Supporting Information

For

Zn^{2+}–Triggered Amide Tautomerization Produces a Highly Zn^{2+}–Selective, Cell–Permeable and Ratiometric Fluorescent Sensor

Zhaochao Xu,[*†,‡] *Kyung-Hwa Baek,*[§] *Ha Na Kim,*[†] *Jingnan Cui,*[||] *Xuhong Qian,*[⊥] *David R. Spring,*[‡] *Injae Shin,*[*§] *and Juyoung Yoon*[*†]

Department of Chemistry and Nano Science and Department of Bioinspired Science, Ewha Womans University, Seoul, 120-750, Korea, Department of Chemistry, University of Cambridge, Cambridge, United Kingdom, and Department of Chemistry, Yonsei University, Seoul, 120-749, Korea, State Key Laboratory of Fine Chemicals, Dalian University of Technology, Dalian 116012, China, Shanghai Key Laboratory of Chemical Biology, East China University of Science and Technology, Shanghai 200237, China

zx214@cam.ac.uk; injae@yonsei.ac.kr; jyoon@ewha.ac.kr

Contents:

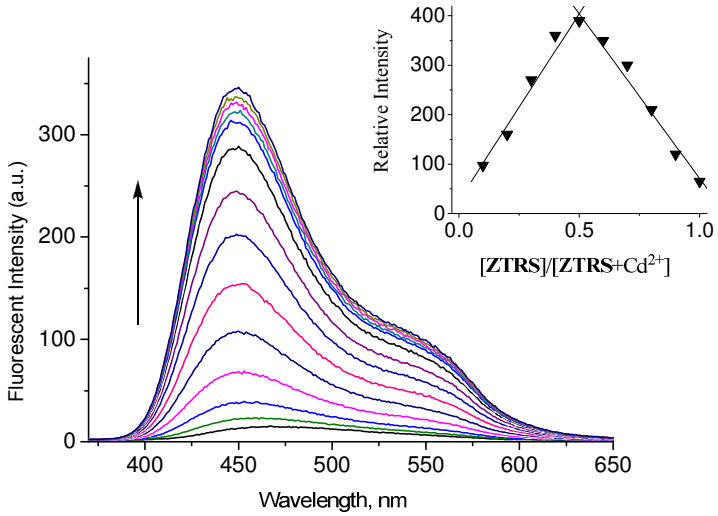

Figure S1. Fluorescence spectra of **ZTRS** in the presence of different concentrations of Cd^{2+} in aqueous solution (CH_3CN:HEPES = 50:50) (HEPES, 0.5 M, pH 7.4). Excitation at 360 nm. [**ZTRS**] = 10 μM. The inset shows the Job plot evaluated from the fluorescence with a total concentration of 10 μM.

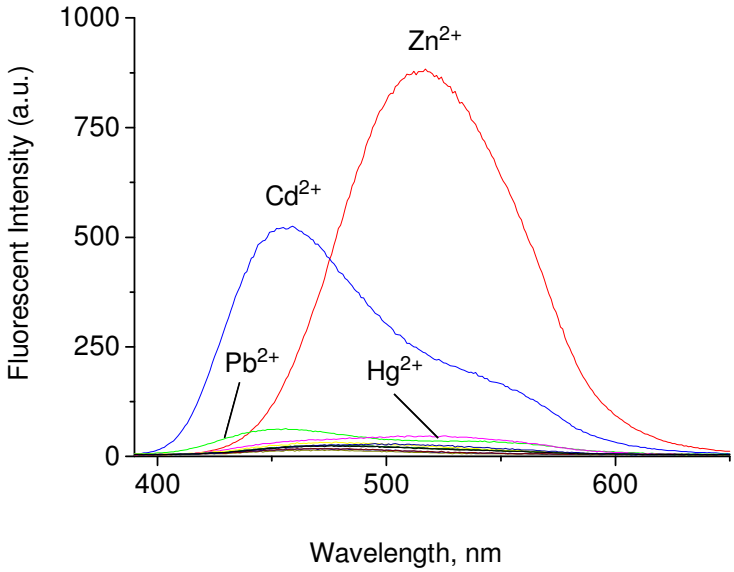

Figure S2. Fluorescence spectra of **ZTRS** in the presence of metal ions in aqueous solution (DMSO:HEPES = 10:90) (HEPES, 0.5 M, pH 7.4). Excitation at 360 nm. [**ZTRS**] = 10 μM.

