Supporting Information (SI)

Click synthesis of a novel triazole bridged AIE active cyclodextrin probe for specific detection of Cd^{2+}

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Contents

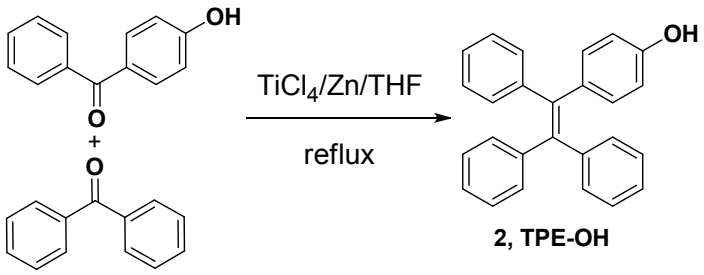
A. Chemicals and Instruments

Diphenyl ketone, 4-hydroxy diphenyl ketone, propargyl bromide and tetrabutyl ammonium bromide were purchased from HEOWNS (Tianjin, China). Sodium azide, $CuSO_4 \cdot 5H_2O$ and pyridine were purchased from Tianjin Chemical Regents (Tianjin, China). Tetrahydrofuran (THF) and dimethylsulfoxide (DMSO) were purchased from JiangTian chemical reagents (Tianjin, China). Ascorbic acid sodium salt was provided by Energy-Chemical (Shanghai, China). Mono-6^A-deoxy-(*p*-tosylsufonyl)-β-cyclodextrin (TsO-CD) was synthesized according to the reported procedure[1]. THF was distilled from sodium and benzophenone ketyl prior to use. Other chemicals were of analytical grade and used without further purification. The metal salts which used for selectivity study were $PbCl_2$, $ZnCl_2$, $CoCl_2$, $FeCl_3$, $MgCl_2$, $CaCl_2$, KCl, $CuCl_2$, $CdCl_2$, $HgCl_2$, NaCl, NH_4Cl, $Al(NO_3)_3$, $AgNO_3$. Deionized water was used in the experiments.

^1H, ^{13}C and 2D ROSEY NMR were recorded on a Bruker ACF400 (400MHz) supplied by Bruker Biospin (Fällanden, Switzerland) in deuterated chloroform ($CDCl_3$), dimethylsulfoxide (DMSO-d_6) or D_2O using tetramethylsilane (δ=0) as internal reference. Fourier-transform infrared (FTIR) spectra were collected on an AVATR360 supplied by Thermo Nicolet (USA). Mass spectra were recorded on LCQ Deca XP MAX system (Thermo Fisher, USA). High resolution mass spectra (HPMS) were measured on a miorOTOF-QII supplied by Bruker Daltonics (USA). The fluorescence spectra were taken on a Cary Eclipse fluorescence spectrophotometer supplied by Varian (USA) at room temperature. Particle size distribution analysis were carried out on a Delsa NaNo C provided by Beckman Coulter (USA). TEM-EDX were taken on a FEI Tecnai G2 F20 TEM (Holland) with EDX equipment at an accelerating voltage of 200 kV. The morphologies of aggregates of compounds in nano-scale were determined on a JEM-2100F supplied by Japan at an accelerating voltage of 200 kV. TEM samples were collected by copper mesh.

B. Synthesis and characterization

1. Synthesis of 1-(4-hydroxyphenyl)-1,2,2-triphenylethylene



Under an nitrogen atmosphere, a three-necked flask equipped with a magnetic stirrer was charged with zinc powder (1.6 g, 24 mmol) and 40 mL dry THF. The mixture was cooled to -5 to 0 ^oC, and $TiCl_4$ (1.3 mL, 12mmol) was slowly added by a syringe with the temperature kept under 10 ^oC. The suspending mixture was warmed to room temperature and stirred for 0.5 h, then heated at reflux for 2.5 h. The mixture was again cooled to -5 to 0 ^oC, charged with pyridine (0.5 mL, 6 mmol) and stirred for

10 min. The solution of diphenyl ketone and 4-hydroxy diphenyl ketone [in 1:1.2 mole ratio, 2.4 mmol] in 15 mL THF was added slowly. After addition, the reaction mixture was heated at reflux until the carbonyl compounds were consumed (monitored by TLC). The reaction was quenched with 10% K_2CO_3 aqueous solution and taken up with CH_2Cl_2. The organic layer was collected. After solvent evaporation, the crude product was purified on a silica gel column using ethyl acetate/petroleum ether (1:10 to 1:7, v/v) as eluent to give the desired product as a white powder in a yield of 76%. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 4.82 (s, 1H), 6.56 (d, 2H), 6.90 (d, 2H), 6.98-7.16 (m, 15H); ^{13}C NMR (400 MHz, $CDCl_3$): δ (ppm) 114.63, 126.42, 126.60, 127.65, 127.75, 131.36, 131.38, 131.40, 132.76, 136.37, 140.21, 140.48, 143.93, 143.94, 144.04, 154.08; ESI (+)-MS: calcd. for $C_{26}H_{20}O$: 347 [M]; found 348.9 $[M+H]^+$; IR (ν, KBr): 1246, 1441, 1516 and 3345 cm^{-1}.

2. Synthesis of TPE-alkyne

The mixture of compound **2** (0.45 g, 1.3 mmol), propargyl bromide (0,225 mL, 1.95 mmol), K_2CO_3 (0.699 g, 5.07 mmol) and NBu_4Br (3.2 mg, 0.001 mmol) in acetone (15 mL) was refluxed overnight under nitrogen. The mixture was then filtered and dried over anhydrous $MgSO_4$. After the solvent evaporation, the crude product was purified by a silica gel column using ethyl acetate/petroleum ether (1:10, v/v) as eluent affording a light yellow syrup in a yield of 95%. ^{1}H NMR (400MHz, $CDCl_3$): δ (ppm) 2.52 (s, 2H), 4.83 (d, 4H), 6.72 (m, 2H), 6.96 (m, 2H), 7.14-7.03 (m, 15H). ^{13}C NMR (400 MHz, $CDCl_3$): δ (ppm) 55.8, 75.4, 78.6, 113.6, 126.5, 127.6, 131.3, 132.5, 137.1, 140.6, 156.3. ESI (+)-MS: calcd. for $C_{29}H_{22}O$: 386 [M]; found 387.5 $[M+H]^+$.

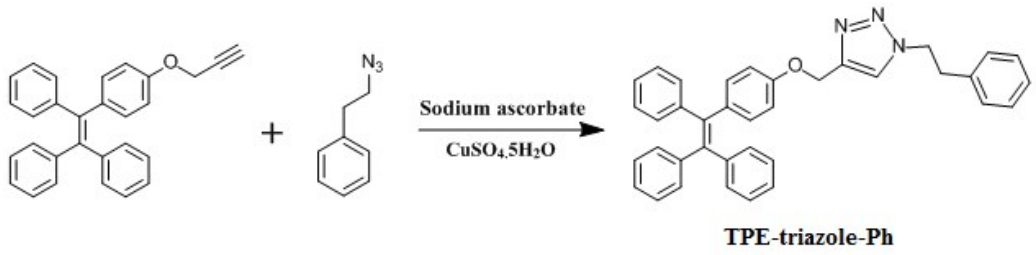
3. Synthesis of mono-(6-azido-6-deoxy)-β-CD

NaN_3 (1.26 g, 19.4 mmol) was added to a solution of TsO-CD (5 g, 3.88 mmol) in water (50 mL). The reaction mixture was stirred at 80 ^{o}C for 12 h, then the clear solution was poured in acetone (300 mL). The white precipitate was isolated by filtration and washed with acetone to afford mono-(6-azido-6-deoxy)-β-CD with a yield of 97%. ^{1}H NMR (DMSO-*d*$_6$): δ (ppm): 5.9-5.6 (14H), 5.0-4.8 (7H), 4.6-4.4 (6H), 3.8-3.2 (42H). IR (ν, KBr): 3357, 2928, 2107, 1032 cm^{-1}; ESI (+)-MS: calcd. for $C_{42}H_{70}O_{34}N_3$: 1160 [M]; found 1161.1 $[M+H]^+$.

