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Supporting Information for

Nanoscale UiO-MOFs-Based Luminescent Sensors for Highly Selective Detection

of Cysteine and Glutathione and Their Application in Bioimaging

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Section 1. Materials and instrumentation

All of the starting materials were purchased from J & K Chemical Technology, unless otherwise noted, and used without further purification. Infrared (IR) samples were prepared as KBr pellets, and spectra were obtained in the 400-4000 cm⁻¹ range using a Perkin-Elmer 1600 FTIR spectrometer. ¹H NMR data were collected using an AM-300 spectrometer. Chemical shifts are reported in δ relative to TMS. Fluorescence spectra were obtained withFLS-920 Edinburgh Fluorescence Spectrometer with a Xenon lamp. The scanning electron microscopy (SEM) micrographs were recorded on a Gemini Zeiss Supra TM scanning electron microscope. The X-ray diffraction (XRD) experiments were obtained on a D8 ADVANCE X-ray powder diffractometer with CuK α radiation (λ = 1.5405 Å). The Brunauer-Emmett-Teller (BET) surface area was measured on an ASAP 2020/TriStar 3000 (Micromeritics) using nitrogen adsorption at 77 K. Confocal fluorescence imaging studies were performed with a TCS SP5 confocal laser scanning microscopy (Leica Co., Ltd. Germany) with an objective lens (× 20). MS spectra were obtained on Thermo LCQ-Fleet machine.

Section 2. Ligands synthesis

1. Synthesis of H₂L1



The 1st step: dimethyl 2-aminobenzene-1,4-dioate (2 mmol, 0.418 g) and 2,5-furandione(2 mmol, 0.196 g) were added to ionic liquid [Bmin][PF₆] (2 mL). The mixture was stirred at 140°C for 2 h and cooled. The product was extracted with Et₂O (3×10 mL). The combined ethereal phase was evaporated under reduced pressure to give crude produce. The product was purified with column chromatography (silica gel, CH₂Cl₂) to give the ester as a white solid (0.536 g, yield: 90.4%). IR (KBr pellet cm⁻¹): 3476 (m), 3092 (m), 2958 (m), 1710 (s), 1441 (s), 1278 (s), 1213 (m), 1160 (w), 1121 (s), 1090 (s), 8328 (m), 710 (w). ¹HNMR (300 MHz, DMSO-*d*⁶, 25 °C, TMS, ppm): 8.15-

8.12 (d, 1H, -C₆H₃-), 8.11-8.08 (d, 1H, -C₆H₃-), 8.02 (s, 1H, -C₆H₃-), 7.26 (s, 2H, -CH=CH-), 3.90 (s, 3H, -CH₃), 3.75 (s, 1H, -CH₃).

The 2st step: a solution of KOH (3.0 g, 53.6 mmpl) in H₂O (10 mL) was added to the solution of carboxylic ester (0.50 g, 1.68 mmol) in THF (20 mL)/MeOH (20 mL) mixed solvent. This mixture was refluxed for 12 h. After cooling down to room temperature. THF and MeOH were removed in vacuum. Additional water was added to the resulting solution and the mixture was heated until the solid was fully dissolved, then the homogeneous solution was acidified with diluted HCl until no further precipitate was detected (pH<2). The yellowish powder (H₂L1) was collected by filtration, washing with water and drying in air (0.34 g, yield: 77.5%). IR (KBr pellet cm⁻¹): 2851 (s), 2571 (s), 1694 (s), 1620 (m), 1554 (s), 1446 (m), 1305 (m), 1230 (w), 979 (m), 909 (w), 764 (m). ¹HNMR (300 MHz, DMSO- d_6 , 25 °C,TMS, ppm): 13.15 (s, 1H, -COOH), 11.25 (S, 1H, -COOH), 9.01 (s, 1H,-C₆H₃-), 8.07-8.05 (d, 1H, -C₆H₃-), 7.71-7.69 (d, 1H, -C₆H₃-), 6.62-6.58 (d, 1H, -CH=CH-), 6.33-6.29 (d, 1H, -CH=CH-).

