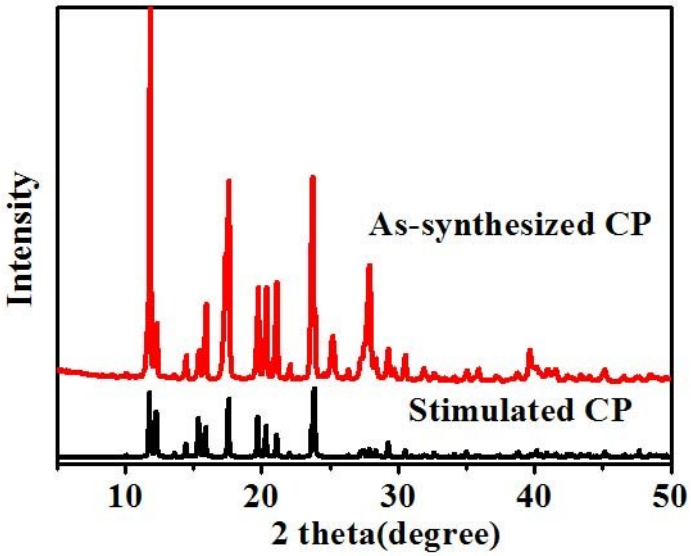

Fig. S4 experimental and simulated PXRD of **CP**.

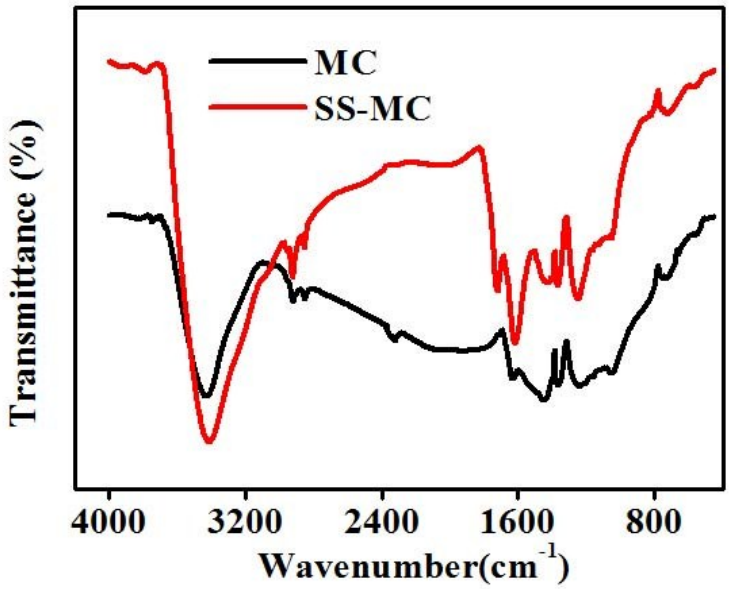

Fig. S5 FTIR of **MC** and **SS-MC**.

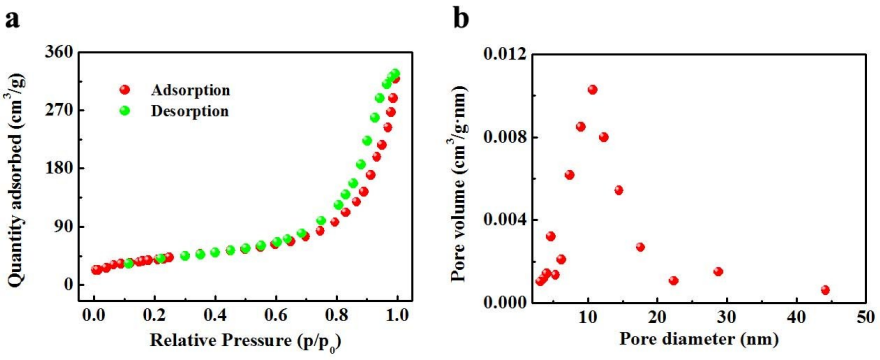

Fig. S6 (a) Nitrogen adsorption/desorption isotherm of **MC**; (b) Pore distribution of **MC**.

Table S1. Crystal data and structure refinement results for **CP**

Empirical formula	$C_{18}H_{16}N_2O_4Zn$
Formula weight	389.70
Crystal system	Orthorhombic
space group	P bcn
a (Å)	6.7317(3)
b (Å)	16.4136(5)
c (Å)	14.9850(5)
Volume (Å^3)	1655.71(11)
Z	4
Calculated density	1.563
F(000)	800
Reflections collected	6868
Reflections unique	2272
R(int)	0.0219
Goodness-of-fit	1.060
R_1[I>2sigma(I)]	0.0407
wR_2[I>2sigma(I)]	0.1391
R_1(all data)	0.0560
wR_2(all data)	0.1518

Note. $R_1 = \Sigma||F_o|-|F_c||/\Sigma|F_o|$; w$R_2 = \Sigma[w(F_o^2-F_c^2)^2]/\Sigma[w(F_o^2)^2]^{1/2}$

Table S2. Selected bond lengths and angles of **CP**

Zn(1)-O(1)	2.124(2)	Zn(1)-O(1)#1	2.124(2)
Zn(1)-O(3)	2.2351(19)	Zn(1)-O(3)#1	2.2351(19)
Zn(1)-N(1)	2.0925(19)	Zn(1)-N(1)#1	2.0925(19)
N(1)#1-Zn(1)-N(1)	78.13(11)	N(1)#1-Zn(1)-O(1)#1	135.59(7)
N(1)-Zn(1)-O(1)#1	95.57(8)	N(1)#1-Zn(1)-O(1)	95.57(8)
N(1)-Zn(1)-O(1)	135.59(7)	O(1)#1-Zn(1)-O(1)	116.99(12)
N(1)#1-Zn(1)-O(3)	126.40(8)	N(1)-Zn(1)-O(3)	88.69(7)
O(1)#1-Zn(1)-O(3)	96.93(8)	O(1)-Zn(1)-O(3)	59.69(7)
N(1)#1-Zn(1)-O(3)#1	88.69(7)	N(1)-Zn(1)-O(3)#1	126.40(8)
O(1)#1-Zn(1)-O(3)#1	59.69(7)	O(1)-Zn(1)-O(3)#1	96.93(8)
O(3)-Zn(1)-O(3)#1	136.88(11)		

Symmetry transformations used to generate equivalent atoms: #1 -x, y, -z+1/2

Reference

[1] a) G. M. Sheldrick, SHLEXL97, *Program for Crystal Structure Refinement*, University of Göttingen, Germany, **1997**; b) G. M. Sheldrick, SHLEXL97, *Program for Crystal structure Solution*, University of Göttingen, Germany, **1997**.

[2] D. Yang, W. L. Chen and J. H. Hu, J. Phys. Chem. B, **2014**, *118*, 12311-12317.