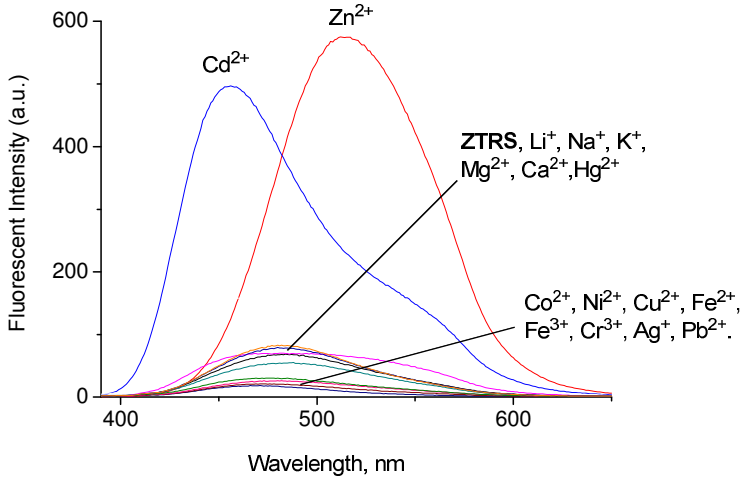

Figure S3. Fluorescence spectra of 10 μM **ZTRS** in the presence of various metal ions in HEPES buffer solutions (0.5 M, pH 7.4). Excitation at 360 nm.

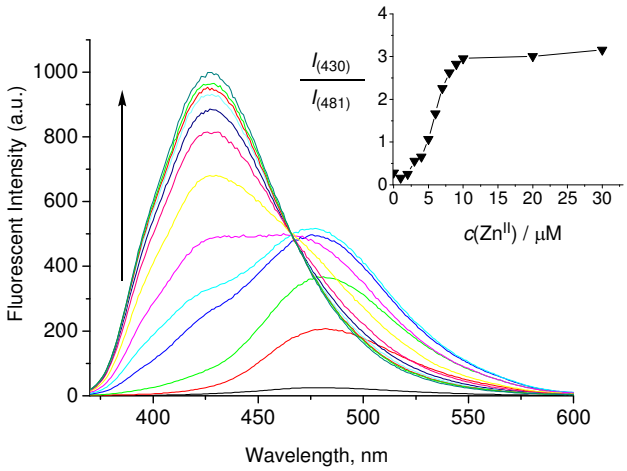

Figure S4. Fluorescence spectra of **ZTRS** in the presence of different concentrations of Zn^{2+} in CH_3CN. Excitation at 360 nm. [**ZTRS**] = 10 μM. Inset: Ratiometric calibration curve I_{430}/I_{481} as a function of Zn^{2+} concentration.

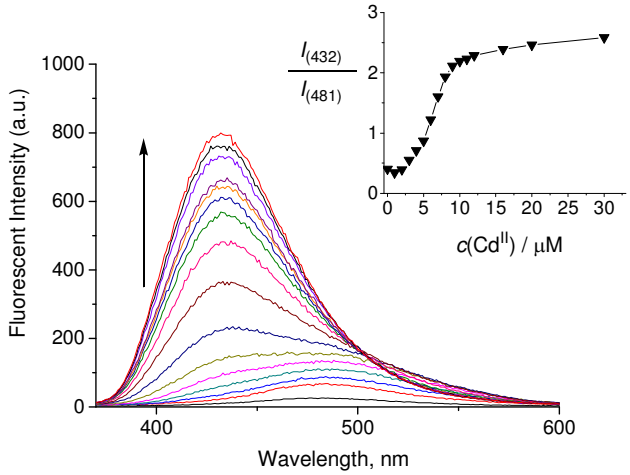

Figure S5. Fluorescence spectra of **ZTRS** in the presence of different concentrations of Cd^{2+} in CH_3CN. Excitation at 360 nm. [**ZTRS**] = 10 μM. Inset: Ratiometric calibration curve I_{432}/I_{481} as a function of Cd^{2+} concentration.

