Electronic Supplementary Material (ESI) for ChemComm.

Electronic Supplementary Information

Coordination responsive tellurium-containing multilayer film for controlled delivery

Wei Cao, Lu Wang and Huaping Xu*

1 EXPERIMENTAL SECTION

1.1 Materials. Cisplatin, spermine, spermidine and sodium borohydride were purchased from Alfa-aesar. 8-bromooctanoic acid was the product of TCI. Tellurium powder was obtained from Aladdin chemical company. Other organic solvents and chemicals used in this work were analytical grade products from Beijing Chemical Reagent Company. Tetrahydrofuran (THF) was dried by Sodium Type A (4A) molecular sieves to remove moisture. (3-Aminopropyl)trimethoxysilane (APTS) was purchased from ACROS. All the solvents and chemicals were used as received unless otherwise stated. DAR (diazo resin) was kindly provided by Prof. Yuping Dong from College of Material Science & Engineering, Beijing Institute of Technology. The number-average molecular weight of DAR was ca. 2640 g mol^{-1}.

1.2 Methods. The ^{1}H NMR spectra and ^{13}C NMR spectra were measured on a JEOL JNM-ECA 400 (400 MHz). ^{125}Te NMR spectra were recorded on a JEOL JNM-ECA 600 (600 MHz) spectrometer.

TEM images were obtained by a JEM-2010 Microscope with an accelerating voltage of 80 kV. Samples were prepared by drop-coating the aqueous solution on the carbon-coated copper grid for 15 min and then observed without staining.

For SEM observation of the film thickness, a JEOL JSM-7401F field-emission scanning electron microscope was used operating at 3.0 kV. The sample was prepared by LbL assembly on a Si substrate and then dried under moist conditions. The sample was first coated with platinum and then mounted onto the microscope for observation. While the morphology of the aggregates was observed using SEM, FEI Quanta 200, FEI Chech.

Atomic force microscope (AFM) analyses were carried out on a commercial MultiMode 8 AFM with ScanAsyst mode using silicon cantilevers (ScanAsyst-Air from Bruker). The LbL films characterized were prepared on silicon substrate. DLS measurements were performed by a Malvern ZEN3690 Zetasizer at 25 ℃. ESI-mass was carried out on a LTQ LC/MS apparatus**.**

To evaluate the release of platinum from the LbL thin films, ELAN DRC-e ICP Mass Spectroscopy was employed. The release rate under different conditions was studied by immersing the quartz slides in 3 ml ligand solution. 1 mL solution was taken out at desired time intervals to test the platinum concentration and another 1 mL fresh solution was supplemented to maintain the whole volume.

Synthesis of 8,8'-tellurodioctanoic acid. The telluride containing monomer was acquired through the reaction of disodium telluride and 8-bromooctanoic acid. Disodium telluride was prepared by the reaction of Te powder and excess amount of sodium borohydride at 50 ^{o}C in water under the atmosphere of nitrogen. 8,8'-tellurodioctanoic acid (denoted as m-TeCOOH) was synthesized through the reaction of disodium telluride and 8-bromooctanoic acid in THF under Ar flow at 50 ^{o}C for 6 h. Product yielded was purified by filtration and recrystallized by acidification. White powder was finally obtained with a yield of ~70 %.

^{1}H NMR (400MHz, D_2O, 298 K) δ (ppm): 2.70(4H, t, TeCH_2), 2. 19(4H, t, CH_2COOH), 1.82-1.25(20H, m, HOOC$CH_2(CH_2)_5CH_2$Te). ^{13}C NMR (400MHz, D_2O, 298 K) with 1,4-dioxane as the external reference (67.19 ppm), δ (ppm): 184.2 (1C, s, *C*OOH), 38.4 (1C, s, CH_2COOH), 29.0-32.5 (1C, s, TeCH_2 $(CH_2)_4CH_2CH_2$COOH), 26.7 (1C, s, CH_2CH_2COOH), 3.9 (1C, s, TeCH_2), 161 (Na_2CO_3, which is added to deprotonate the –COOH groups). ^{125}Te NMR (600MHz, D_2O, 298 K) δ (ppm): 191 (1Te, m, *Te*). MS (ESI) m/z = 415.11 $[M-H]^-$.

