

## Supporting information

### Light-regulated release of entrapment drug from photoresponsive gold nanoparticles

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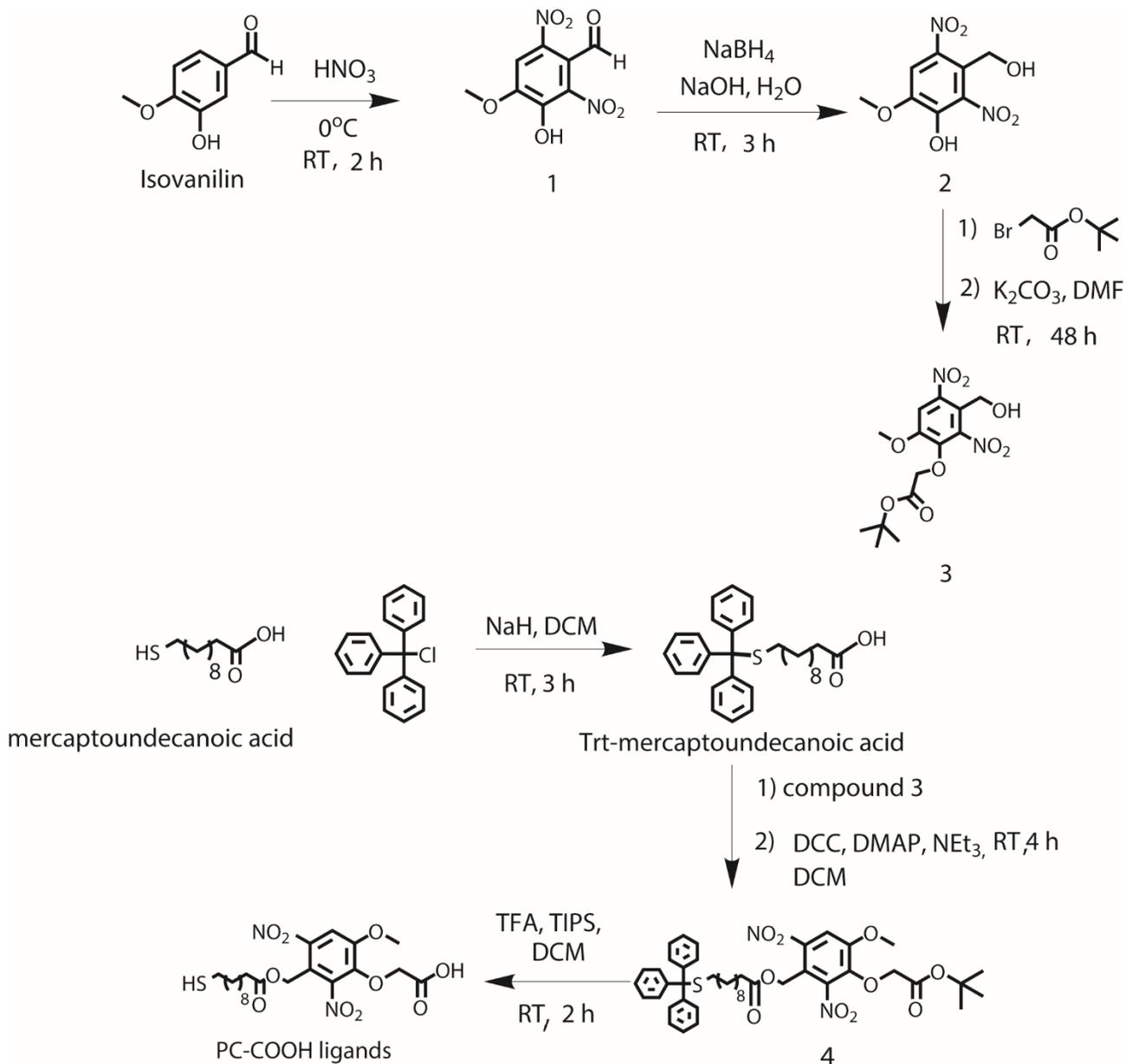
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## Materials.