2. Synthesis of H₂L2



The 1st step: 3-Amino-dimethyl biphenyl-4,4'-dicarboxylate (2 mmol, 0.570 g) and 2,5furandione (2 mmol, 0.196 g) were added to ionic liquid [Bmin][PF₆] (2 mL). The mixture was stirred at 140°C for 2 h and cooled. The product was extracted with Et₂O (3 × 10 mL). The combined ethereal phase was evaporated under reduced pressure to give crude produce. The product was purified with column chromatography (silica gel, CH2Cl2) to give the ester as a white solid (0.638 g, yield: 87.4%). IR (KBr pellet cm⁻¹): 3109 (m), 2952 (m), 1715 (s), 1606 (w), 1437 (s), 1288 (s), 1208 (m), 1153 (w), 1110 (w), 828 (w), 763 (w), 694 (w), 466 (w). ¹HNMR (300 MHz, DMSO-*d*⁶, 25 °C,TMS, ppm): 8.15-8.12 (d, 1H, -C6H3-), 8.07 (s, 1H,-C₆H₃-), 7.98-7.95 (d, 2H,

-C₆H₄-), 7.71-7.68 (d, 1H, -C₆H₃-), 7.35-7.32 (d, 2H, -C₆H₄-), 7.07 (s, 2H, -CH=CH-), 3.90 (s, 3H, -CH₃), 3.85 (s, 1H, -CH₃).

The 2st step: The carboxylic ester (0.50 g, 1.37mmol) was stirred in THF (20 mL) and MeOH (20 mL) mixed solvent, to which a solution of KOH (3.0 g, 53.6 mmpl) in H₂O (10 mL) was introduced. This mixture was refluxed for 12 h. After cooling down to room temperature. THF and MeOH were evaporated in vacuum. Additional water was added to the resulting solution and the mixture was heated until the solid was fully dissolved, then the homogeneous solution was acidified with diluted HCl until no further precipitate was detected (pH<2). The yellowish powder (H_2L2) was collected by filtration, washing with water and drying in air (0.37 g, yield: 80.1%). IR (KBr pellet cm⁻¹): 3109 (m), 2953 (m), 1715 (s), 1606 (w), 1437 (s), 1370 (w), 1288 (s), 1208 (s), 1153 (m), 1110 (m), 828 (w),763 (w), 694 (w), 637 (w), 466 (w).¹HNMR (300 MHz, DMSO- d^6 , 25 °C, TMS, ppm): 12.93 (s, 1H, -COOH), 9.96 (S, 1H, -COOH), 8.22 (s, 1H, -C₆H₃-), 8.01-7.99 (d, 2H, -C₆H₄-), 7.88-7.85 (d, 1H, -C₆H₃-), 7.54-7.49 (d, 2H, -C₆H₄-), 7.51-7.49 (d, 1H, -C₆H₃-), 6.45-6.41 (d, 1H, -CH=CH-), 6.23-6.19 (d, 1H, -CH=CH-).

Section 3. Synthesis of Mi-UiO-66 and Mi-UiO-67

Synthesis of Mi-UiO-66: acetic acid (120 μ L) was added to a solution of ZrCl₄ (9.60 mg, 0.040 mmol) and H₂L1 (10.7 mg, 0.040 mmol) in DMF (1.6 mL). The mixture was heated to 120 °C for 24 h and then cooled to room temperature. The product was collected by centrifugation and washed with DMF three times. After that, the obtained yellowish powder was soaked in fresh DMF at 80 °C for 6 h, then in alcohol at 60 °C for 2 days with replacing the soaking solvent every 12 h to exchange alcohol. Finally, the product was washed three times with alcohol and dried at 80 °C in an oven.

Synthesis of Mi-UiO-67: HCl (250 μ L conc.) was added to a solution of ZrCl₄ (45 mg, 0.20 mmol) in DMF (2.5 mL). The resulting mixture was sonicated for 20 min until fully dissolved. The reaction was diluted with DMF (5 mL) and **H₂L2** (67.4 mg, 0.20 mmol) was added. The mixture was heated in an oven at 80 °C for 12 h and then cooled to room temperature. The product was collected by centrifugation and washed with DMF three times. After that, the obtained

yellowish powder was soaked in fresh DMF at 80 °C for 6 h, then in alcohol at 60 °C for 2 days with replacing the soaking solvent every 12 h to exchange alcohol. Finally, the product was washed three times with alcohol and dried at 80 °C in an oven.