Coordination of m-TeCOOH with cisplatin. The m-TeCOOH was suspended in 10 mM phosphate buffered saline (PBS) initially, then gradually neutralized to pH 7.4 through sequential addition of 0.4 M Na_2CO_3 under sonication. Cisplatin was added to the previous solution and kept still for 30 min before further characterization. After coordination, the m-TeCOOH/cisplatin complex, ^{1}H NMR (400MHz, D_2O, 298 K) δ (ppm): 3.6-3.2 (4H, b, TeCH_2), 2. 19(4H, t, CH_2COOH), 1.95-1.25(20H, m, HOOC$CH_2(CH_2)_5CH_2$Te). ^{125}Te NMR (600MHz, D_2O, 298 K) δ (ppm): 283 (1Te, m, *Te*). MS (ESI) m/z = 679.11 $\{Pt(m\text{-}TeCOOH)(NH_3)_2Cl\}^+$, 723.06 $\{Pt(m\text{-}TeCOONa)(NH_3)_2Cl\}^+$.

Preparation of the aggregates of m-TeCOOH/cisplatin complex. 3 mg m-TeCOOH was dissolved in PBS as described above and coordinated with cisplatin for 30 min followed by centrifugation to separate the unreacted cisplatin. The solution was added dropwise in 3 mL pH 4 buffer under sonication.

Substrate preparation. Quartz slides and silicon slides were treated in hot piranha solution overnight (98% H_2SO_4/30% H_2O_2 = 7/3, v/v. *CAUTION: piranha solution is extremely dangerous and corrosive. Appropriate safety precautions should be utilized*) and then rinsed carefully with deionized water and dried in an oven overnight. The substrates were then immersed in a 10μM APTS toluene solution overnight to form a self-assembled silane monolayer terminated with NH_2 groups on the exposed surface. The substrates were subjected to ultrasonic agitation in toluene, THF, and acetone for 1 min to remove the physically adsorbed APTS.

Multilayer formation and photoreaction. The quartz slides prepared were first immersed in the m-TeCOOH/cisplatin suspension for 2 min, followed by rinsing with deionized water and drying with nitrogen. The slides were then immersed in a DAR aqueous solution (1 mg mL^{-1}) for 2 min, followed by the same rinsing and drying cycle. By repeating both immersion processes alternately, films of ten bilayers and a DAR outmost layer were prepared. The multilayer films were irradiated by a photo-chemical reactor equipped with a 100 W UV lamp with the peak wavelength of 365 nm for 10 min to form cross-linked films.

2 DETAILED CHARACTERIZATION.

2.1 Synthesis route for the tellurium-containing molecules.

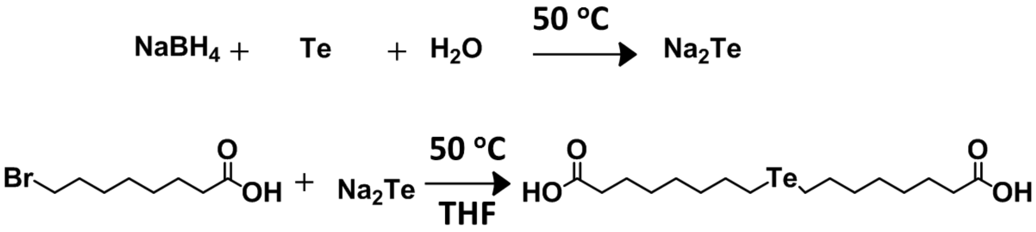

Fig. S1. Synthesis route for the tellurium-containing molecules, m-TeCOOH.

2.2 Characterization for the tellurium-containing molecules and the self-assembly behaviors.

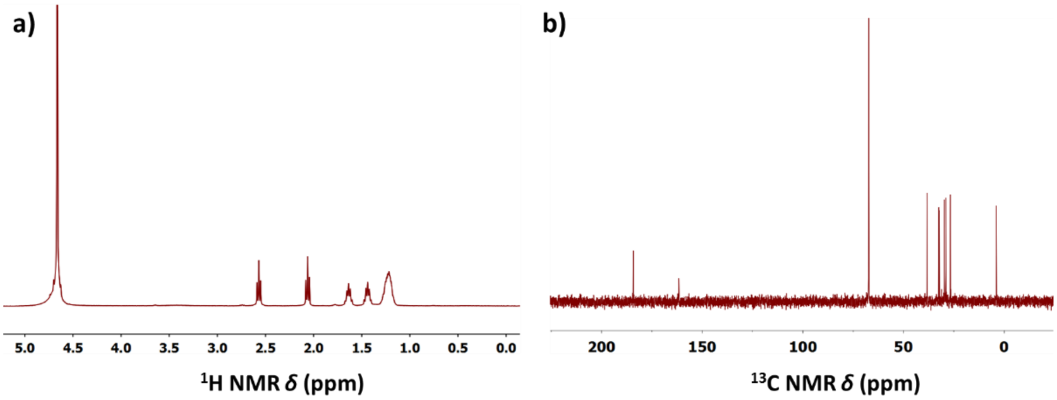

Fig. S2. a) ^1H NMR and b)^{13}C NMR spectrum of the m-TeCOOH (400MHz, D_2O).