4. Synthesis of TPE-Triazole-CD *via* click chemistry

Mono-(6-azido-6-deoxy)-β-CD (1.454 g, 1.46 mmol) was added to a solution of **3** (0.88 g, 2.2 mmol) in DMF (30 mL) followed by addition of $CuI(PPh_3)$ (99.5 mg, 0.22 mmol) in one portion. The reaction mixture was stirred at 90 ^{o}C for 2 days under nitrogen atmosphere. After removing the solvent, the crude product was purified by flash chromatography using silica gel with water and acetonitrile (1:2, v/v) as the eluent. Yellow solid was obtained in a yield of 90%. ^{1}H NMR (400 MHz, DMSO-*d*$_6$) δ (ppm): 3.99 (s, 1H), 4.27 (s, 1H), 4.46-4.52 (m, 4H), 4.77-5.09 (m, 8H), 5.64-5.90 (m, 14H), 6.19 (d, 2H), 6.95 (d, 2H), 7.01-7.19 (m, 15H), 8.14 (s, 1H). ^{13}C NMR (400 MHz, DMSO-*d*$_6$) δ (ppm): 60.4, 72.8, 82.1, 102.5, 114.4, 126.0, 126.1, 126.9, 128.4, 131.2, 132.4, 136.2, 140.3, 140.7, 142.9, 143.9, 157.2. IR (ν, KBr): 3379.53, 2930.44, 1411.74, 1155.08 and 1032.89 cm^{-1}. ESI (+)-HR-MS: calcd. for $C_{71}H_{92}O_{35}N_3$: 1546 [M]; found 1568.5270 $[M+Na]^+$.

5. Synthesis of TPE-Triazole-Ph *via* click chemistry



To a solution of **3** (340 mg, 0.88 mmol) in THF (5 mL), azide ethyl benzene (117 mg, 0.8 mmol) in THF (5 mL) was added with stirring. To the resulting solution, $CuSO_4 \cdot 5H_2O$ (5.5 mg) and then sodium ascorbate (87 mg) dissolved in water (2 mL) were added. The color of the mixture turned brown immediately and then dark purple in a few minutes. The solution was heated at about 65 °C for 18 h. The reaction mixture was diluted with H_2O (5 mL) and extracted with CH_2Cl_2 (3 x 20 mL). The combined organic phases afforded. After solvent evaporation, the crude product was purified by a silica gel column using ethyl acetate/petroleum ether (1:2, v/v) as eluent affording a white solid in a yield of 85%. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 3.16 (m, 2H), 4.62 (m, 2H), 5.02 (s, 2H), 6.75 (d, 2H), 6.85 (d, 2H), 6.95-7.21 (m, 20H), 8.12 (s, 1H). IR (ν, KBr): 3075.28, 1503.66, 1242.46, 1024.56 cm^{-1}. ESI (+)-MS: calcd. for $C_{37}H_{31}N_3O$: 533 [M]; found 555.9 $[M+Na]^+$.

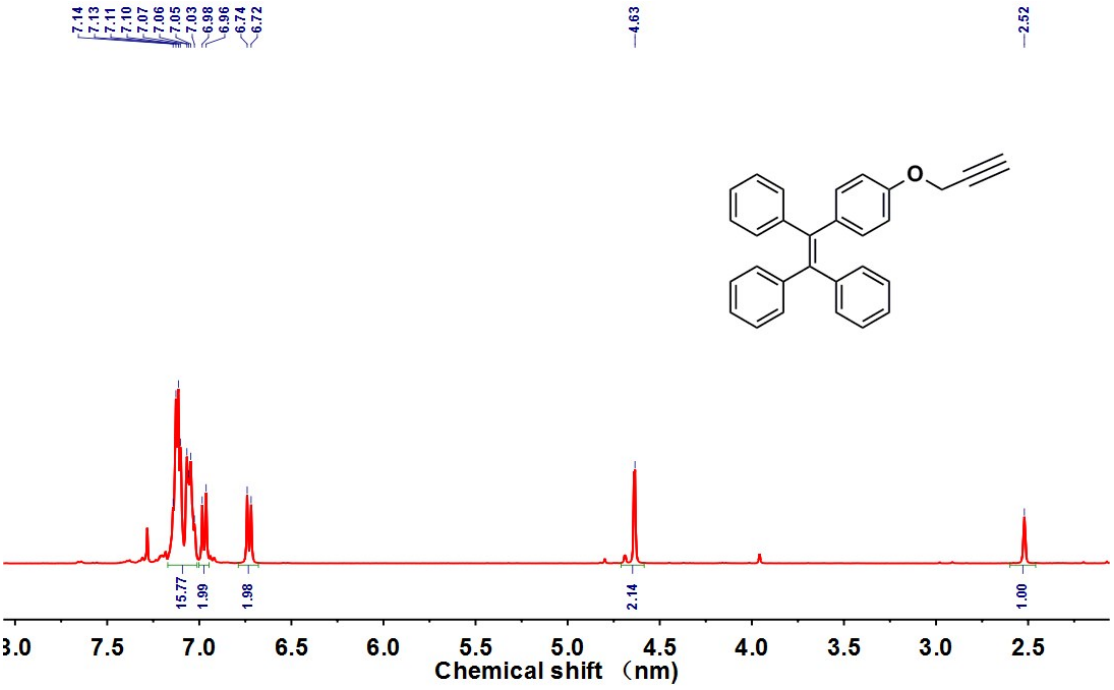


Fig. S1. ^{1}H NMR of TPE-alkyne in $CDCl_3$.