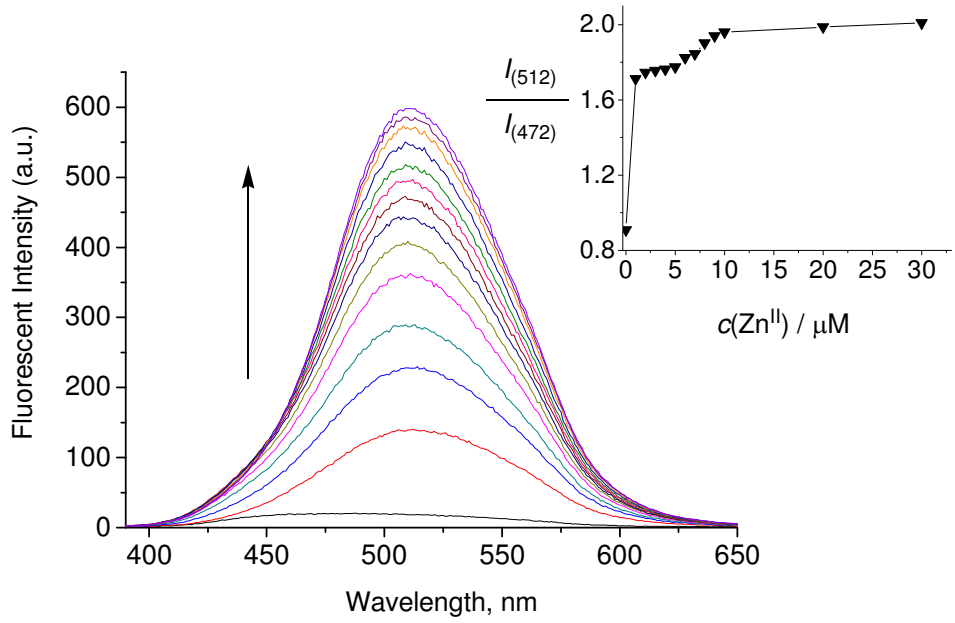

Figure S6. Fluorescence spectra of **ZTRS** in the presence of different concentrations of Zn^{2+} in DMSO. Excitation at 360 nm. [**ZTRS**] = 10 μM. Inset: Ratiometric calibration curve I_{512}/I_{472} as a function of Zn^{2+} concentration.

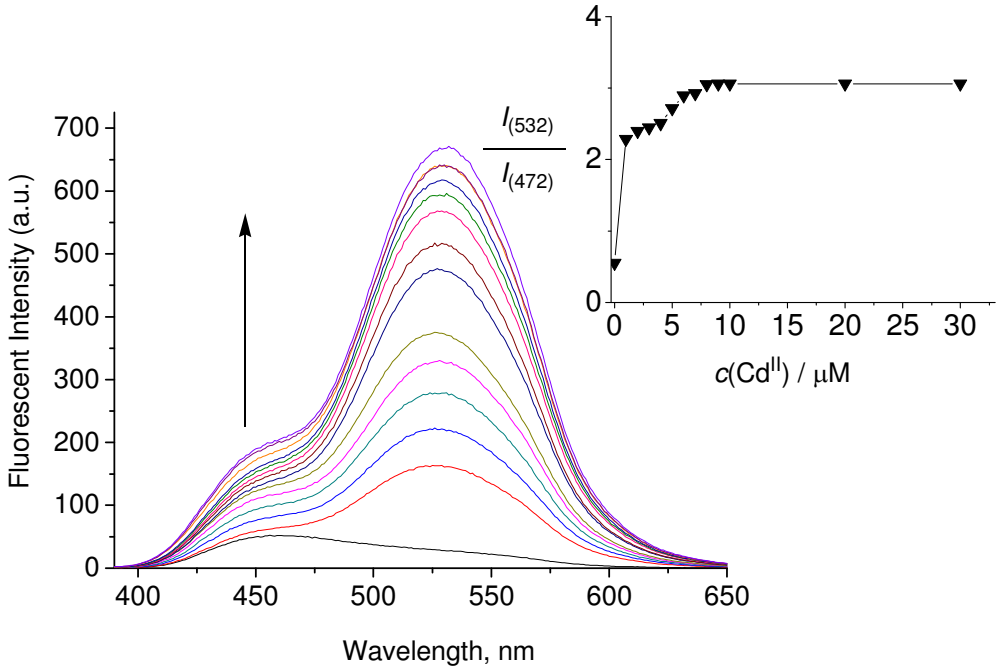

Figure S7. Fluorescence spectra of **ZTRS** in the presence of different concentrations of Cd^{2+} in DMSO. Excitation at 360 nm. [**ZTRS**] = 10 μM. Inset: Ratiometric calibration curve I_{532}/I_{472} as a function of Cd^{2+} concentration.

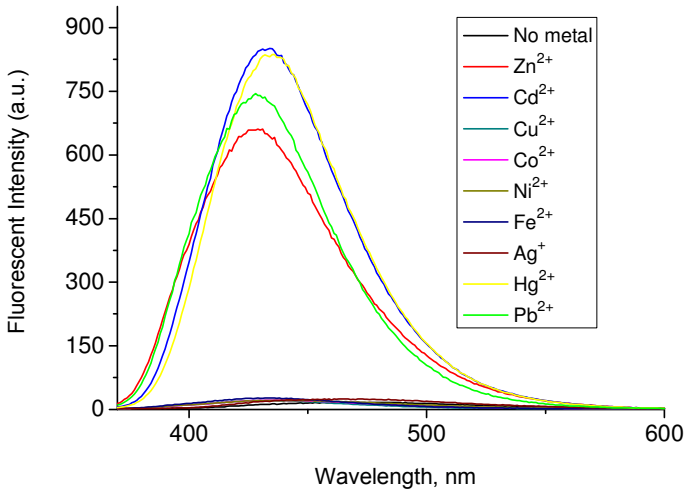

Figure S8. Fluorescence spectra of **ZTRS** in the presence of different metal ions in CH_3CN. Excitation at 360 nm. [**ZTRS**] = 10 μM.