All materials were used as received unless otherwise noted. Chlorotriphenylmethane (99.5%), acetone (HPLC grade), hydrochloric acid (HCl, 37%), isovanillin, nitric acid (HNO<sub>3</sub>, 65%), potassium carbonate (K<sub>2</sub>CO<sub>3</sub>, >99%), sodium borohydride (NaBH<sub>4</sub>, >98%), sodium hydroxide (NaOH, >99%), *tert*-butyl bromoacetate, triethylamine (99%), and triisopropylsilane (TIPS, 99%) were purchased from Merck chemicals. Gold (III) Chloride trihydrate (HAuCl<sub>4</sub>, 49%), 1-dodecanethiol (>98%), 4-(dimethylamino) pyridine (DMAP, >98%), N,N'-dicyclohexylcarbodiimide (DCC, >98%), N,N'-dimethylformamide (DMF), 11-mercaptoundecanoic acid (95%), and tetraoctylammonium bromide (98%), DL-Dithiothreitol (DTT) were purchased from Sigma-Aldrich. Dichloromethane (DCM, 99.5%), ethanol (99.9%), sodium chloride (NaCl), and sodium sulfate anhydrous (Na<sub>2</sub>SO<sub>4</sub>) were purchased from Quality Reagent Chemical. Toluene (99.9%) and trifluoroacetic acid (TFA, 99%) were purchased from RCI Labscan limited. The dye were gifted from Dr. Panawan Moosophon Department of Chemistry, Faculty of Science, Khon Kaen University.

<sup>1</sup>H NMR spectra was recorded using Varian Mercury Plus 400 spectrometer. UV-vis spectra were recorded in shimadzu, UV-1800. Fluorescent Spectra wer measured by fluorescence spectrometer (JASCO, FP-8200). Dynamic light scattering (DLS) was measured using Zetasizer Nano ZS.



**Scheme S1.** Synthetic scheme for the preparation of PC-COOH ligands.

### Synthesis of compound 1

Isovanilin (18.3 g, 120 mmol) was placed in a 250 mL round bottom flask. The flask was cooled down to 0 °C using an ice bath. Then, HNO<sub>3</sub> (40 mL) was added dropwise to the isovanilin

under stirring condition. The reaction mixture changes into to a dark yellow mixture and finally turns to brown. The mixture was kept at room temperature and further stirred for 2 h. The reaction mixture was then poured into a 200 mL of ice cold water, filtered, and evaporated under vacuum to yield compound **1** 17.8671 g ( 61.52% yield).

$^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  10.48 (s, 1H,  $-\text{CHO}$ ), 7.85 (s, 1H, HAr), 4.10 (s, 3H,  $-\text{OCH}_3$ ).

### *Synthesis of compound 2*

Compound **1** (1.03 g, 4.3 mmol) was dissolved in water (20 mL) in a 100 mL round bottom flask. NaOH pellet (0.17 g, 4.3 mmol) was added into the solution of compound **1**.  $\text{NaBH}_4$  (0.085g, 2.2 mmol) was then added to the solution after 10 min of stirring. The reaction mixture was further stirred at room temperature and kept for 3h. Then, solution of 1 M HCl was used to adjust the pH of the solution to be  $\sim 2$ . A dark brown solid was precipitated out from the acidic solution. The solid was extracted using ethyl acetate (3x 20 mL). The organic layers were combined and washed with water and brine. After drying over  $\text{Na}_2\text{SO}_4$ , removal of the ethyl acetate under reduced pressure afforded compound **2** 0.7158 g (68.22% yield). Compound **2** was used in the next step of reaction without any purification.

$^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.70 (s, 1H, HAr), 4.80 (s, 2H,  $-\text{PhCH}_2\text{O}-$ ), 4.07 (s, 3H,  $-\text{OCH}_3$ )

### *Synthesis of compound 3*

$\text{K}_2\text{CO}_3$  (10.5 g, 76 mmol) was suspended in dry DMF (100 mL). Compound **2** (2.8 g, 11.5 mmol) was added to the suspended solution of  $\text{K}_2\text{CO}_3$ . The mixture was stirred for 1 h and then *tert*-butyl bromoacetate (2.54 g, 13 mmol) was added to the solution. The reaction was stirred for 48 h at room temperature. The insoluble solid was filtered off. The filtrate was transferred into water ( $\sim 300$  mL). The mixture was extracted with ethyl acetate (3x150 mL). The ethyl acetate layers were combined, washed with a saturated solution of brine (100 mL), dried over anhydrous  $\text{Na}_2\text{SO}_4$ ,

filtered, and concentrated under reduced pressure. The product was purified by silica-gel chromatography (eluent: 50% ethyl acetate in hexane v/v) to afford compound **3** 2.3111 g (56.09% yield).

<sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): δ 7.70 (s, 1H, HAr), 4.79 (s, 2H, -OCH<sub>2</sub>C(O)-), 4.72 (d, J = 7.32 Hz, 2H, -PhCH<sub>2</sub>O-), 3.97 (s, 3H, -OCH<sub>3</sub>), 2.69 (t, J = 7.44 Hz, 1H, Benzyl-OH), 1.45 (s, 9H, -C(CH<sub>3</sub>)<sub>3</sub>).

### *Synthesis of Trt-mercaptoundecanoic acid*

Mercaptoundecanoic acid (1 g, 4.58 mmol) was dissolved in DCM (10 mL) and placed in a 100 mL round bottom flask. NaH (0.1214 g, 5.05 mmol) was added to the clear solution and stirred for 10 min. Chlorotriphenylmethane (2.8212 g, 10.11 mmol) was added into the mixture of mercaptoundecanoic acid. The reaction mixture was further stirred at room temperature for another 3 h. The solvent was removed under reduced pressure. The product was purified by silica-gel chromatography (eluent: a gradient eluent of hexane to ethyl acetate) to yield Trt-mercaptoundecanoic acid 0.78 g (37% yield).

<sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): δ 7.41 (m, 6H, Ar-H), 7.27 (m, 6H, Ar-H), 7.20 (m, 3H, Ar-H), 2.30 (t, 2H, -S-CH<sub>2</sub>-), 2.10 (t, 2H, -CH<sub>2</sub>-C(O)OH), 1.80-1.85 (m, 4H, -CH<sub>2</sub>-), 1.50-1.70 (m, 12H, -(CH<sub>2</sub>)<sub>6</sub>).

### *Synthesis of PC-COOH ligand*

#### *Synthesis of compound 4 (part 1)*

Trt-mercaptoundecanoic acid (0.7 g, 1.52 mmol) was dissolved in DCM (25 mL) and placed in a 100 mL round bottom flask to the clear solution after 10 min of stirring. DCC (0.3357 g, 1.67 mmol), NEt<sub>3</sub> (0.23 mL, 0.1689 mmol), DMAP (cat.) were added to a suspended solution of Trt-mercaptoundecanoic acid. Compound **3** (0.5446 g, 1.52 mmol) was suspended in DCM (20 mL) and added into the reaction mixture of Trt-mercaptoundecanoic acid. The mixture was stirred for 4 h.