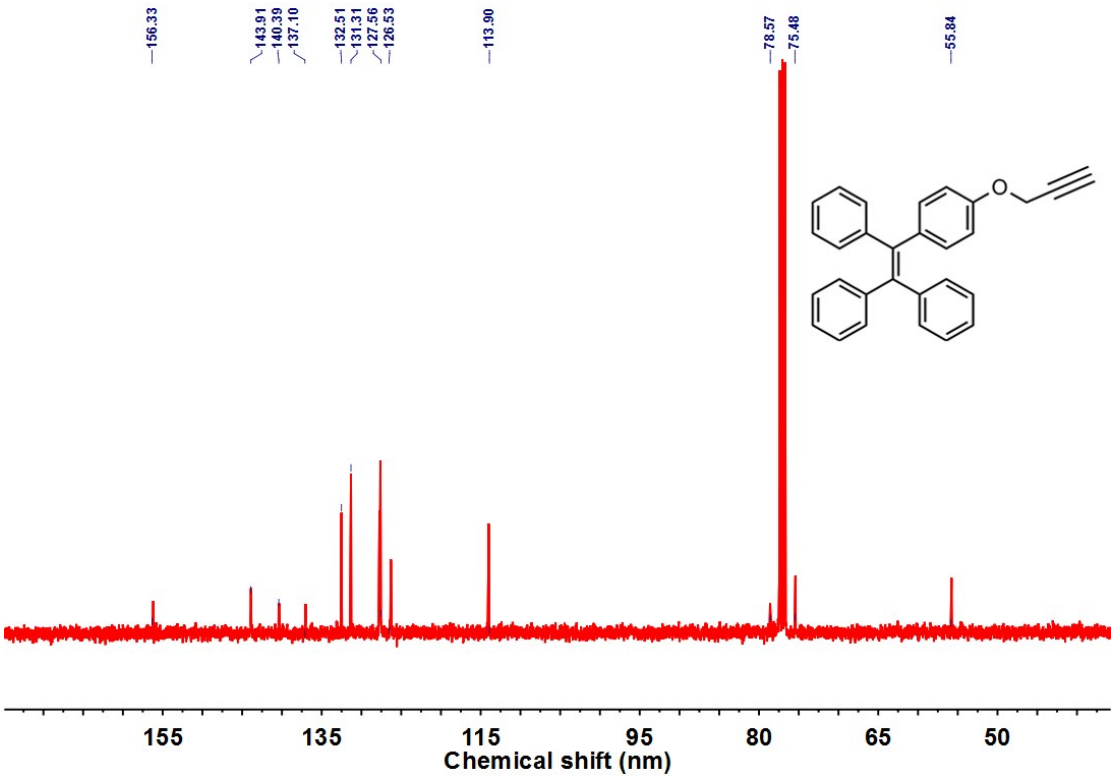


Fig. S2. ^{13}C NMR of TPE-alkyne in $CDCl_3$

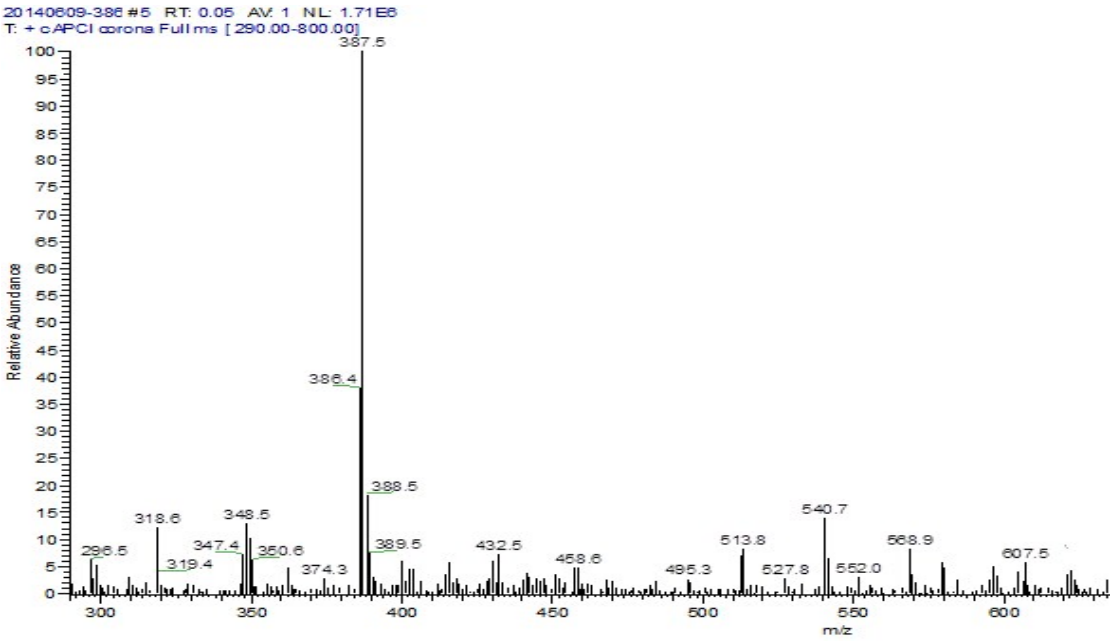


Fig. S3. Mass spectra of TPE-alkyne

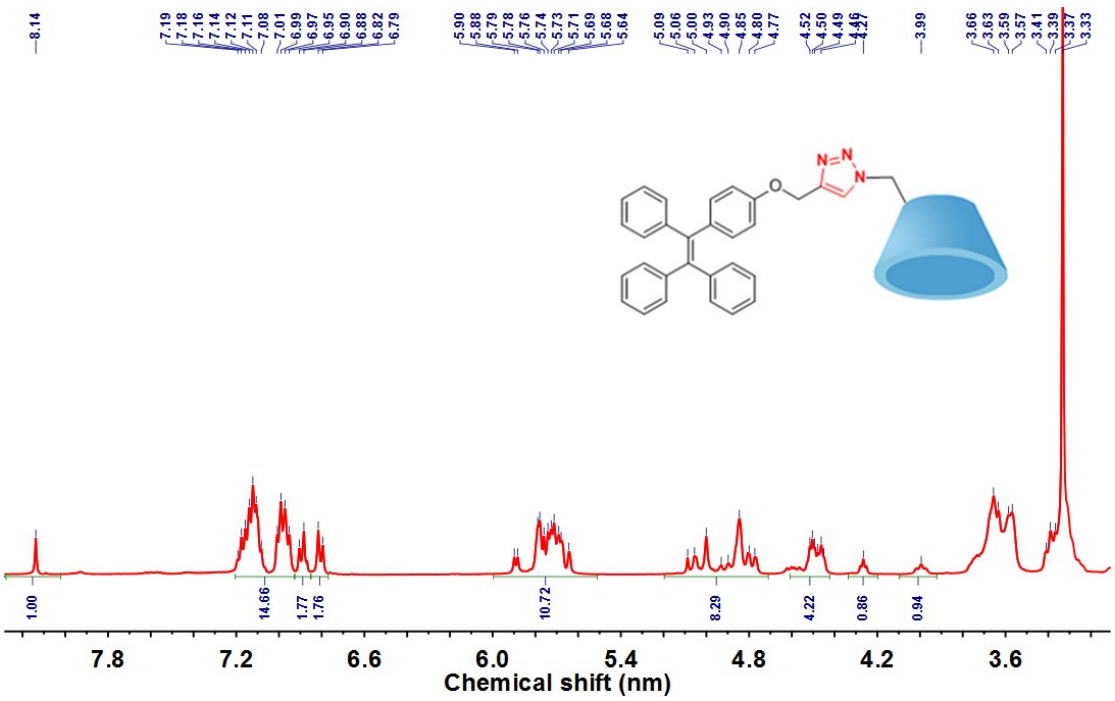


Fig. S4. ^{1}H NMR of TPE-triazole-CD in DMSO-d_6

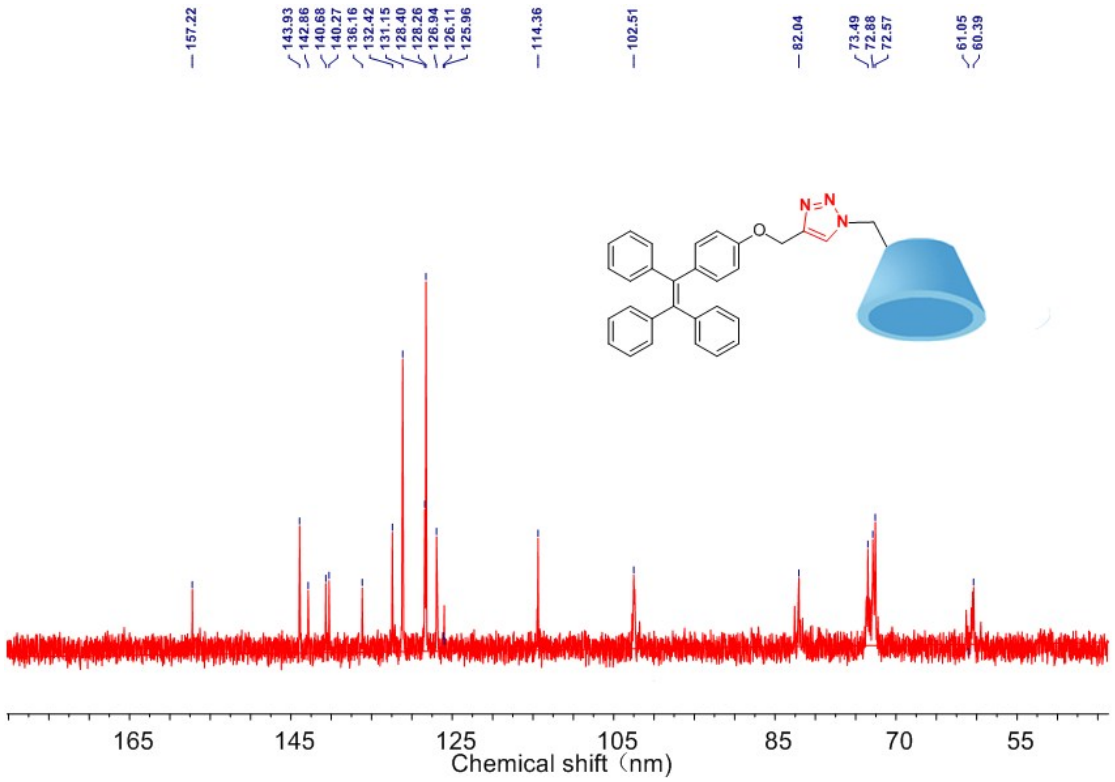