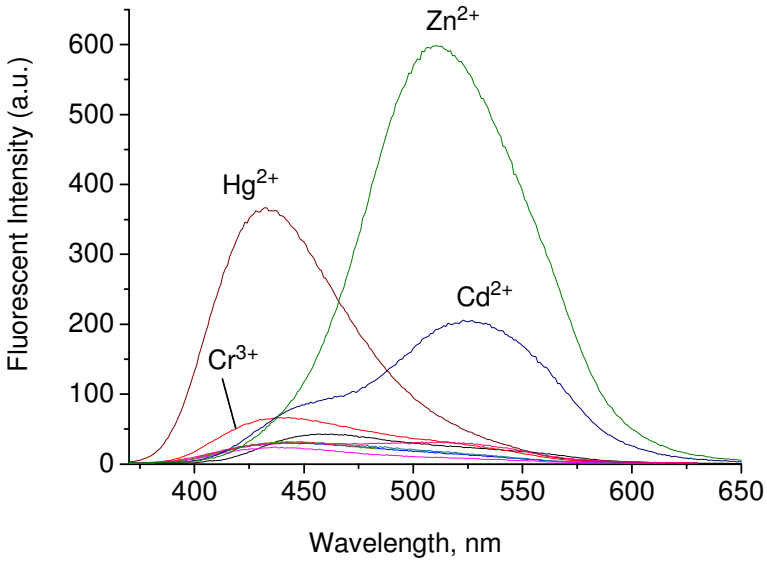

Figure S9. Fluorescence spectra of **ZTRS** in the presence of different metal ions in DMSO. Excitation at 360 nm. [**ZTRS**] = 10 μM.

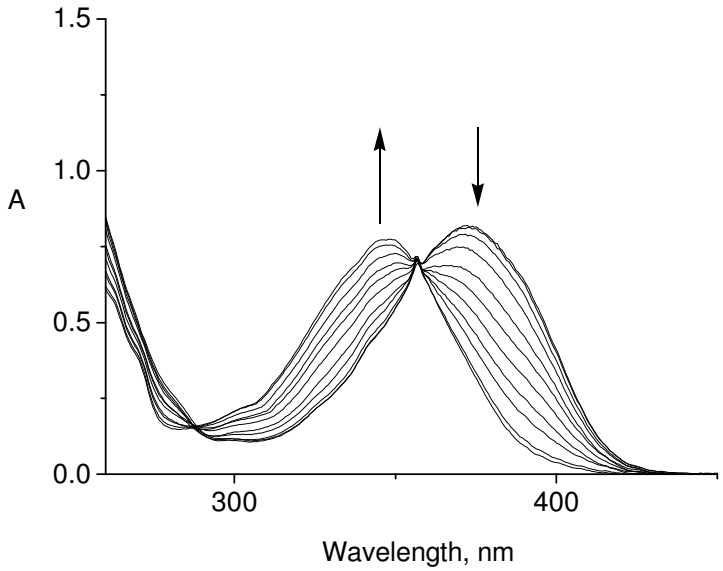

Figure S10. UV-Vis absorption spectra of **ZTRS** in the presence of different concentrations of Zn^{2+} in acetonitrile. [**ZTRS**] = 10 μM, [Zn^{2+}] = 0-10 μM.

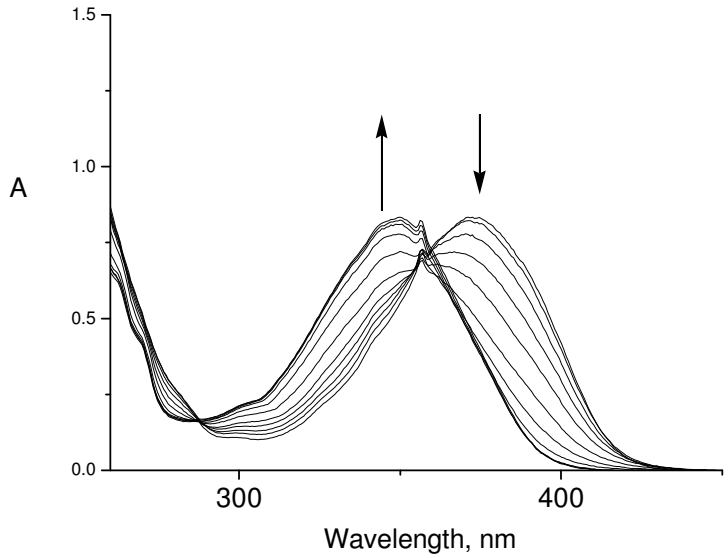

Figure S11. UV-Vis absorption spectra of **ZTRS** in the presence of different concentrations of Cd^{2+} in acetonitrile. [**ZTRS**] = 10 μM, [Cd^{2+}] = 0-10 μM.