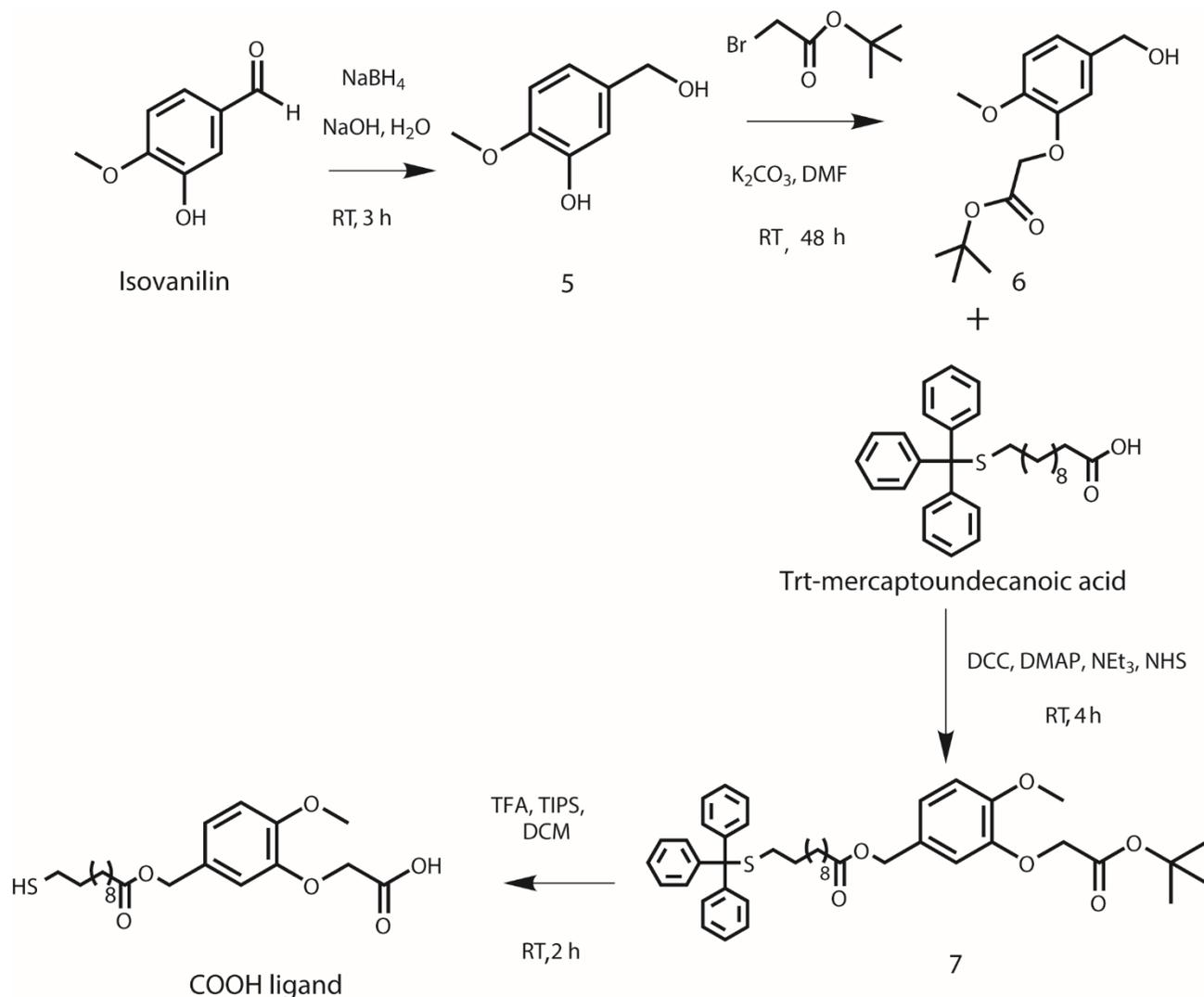
The solvent was removed under reduced pressure and the residue was loaded purified by silica-gel chromatography (eluent: a gradient eluent of hexane to ethyl acetate) to yield compound **4** 0.5417 g (44.5% yield).

<sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): δ 7.65 (s, 1H, Ar-H), 7.41 (m, 6H, Ar-H), 7.27 (m, 6H, Ar-H), 7.20 (m, 3H, Ar-H), 5.30 (s, 2H, O-CH<sub>2</sub>-Ph-), 4.75 (s, 2H, -O-CH<sub>2</sub>-C(O)), 3.95 (s, 3H, CH<sub>3</sub>-O), 2.25 (t, 2H, -S-CH<sub>2</sub>-), 2.10 (t, 2H, -CH<sub>2</sub>-C(O)), 1.58 (m, 2H, -(CH<sub>2</sub>)<sub>2</sub>-), 1.45 (9H, (CH<sub>3</sub>)<sub>3</sub>-C-), 1.39 (m, 2H, -(CH<sub>2</sub>)<sub>2</sub>-), 1.10-1.35(m, 12H, -(CH<sub>2</sub>)<sub>6</sub>-).