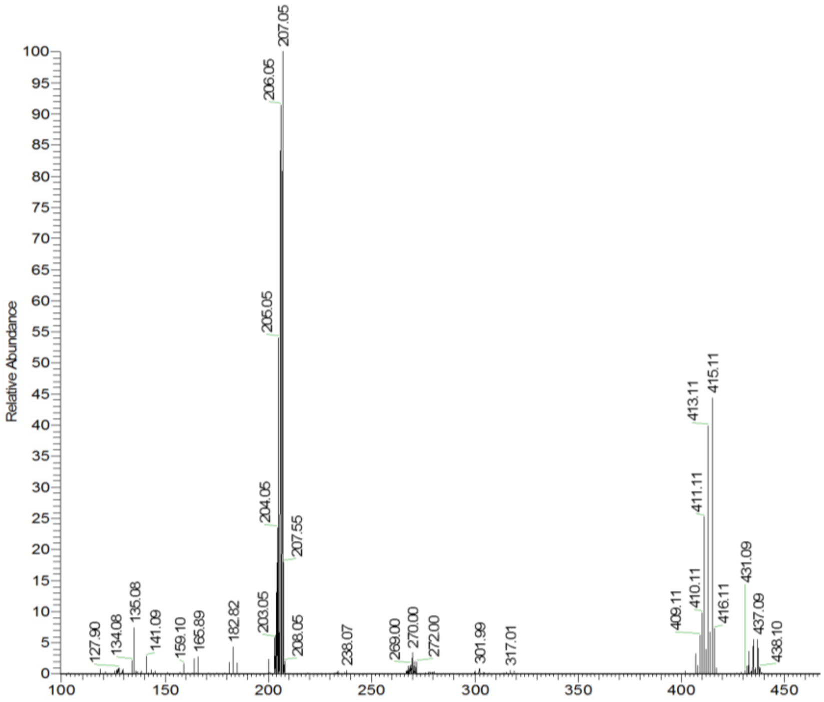

Fig. S3. ESI-MS spectrum (negative spectrum) for m-TeCOOH.

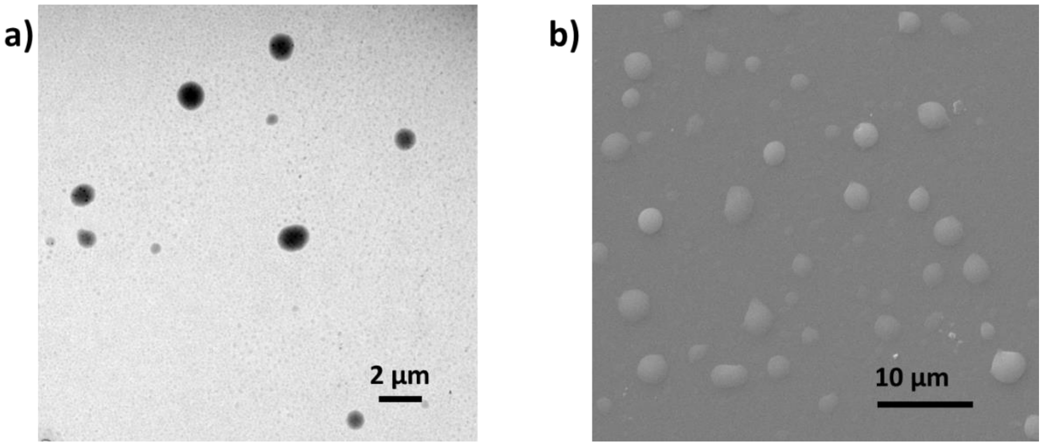

Fig. S4. Self-assembly behaviors of m-TeCOOH in pH 4 buffer. a) TEM and b) SEM image of the aggregates.