Fig. S5. ^{13}C NMR of TPE-triazole-CD in DMSO-d_6

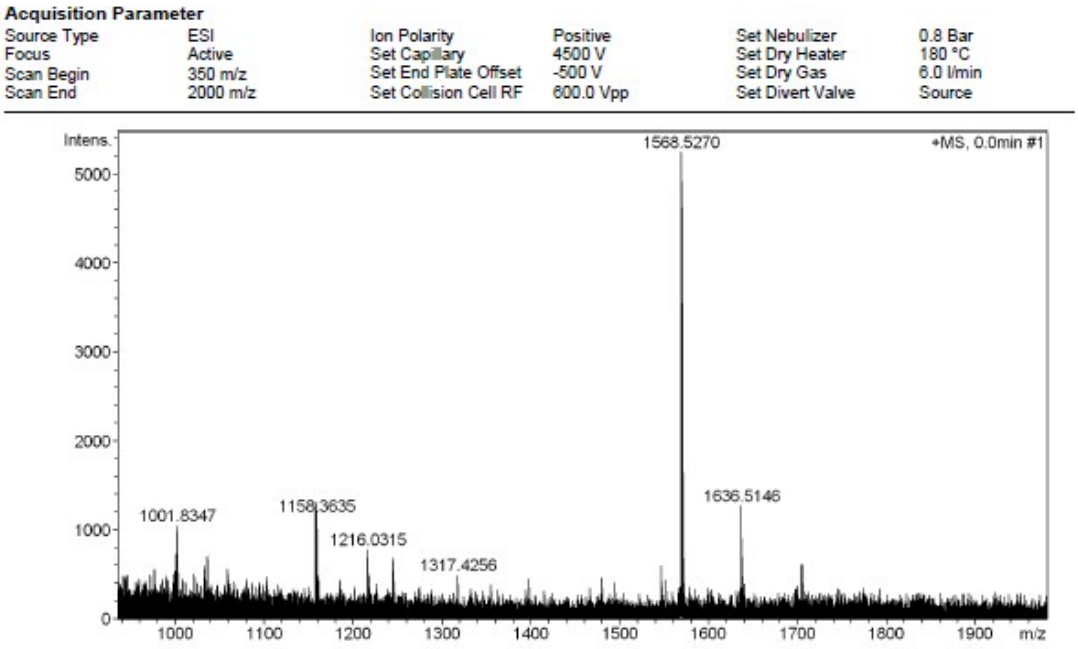


Fig. S6. High resolution mass spectra of TPE-triazole-CD

C. Analytical Data

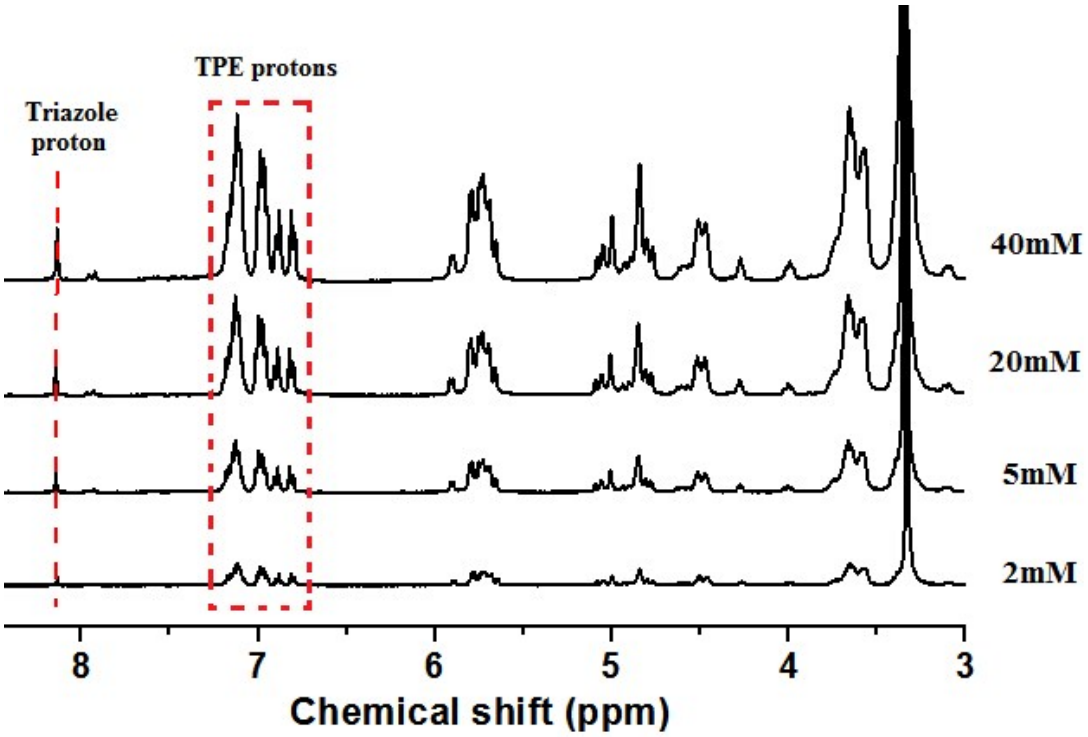


Fig. S7. [1] H NMR spectra of TPE-triazole-CD in DMSO-d_6. Solution concentration: 2 mM, 5 mM, 20 mM, 40 mM from bottom to top.