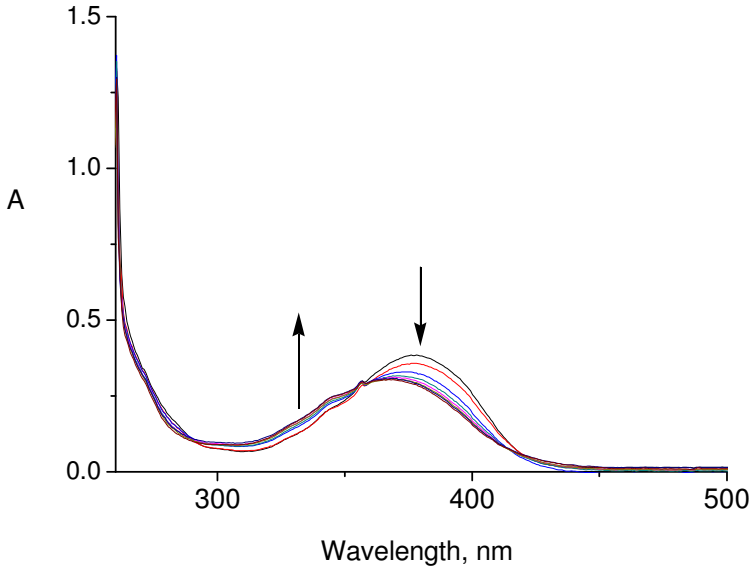

Figure S12. UV-Vis absorption spectra of **ZTRS** in the presence of different concentrations of Zn^{2+} in DMSO. [**ZTRS**] = 10 μM, [Zn^{2+}] = 0-10 μM.

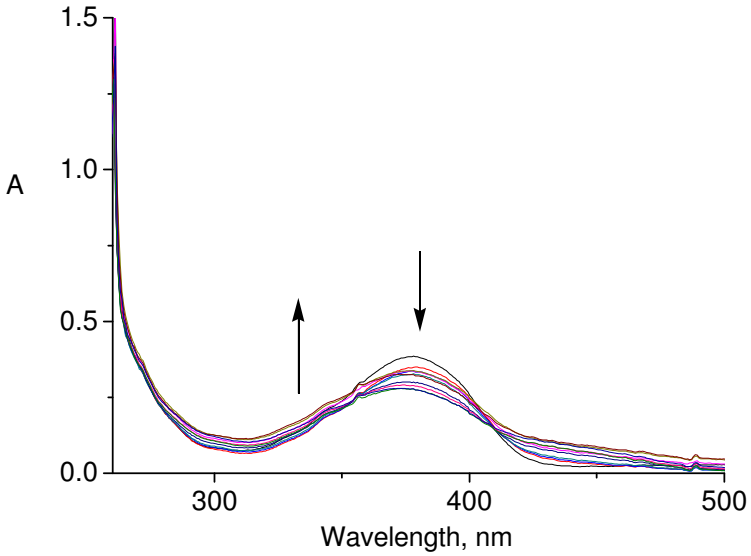

Figure S13. UV-Vis absorption spectra of **ZTRS** in the presence of different concentrations of Cd^{2+} in DMSO. [**ZTRS**] = 10 μM, [Cd^{2+}] = 0-10 μM.

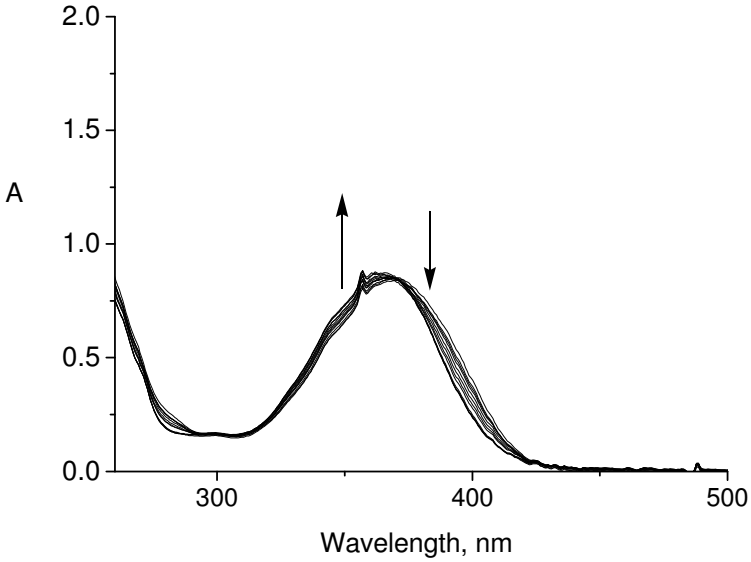

Figure S14. UV-Vis absorption spectra of **ZTRS** in the presence of different concentrations of Zn^{2+} in aqueous solution (CH_3CN:HEPES = 50:50) (HEPES, 0.5 M, pH 7.4). [**ZTRS**] = 10 μM, [Zn^{2+}] = 0-10 μM.