2.3 Characterization of the m-TeCOOH/cisplatin complex and the self-assembly behaviors.

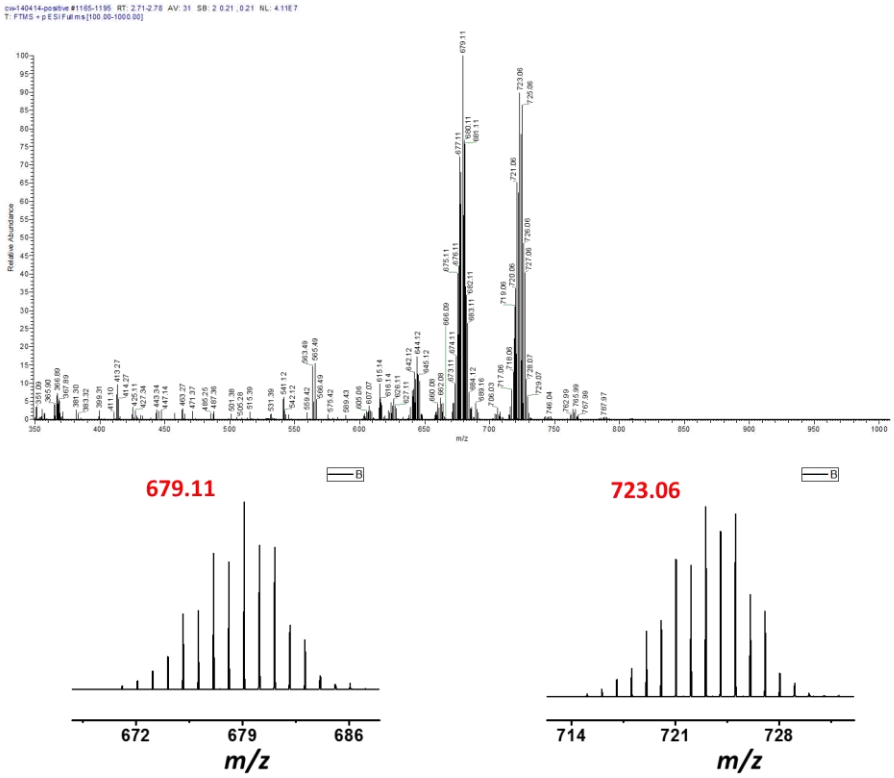

Fig. S5. ESI-MS spectrum (positive spectrum) for m-TeCOOH/cisplatin complex and the zoomed spectra for the two main peaks.

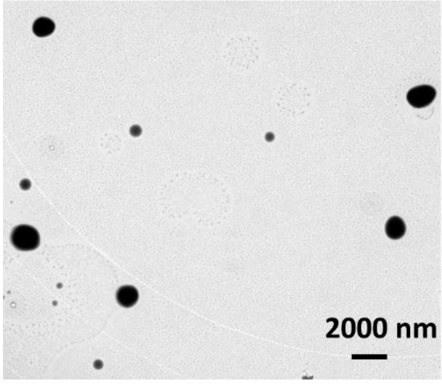

Fig. S6. TEM images for the self-assembly aggregates of m-TeCOOH-cisplatin in pH 4 buffer.

2.4 Characterization of the ten-bilayer film by AFM and SEM.

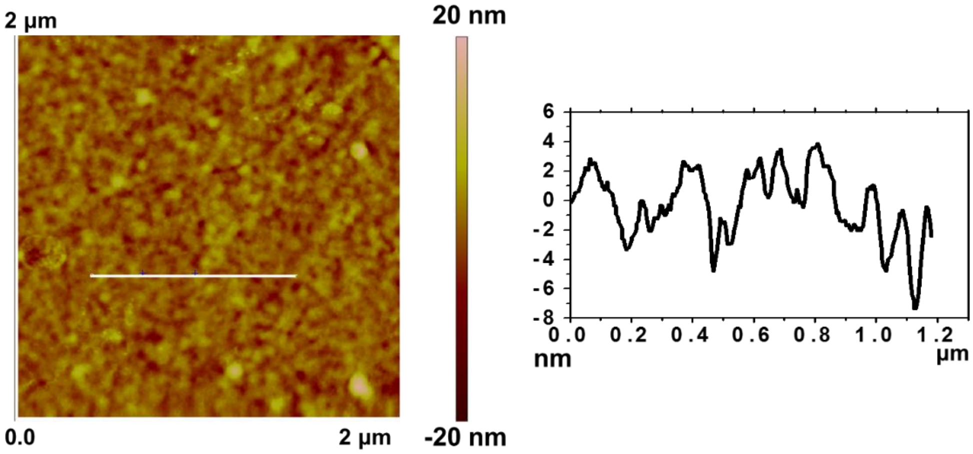

Fig. S7. The AFM image of the ten-bilayer film prepared on the silicon substrate.