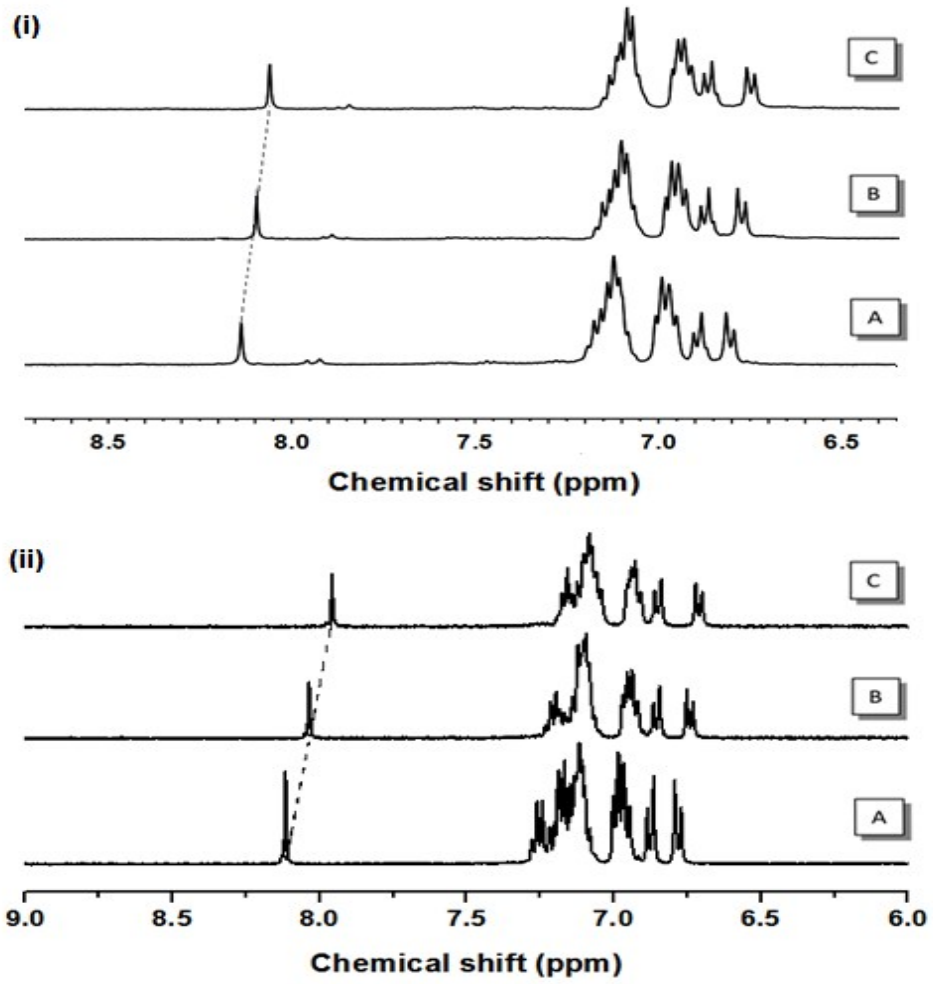


Fig. S8. ^{1}H NMR of (i) TPE-triazole-CD (2 mM) and (ii) TPE-triazole-Ph in DMSO-d_6/D_2O mixture. (The volume fraction of water: A. 0%; B. 10%; C. 20%).

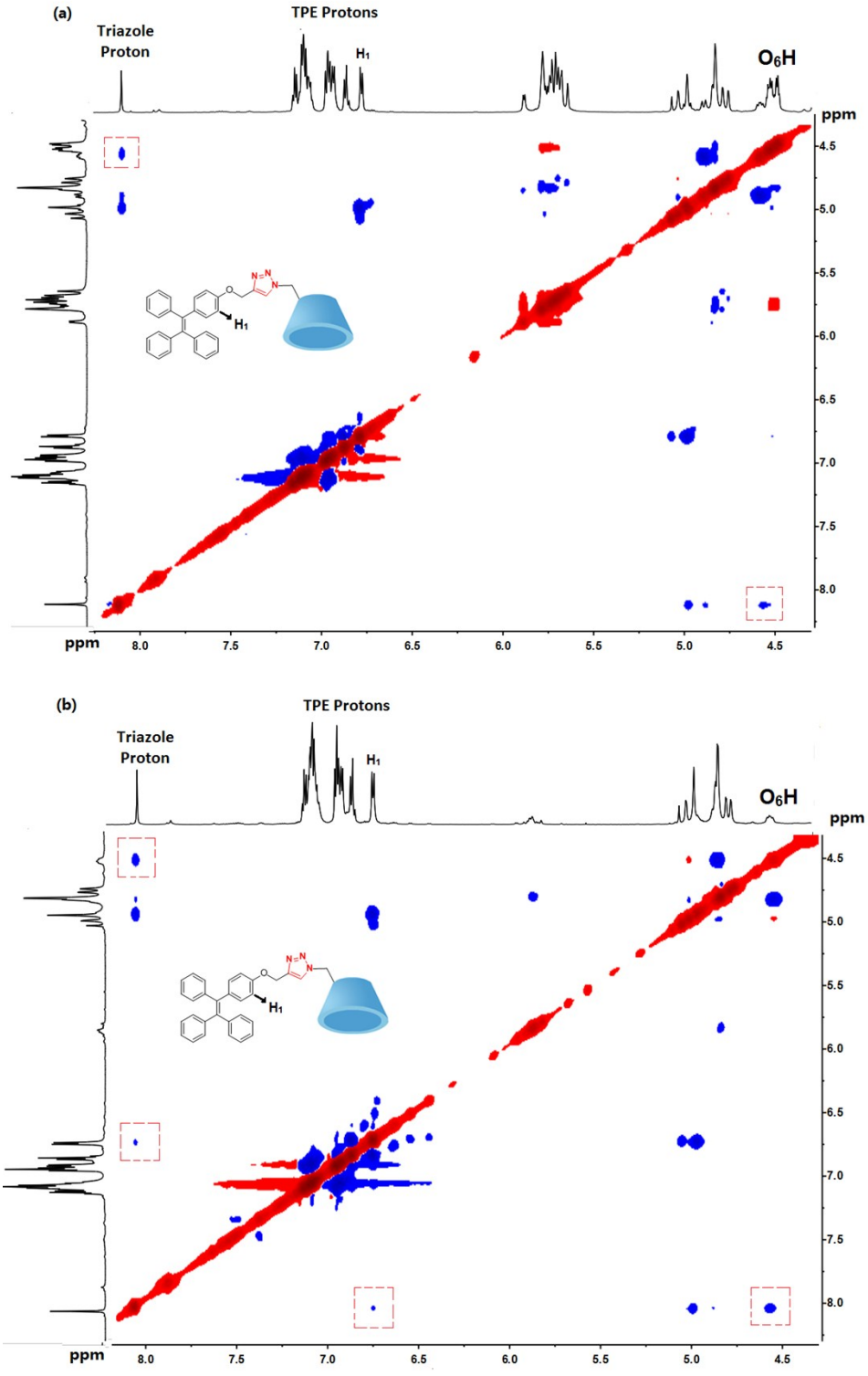


Fig. S9. 2D ROESY NMR spectra of TPE-triazole-CD in DMSO-d_6/D_2O mixture. (The volume fraction of water: A. 0%; B. 25%).

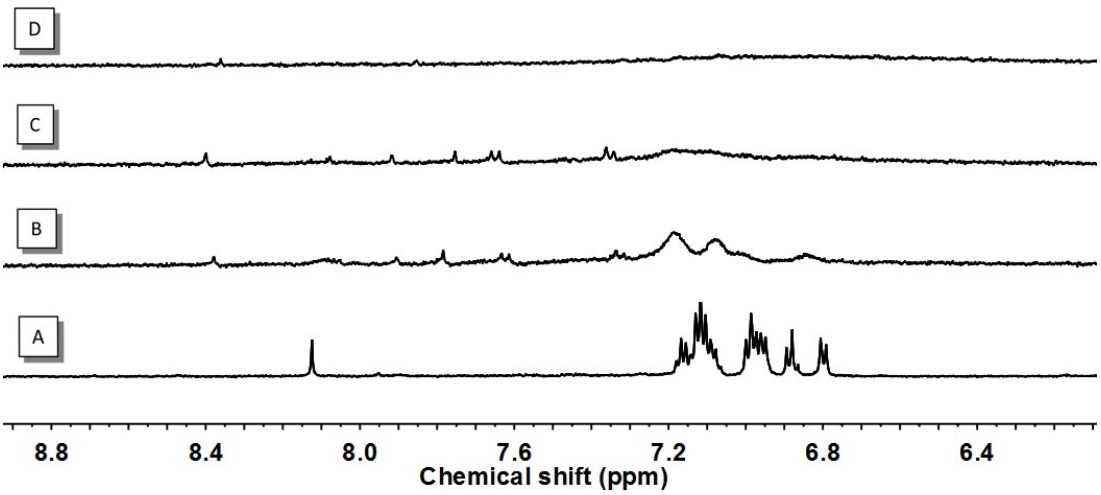


Fig. S10. ^{1}H NMR of TPE-triazole-CD (2 mM) in DMSO-d_6/D_2O mixture. (The volume fraction of water: A. 0%; B. 60%; C. 80%; D. 95%).