*Synthesis of compound PC-COOH (part 2)*

Compound **4** (0.5 g, 0.625 mmol) was suspended in DCM (5 mL) and placed in a 25 mL round bottom flask. Trifluoroacetic acid (TFA, 0.5mL, 0.688 mmol) was added to the color of the solution was turned to yellow. Triisopropylsilane (TIPS) was added carefully to the reaction mixture and the color of mixture slowly recovered to colorless. The reaction was continued for 1 h at room temperature under stirring condition. The volatile components (solvent, TFA and TIPS) were distilled off under reduced pressure. The pale yellow residue was further purified by washing with hexane (4x15mL). The solvent was removed under reduced pressure to yield compound **4** 0.24 g (78.86%yield).

<sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): δ 7.65 (s, 1H, Ar-H), 5.30 (s, 2H, O-CH<sub>2</sub>-Ph-), 4.90 (s, 2H, -O-CH<sub>2</sub>-C(O)), 3.99 (s, 3H, CH<sub>3</sub>-O), 2.5 (m, 2H, -S-CH<sub>2</sub>-), 2.22 (t, 2H, -CH<sub>2</sub>-C(O)), 1.65-1.50 (m, 4H, -(CH<sub>2</sub>)<sub>2</sub>-), 1.42-1.10 (m, 12H, -(CH<sub>2</sub>)<sub>6</sub>-).



**Scheme S1.** Synthetic scheme for the preparation of Au-COOH ligands.

### Synthesis of compound 5

Isovanillin (4.56 g, 30 mmol) was dissolved in 150 mL and placed in a 250 mL round bottom flask.  $\text{NaOH}$  pellet (1.2005 g, 30 mmol) was added carefully into the suspended solution of isovanillin solution. The solution became homogeneous solution.  $\text{NaBH}_4$  (0.601 g, 15 mmol) was added to the clear solution after 10 min of stirring. The reaction mixture was further stirred at room temperature for 3 h. Then, 1M  $\text{HCl}$  was used to adjust the pH of the solution at  $\sim 2$ . The solid was extracted using ethyl acetate (3X30 mL). The organic layers were combined and washed thoroughly

with water and brine. After drying over Na<sub>2</sub>SO<sub>4</sub>, removal of the ethyl acetate under reduced pressure afforded compound **5** pure enough for the next step of reaction. Compound **5** was obtained 3.816 g (82.59% yield).

<sup>1</sup>H-NMR (400MHz, CDCl<sub>3</sub>): δ 6.85 (m, 1H, HAr), 6.75 (m, 2H, HAr), 4.50 (s, 2H, -PhCH<sub>2</sub>O-), 4.40 (s, 2H, -OCH<sub>2</sub>C(O)-), 3.8 (s, 3H, -OCH<sub>3</sub>), 2.60 (br, 1H, Benzyl-OH).

### ***Synthesis of compound 6***

A suspended solution of K<sub>2</sub>CO<sub>3</sub> (10.5 g, 76 mmol) in dry DMF (100 mL) was prepared. Compound **5** (1.7505 g, 11.36 mmol) was added to K<sub>2</sub>CO<sub>3</sub> solution. The mixture was stirred for another 1h. Then, *tert*-butyl bromoacetate (2.54 g, 13 mmol) was added to the solution. The reaction was continued for 48 h at room temperature under stirring condition. The reaction mixture was filtered through a filter paper. The filtrate was poured into DI water (~300 mL). The aqueous solution was extracted with ethyl acetate (3x30 mL). The ethyl acetate layers were combined, washed with a saturated solution of NaCl (100 mL), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, filtered, and concentrated under reduced pressure. The residue was purified by silica-gel chromatography (eluent: 50% ethyl acetate in hexane v/v) to afford compound **3** as a bright yellow solid. 0.2119 g (7.28% yield)

<sup>1</sup>H-NMR (400MHz, CDCl<sub>3</sub>): δ 6.85 (m, 1H, H-Ar), 6.75 (m, 2H, H-Ar), 4.50 (s, 2H, -PhCH<sub>2</sub>O-), 4.40 (s, 2H, -OCH<sub>2</sub>C(O)-), 3.8 (s, 3H, -OCH<sub>3</sub>), 2.60 (br, 1H, Benzyl-OH), 1.46 (s, 9H, -C(CH<sub>3</sub>)<sub>3</sub>).