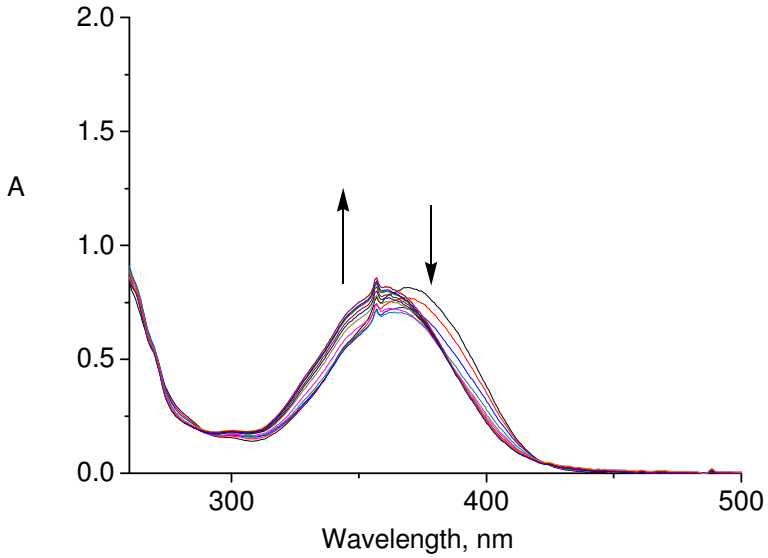

Figure S15. UV-Vis absorption spectra of **ZTRS** in the presence of different concentrations of Cd^{2+} in aqueous solution (CH_3CN:HEPES = 50:50) (HEPES, 0.5 M, pH 7.4). [**ZTRS**] = 10 μM, [Cd^{2+}] = 0-10 μM.

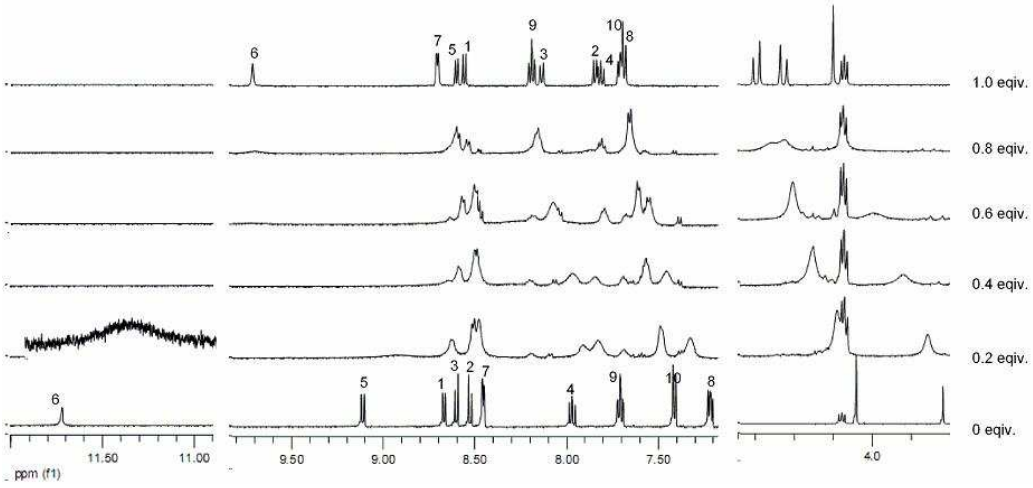

Figure S16. ^{1}H-NMR spectra of **ZTRS** in the prescence of a different amount of Zn^{2+} in CD_3CN.