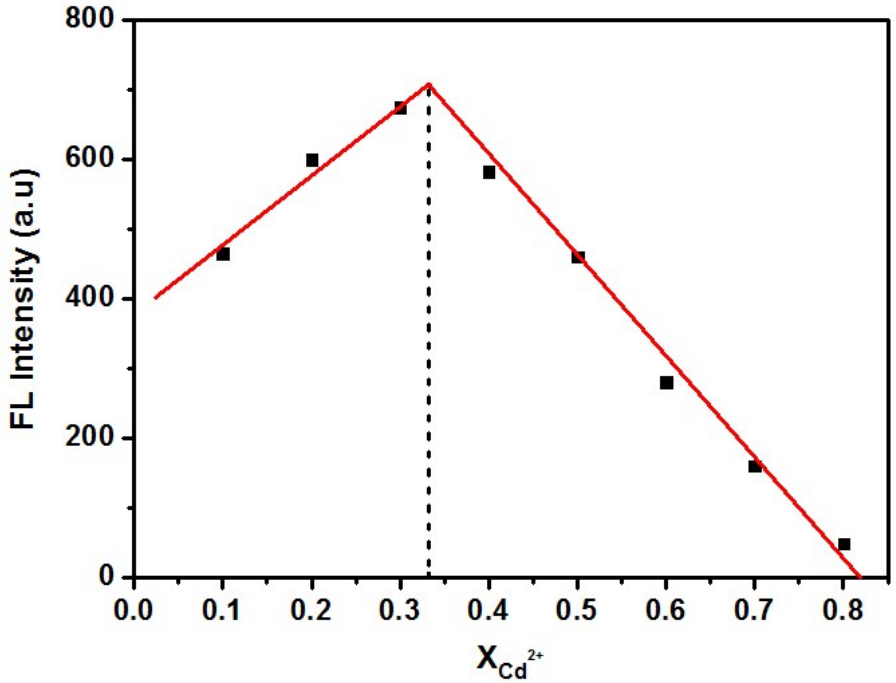


Fig. S11. Job's plot for evaluating the chelating ratio of probe **1** to Cd^{2+}. The total concentration of **1** and Cd^{2+} was 30 μM. The wavelength of absorbance was 476 nm.

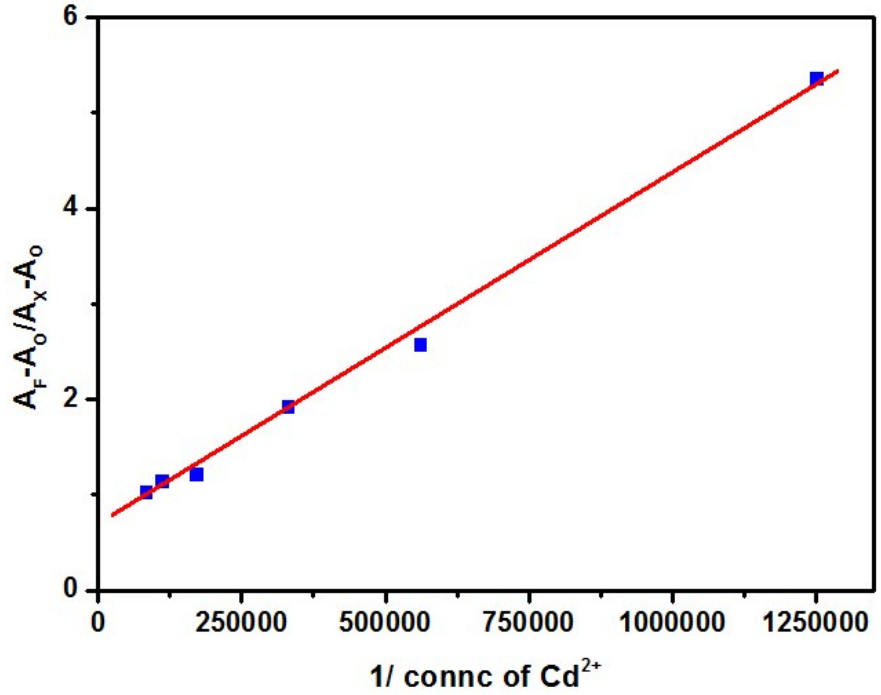


Fig. S12. Calculation of binding constant for Cd^{2+} with probe **1** from the plot $(A_F-A_0)/(A_X-A_0)$ vs $1/[Cd^{2+}]$.

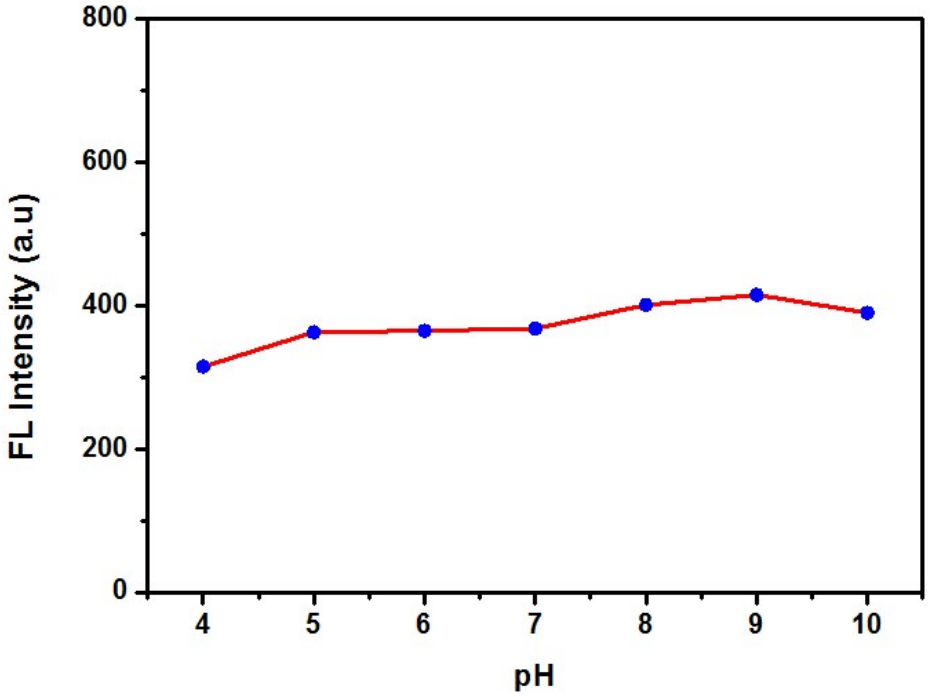


Fig. S13. Fluorescence intensity change of **1** (25 μM) after addition of Cd^{2+} (12 μM) in 10 mM Tris-HCl buffer with a pH range of 4.0-10.0.