## *Synthesis of compound COOH ligands*

### *Synthesis of compound 7 (part 1)*

Trt-mercaptopundecanoic acid (2 g, 4.34 mmol) was dissolved in DCM (20 mL) and placed in a 50 mL round bottom flask to the clear solution after 10 min of stirring. DCC (0.9842 g, 4.77 mmol),  $\text{NEt}_3$  (0.66 mL, 4.82 mmol), DMAP (cat.), NHS (0.5489 g, 4.77 mmol) were added to a suspended solution of Trt-mercaptopundecanoic acid. Compound **6** (0.9815 g, 4.34 mmol) was suspended in DCM (20 mL) and added into the reaction mixture of Trt-mercaptopundecanoic acid. The mixture was stirred for 4 h. The solvent was removed under reduced pressure and the residue was loaded purified by silica-gel chromatography (eluent: a gradient eluent of hexane to ethyl acetate) to yield compound **7** 0.4265 g (13.9% yield).

$^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.41 (m, 6H, Ar-H), 7.27 (m, 6H, Ar-H), 7.20 (m, 3H, Ar-H), 6.85 (m, 1H, H-Ar), 6.75 (m, 2H, H-Ar), 5.30 (s, 2H, -O- $\text{CH}_2$ -Ph), 4.58 (s, 2H, O - $\text{CH}_2$ -C(O)-), 3.8 (s, 3H, - $\text{OCH}_3$ ), 2.25 (t, 2H, -S- $\text{CH}_2$ -), 2.10 (t, 2H, - $\text{CH}_2$ -C(O)), 1.90 (m, 2H, - $\text{CH}_2$ -), 1.70 (m, 2H, - $\text{CH}_2$ -), 1.45 (s, 9H,  $(\text{CH}_3)_3\text{-C-}$ ), 1.40-1.10 (12H,  $-(\text{CH}_2)_6-$ ).

### *Synthesis of compound COOH ligand (part 2)*

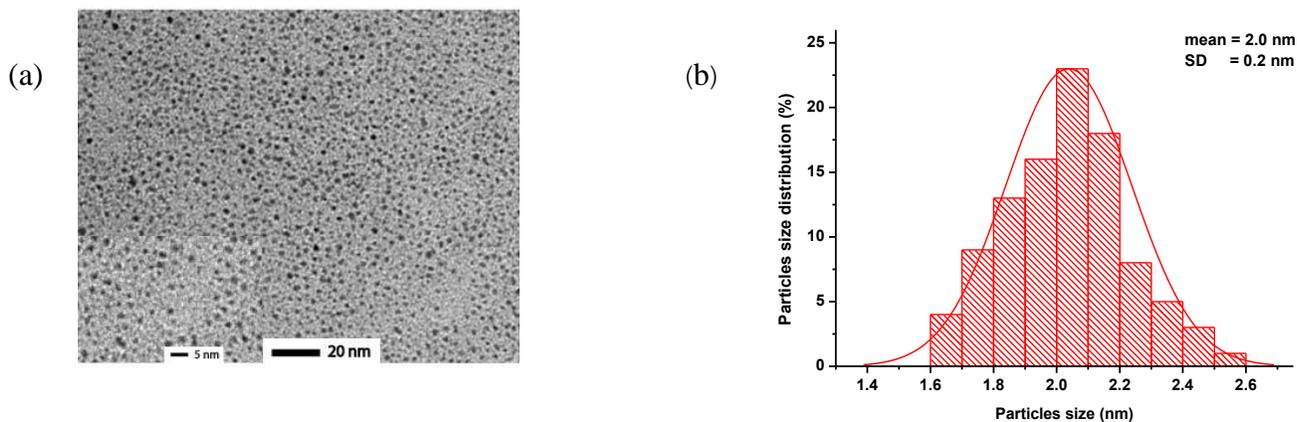
Compound **7** (0.4265 g, 6.04 mmol) was suspended in DCM (5 mL) and placed in a 25 mL round bottom flask. Trifluoroacetic acid (TFA, 0.5 mL, 0.66 mmol) was added to the color of the solution was turned to yellow. Triisopropylsilane (TIPS) was added carefully to the reaction mixture and the color of mixture slowly recovered to colorless. The reaction was continued for 1 h at room temperature under stirring condition. The volatile components (solvent, TFA and TIPS) were distilled off under reduced pressure. The pale yellow residue was further purified by washing

with hexane (4x15mL). The solvent was removed under reduced pressure to yield compound **4** 0.2962 g (17.19% yield).