Reaction of Mi-UiO-66 and Mi-UiO-67 with Cys and GSH: nano-sized Mi-UiO-66 or Mi-UiO-67

(15 mg) were immersed in aqueous solution of Cys or GSH (0.2 %) for 2 h, the resulting solids were collected by centrifugation, washed by water (2 times) and dried in air. The elemental analysis (based on N/S ratios) indicated that the thiolated yields are 69.7 (**Mi-UiO-66** + Cys), 54.7 (**Mi-UiO-66** + GSH), 76.0 (**Mi-UiO-67** + Cys), and 58.4 % (**Mi-UiO-67** + GSH), respectively.

Section 4. Theoretical calculation

The structures of H₂L1, H₂L1', H₂L2 and H₂L2' were optimized at the B3LYP level of density functional theory (DFT) with 6-31G** basis set by using Gaussian 09 software.¹ Frequency calculations were carried out to confirm each structure is a local minimum. Evident intramolecular charge transfer (ICT) effects were observed at H₂L1' and H₂L2' compared with H₂L1 and H₂L2, indicating increases of luminescence intensity after introduction of Cys substituent group.

Section 5. Cell culture and treatments

The HeLa and ECV304 cell lines were provided by Institute of Basic Medicine, Shandong Academy of Medical Sciences (China). The cells were grown in RPMI-1640 (Invitrogen, CA, USA) containing 10 % heat-inactivated new born calf serum and 100U/mL penicillin, 100 mg/mL streptomycin in an atmosphere of 5 % CO₂, 95 % air at 37 °C. For confocal fluorescence imaging, cells were incubated in glass bottom dishes for 24 h. Cells were incubated at 37 °C with **Mi-UiO-66** or **Mi-UiO-67** (10^{-4} mg/mL) in PBS (Phosphate Buffered Saline) for 1 h, washed with PBS and fluorescence images were captured. In a control experiment, Hale cells were pre-treated with N-ethylmaleimide (500 μ M) for 20 min in an atmosphere of 5 % CO₂, 95 % air at 37 °C, and then washed with PBS. These cells were further loaded with **Mi-UiO-66** or **Mi-UiO-67** (10^{-4} mg/mL) for 1 h, washed with PBS. Samples were excited at 405 nm and observed between 500-550 nm.

Section 6. The products characterization of esterified H_2L1 and H_2L2 with Cys and GSH



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Fig. S1 MS spectra of the thiolated products of the esterified H₂L1 and H₂L2 with Cys and GSH.

Section 7. SEM images of Mi-UiO-66 and Mi-UiO-67



Fig. S2 SEM images of Mi-UiO-66 and Mi-UiO-67.

Section 8. Brunauer-Emmett-Teller (BET) plots for Mi-UiO-66 and Mi-UiO-67



Fig. S3 Left: the Brunauer-Emmett-Teller (BET) plot for **Mi-UiO-66** in the chosen range ($P/P_0 = 0.07 - 0.20$). Right: the Brunauer-Emmett-Teller (BET) plot for **Mi-UiO-67** in the chosen range ($P/P_0 = 0.07 - 0.20$).



Section 9. Detecting limits of Mi-UiO-66 and Mi-UiO-67 for Cys and GSH

Fig. S4 The reactions of NMOFs with Cys and GSH at different concentrations, the good linearity between relative luminescent intensities and concentrations of RSH species in the range of 10^{-11} - 10^{-3} M were observed (with the linear coefficient of 0.9902-0.9923), indicating that the detecting limit for Cys and GSH based on the proposed method is ca. 10^{-11} M.







Fig. S5 XRPD patterns of Mi-UiO-66 and Mi-UiO-67 during the sensing processes.

Reference

M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G. A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H. P. Hratchian, A. F. Izmaylov, J. Bloino, G. Zheng, J. L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, J. A. Montgomery, Jr., J. E. Peralta, F. Ogliaro, M. Bearpark, J. J. Heyd, E. Brothers, K. N. Kudin, V. N. Staroverov, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, N. Rega, J. M. Millam, M. Klene, J. E. Knox, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, R. L. Martin, K. Morokuma, V. G. Zakrzewski, G. A. Voth, P. Salvador, J. J. Dannenberg, S. Dapprich, A. D. Daniels, Ö. Farkas, J. B. Foresman, J. V. Ortiz, J. Cioslowski, and D. J. Fox, Gaussian, 09, Revision D.01, Gaussian, Inc., Wallingford CT, 2009.