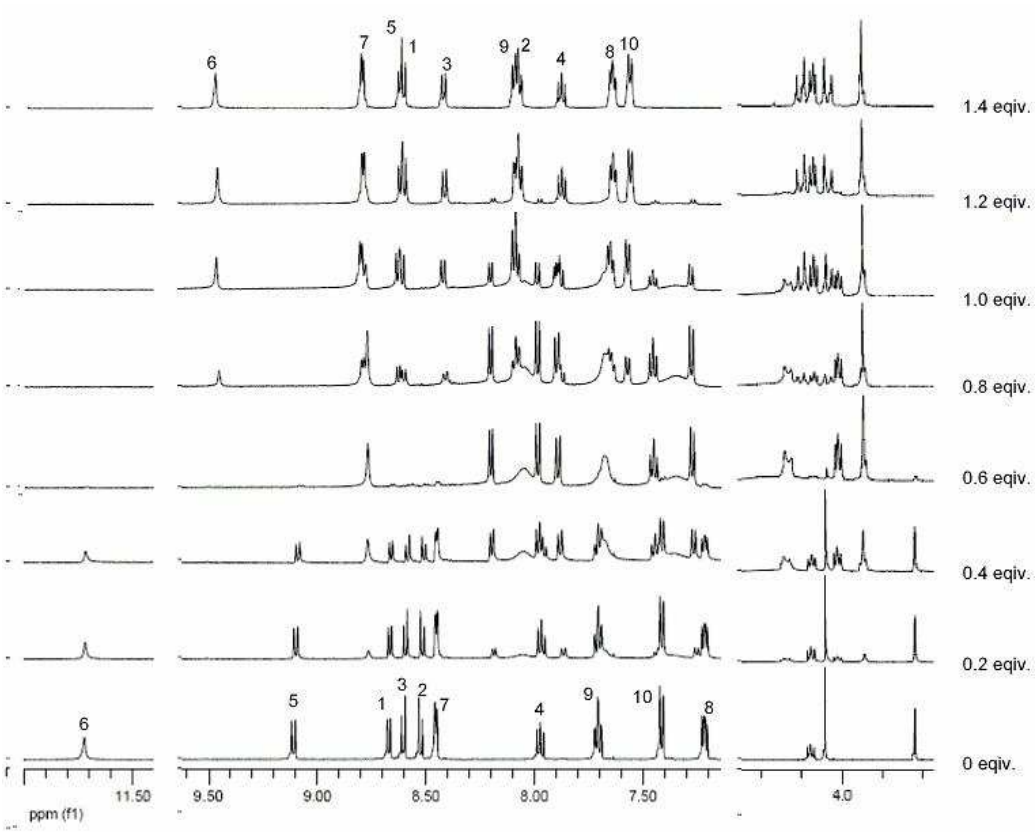

Figure S17. ^{1}H-NMR spectra of **ZTRS** in the prescence of a different amount of Cd^{2+} in CD_3CN.

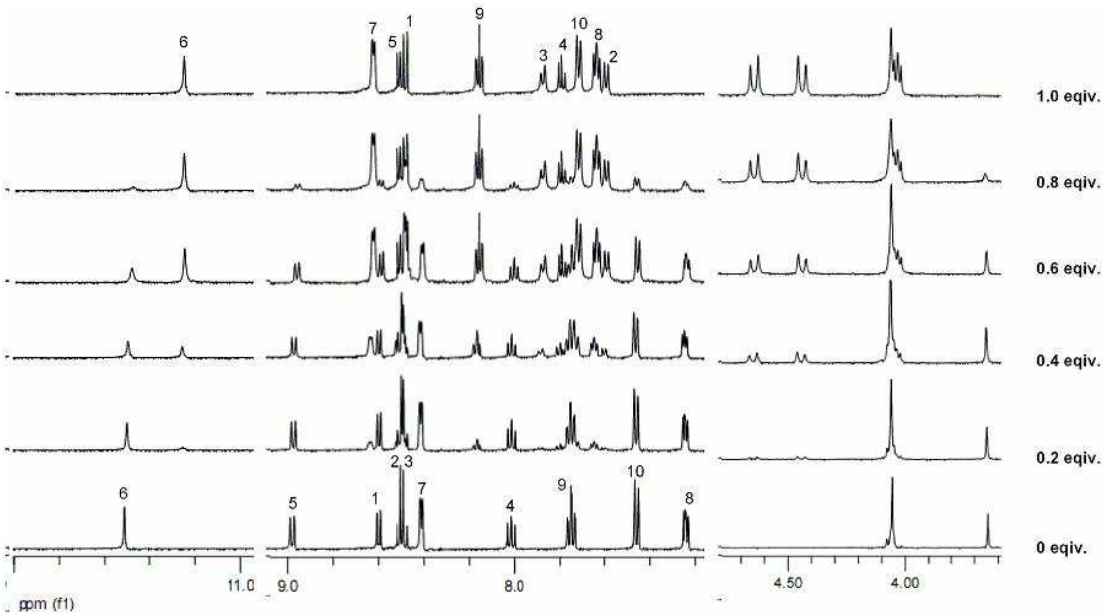

Figure S18. ^{1}H-NMR spectra of **ZTRS** in the prescence of a different amount of Zn^{2+} in DMSO-*d6*.