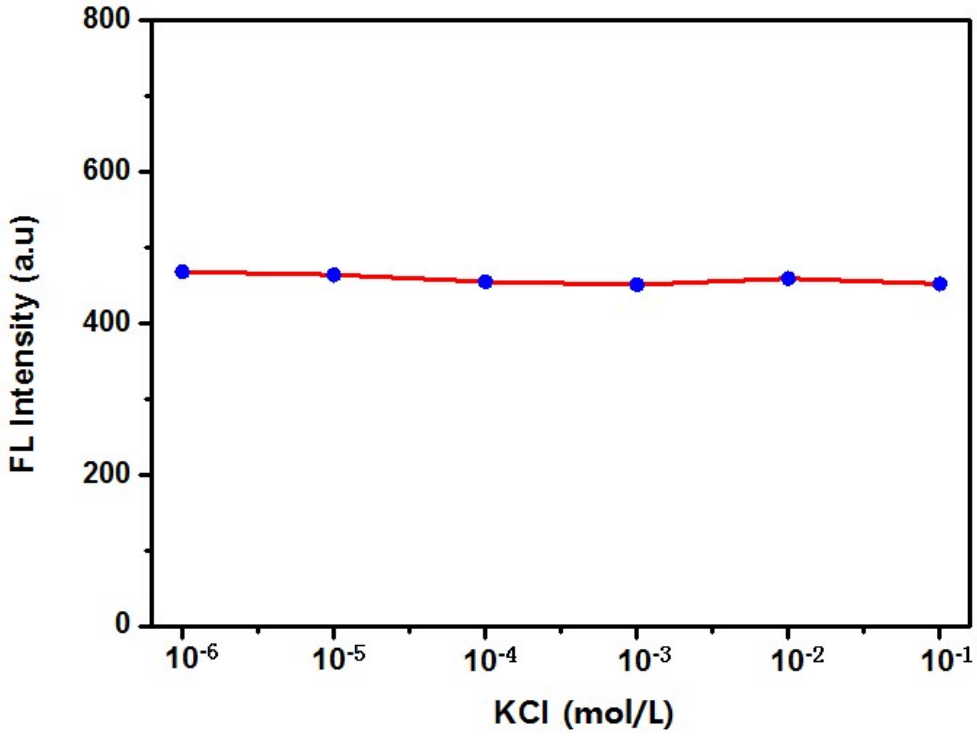


Fig. S14. Fluorescence response of **1** (25 μM) to Cd^{2+} (12 μM) upon addition of various concentrations of KCl (10^{-6}-10^{-1}M) in 10 mM Tris-HCl buffer at pH 7.0.

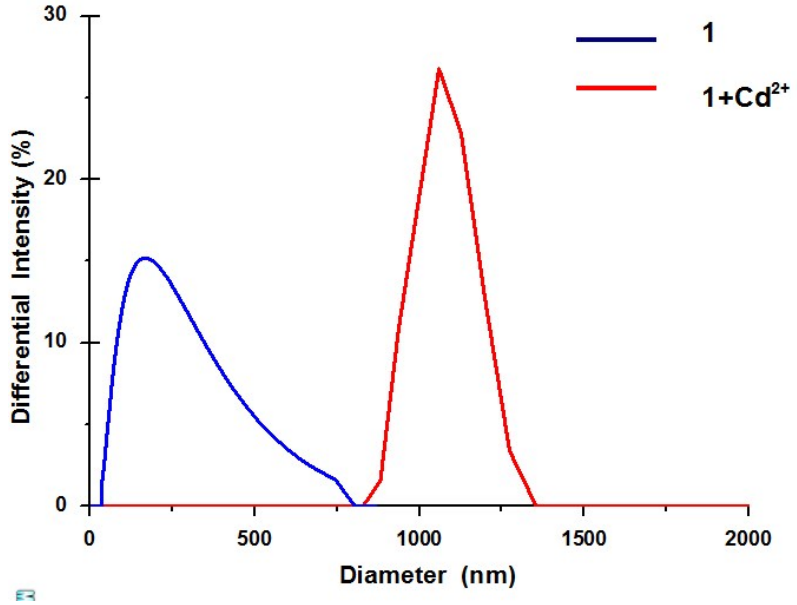


Fig. S15. Particle size distribution of TPE-triazole-CD (100 μM) in DMSO/H_2O (1/1, v/v) solution before and after addition of Cd^{2+} (0.5 equiv).

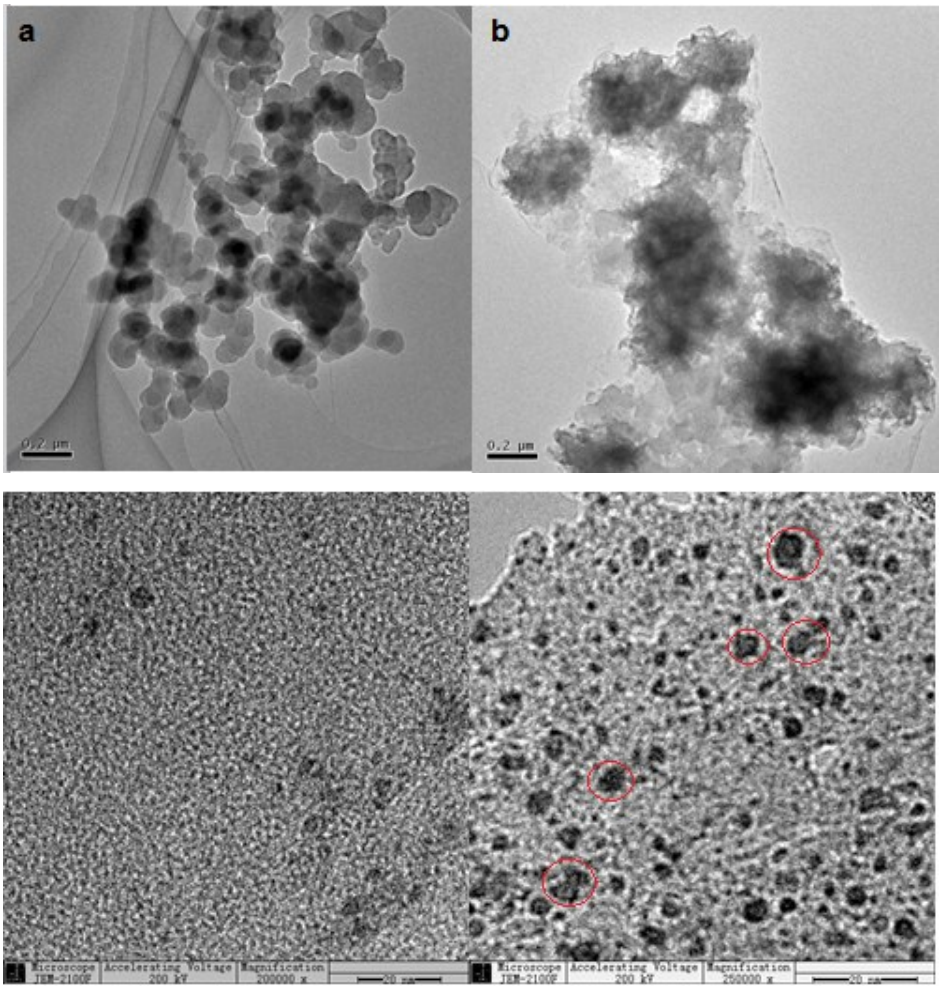


Fig. S16. TEM images sensor **1** (100 μM) in DMSO/H_2O (1:1, v/v) before (left) and after (right) addition of 0.5 equiv Cd^{2+}.