$^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  6.85 (m, 1H, H-Ar), 6.75 (m, 2H, H-Ar), 4.65 (s, 2H, -O-CH<sub>2</sub>-Ph), 4.60 (s, 2H, O -CH<sub>2</sub>-C(O)-), 3.85 (s, 3H, -OCH<sub>3</sub>), 2.25 (t, 2H, -S-CH<sub>2</sub>-), 2.10 (t, 2H, -CH<sub>2</sub>-C(O)), 1.90 (m, 2H, -CH<sub>2</sub>-), 1.70 (m, 2H, -CH<sub>2</sub>-), 1.40-1.10 (12H, -(CH<sub>2</sub>)<sub>6</sub>-).

### *Morphology of Au-PC-COOH*

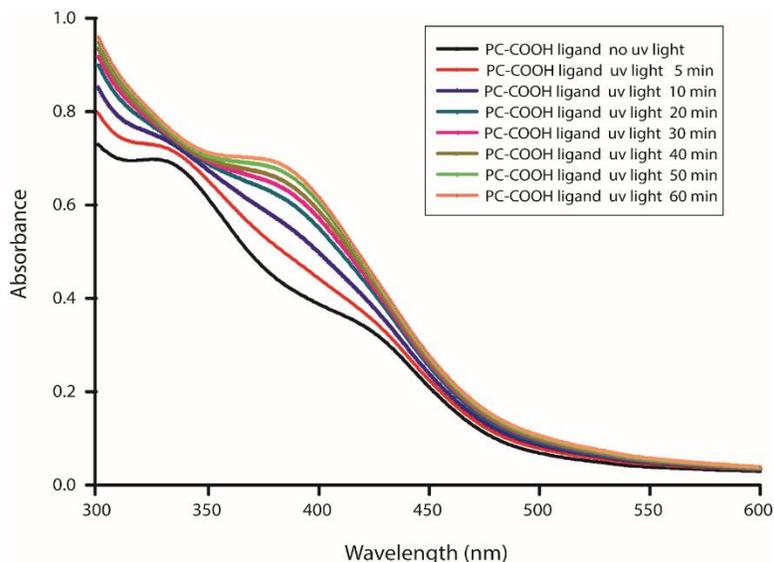
Figure S1 (a) showed the TEM image of Au-PC-COOH. The Au-PC-COOH have sizes between 1.6-2.6 nm. The size of Au-PC-COOH was determined from randomly selected images using the Image J program. The size of Au-PC-COOH particles was found to be  $2 \pm 0.2$  nm (Figure S1(b)). It was found that the Au-PC-COOH were well dispersed and no aggregation of nanoparticles was observed.



**Figure S1:** TEM images of Au-PC-COOH (b) the size distribution of Au-PC-COOH calculated using program Image J and randomly selected 100 particles.

### ***Photoresponsive property of PC-COOH ligand***

A solution of PC-COOH ligand (1 mg/mL, 3010  $\mu$ L) in PBS buffer was irradiated using a hand-held UV light source ( $\sim$ 365 nm) for one of several predetermined times (5, 10, 20, 30, 40, 50, and 60 min). After irradiation, the absorbance behavior of the solution between 300-600 nm was recorded. Upon exposure to UV light (365 nm), UV-vis spectra of a ligand solution changes were observed. The main peak at 380 nm increased with increasing irradiation time, indicating a photoreaction and release of nitroso benzaldehyde compounds.



**Figure S2:** UV-vis spectra of PC-COOH ligand (1 mg/mL) in PBS solution under UV irradiation at 365 nm for different time

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<sup>1</sup> Agasti, S. S.; Chompoosor, A.; You, C.-C.; Ghosh, P.; Kim, C. K. and Rotello, V. M.

“Photoregulated Release of Caged Anticancer Drugs from Gold Nanoparticles”

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