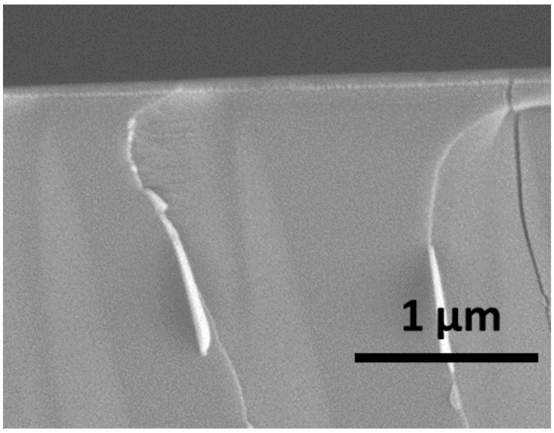

Fig. S8. Cross-sectional SEM image of a UV-irradiated ten-bilayer film.

2.5 The release kinetics studies of the films under different conditions.

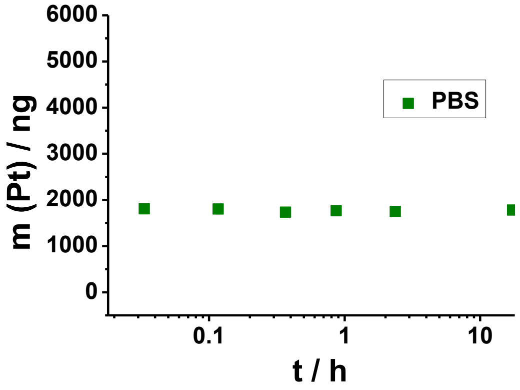

Fig S9. Controlled release profiles of cisplatin for the multilayer film in 10 mM PBS (pH 7.4).

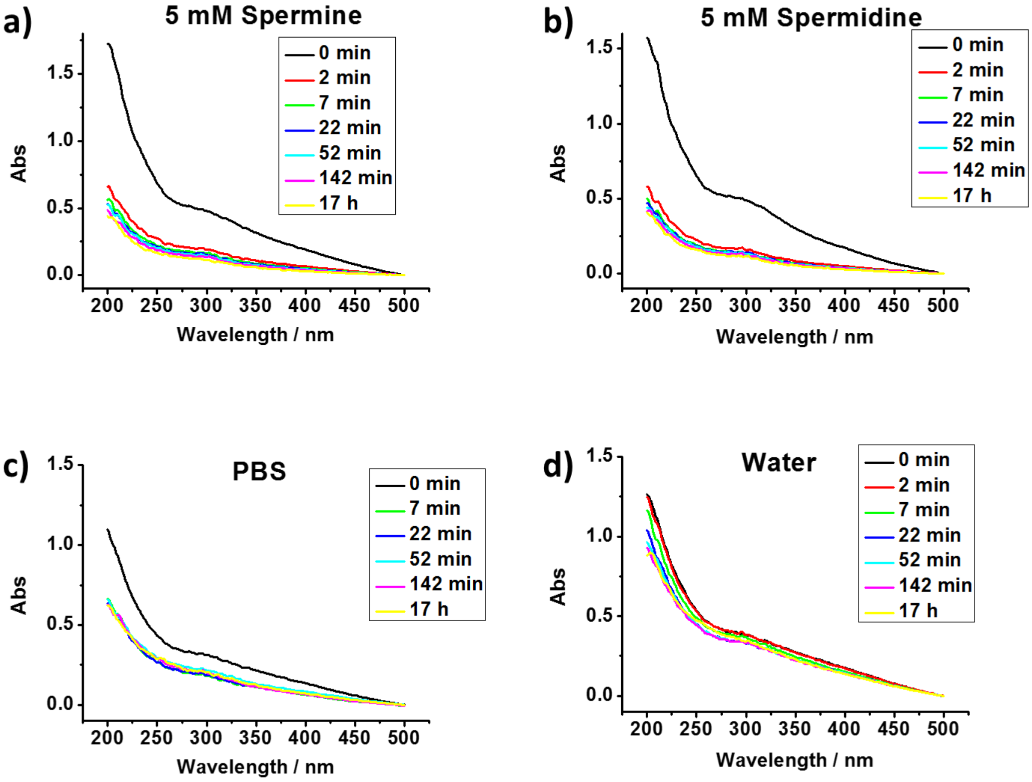

Fig. S10. Release process monitored by UV-Vis spectra. The quartz substrates coated with 10-bilayer films were immersed in outer solution a) 5 mM spermine b) 5 mM spermidine c) 10 mM PBS and d) water. They were taken out and washed with deionized water for measurement, and then put back into the solutions respectively.