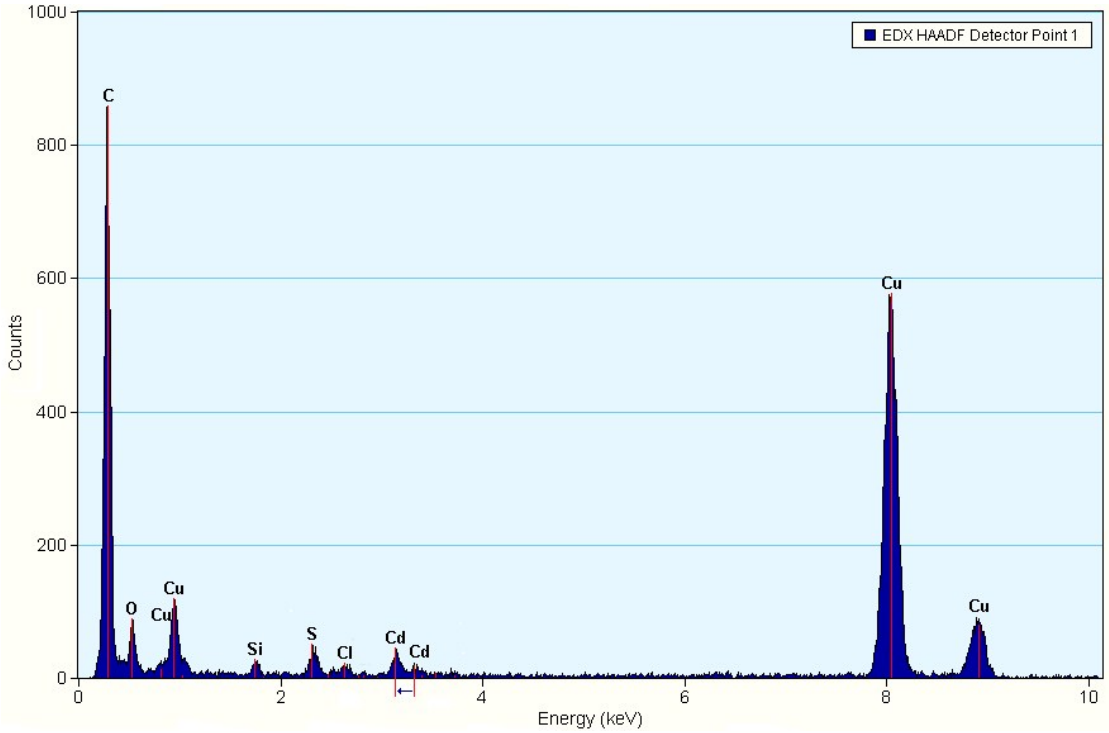


Fig. S17. Energy dispersive X-ray (EDX) spectrum of **1** in the presence of 0.5 equiv Cd^{2+}.

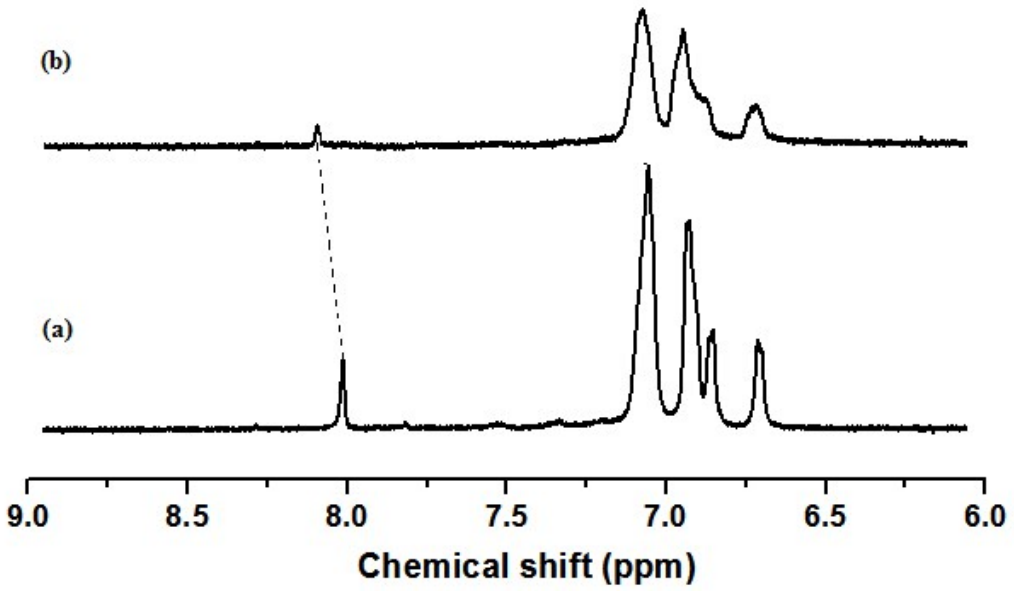


Fig. S18. ^{1}H NMR spectra change of **1** (a) in the absence of and (b) in the presence of 0.5 equiv of Cd^{2+} in DMSO-d_6/D_2O (v/v, 1:1) ([**1**] = 1.0×10^{-3} M, [Cd^{2+}] = 5.0×10^{-4} M).

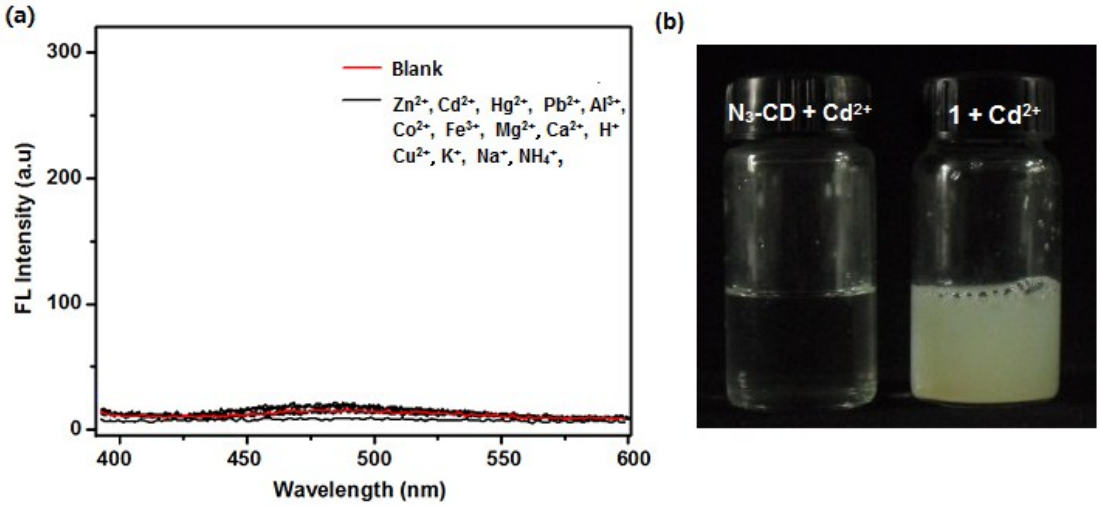


Fig. S19. (a) FL spectra of TPE-triazole-Ph (10 μM) in the presence of different metal ions (30 μM) in THF/H_2O=1:9 (v/v); (b) The images of N_3-CD and **1** under daylight in DMSO-H_2O (1/1, v/v) (100 mM) upon addition of 0.5 equiv of Cd^{2+}.

5. References

1. Y. Wang, H. Chen, Y. Xiao, C. H. Ng, T. S. Oh, T. T. Y. Tan and S. C. Ng, *Nat. Protoc.*, 2011, **6**, 935.