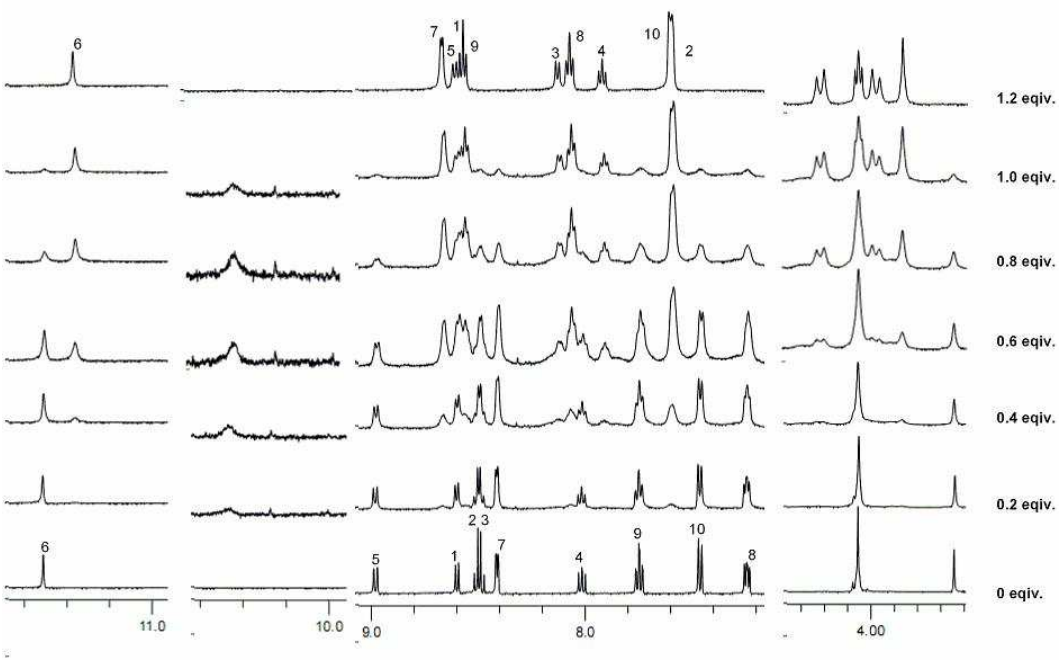

Figure S19. ^{1}H-NMR spectra of **ZTRS** in the prescence of a different amount of Cd^{2+} in DMSO-*d6*.

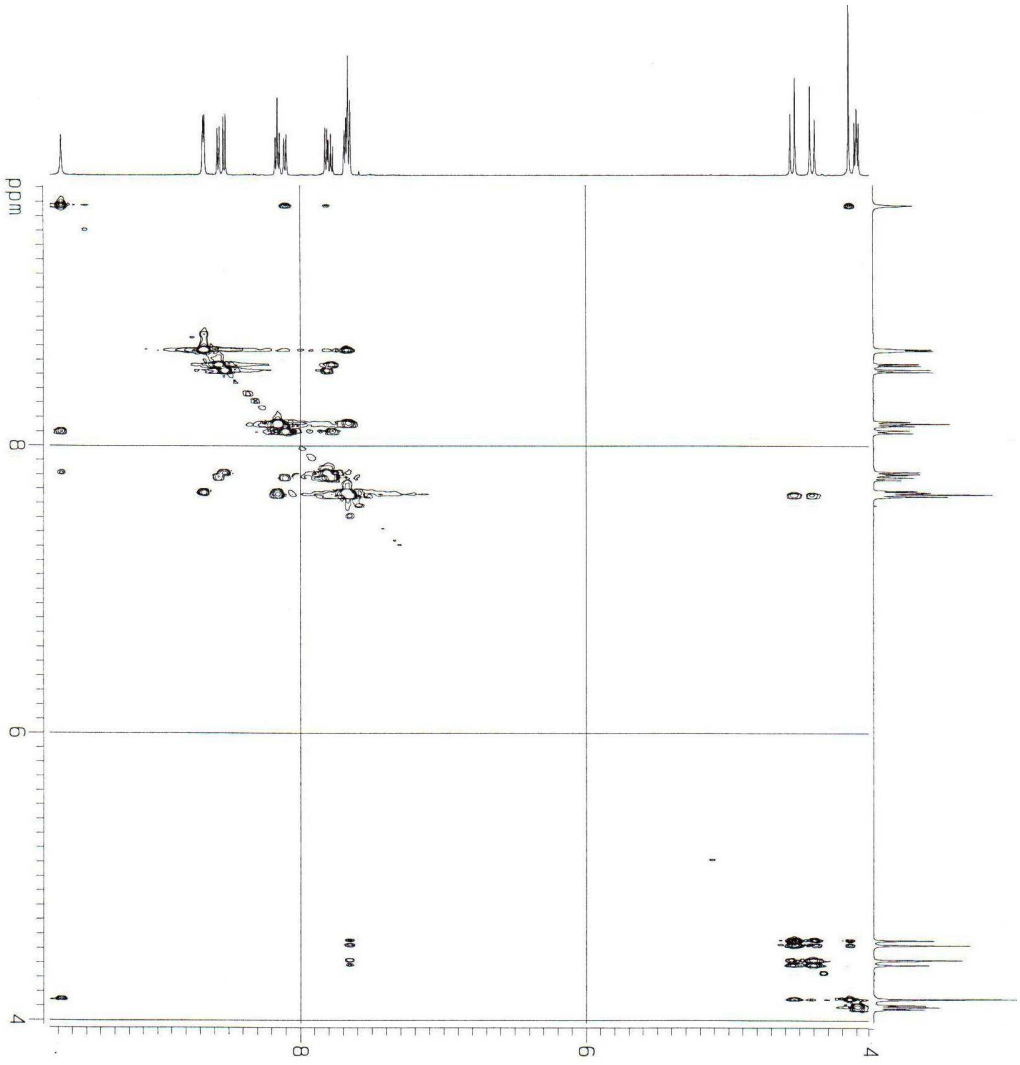

Figure S20. 500 MHz ^{1}H-^{1}H NOESY spectrum of **ZTRS** with 1 eq. of Zn^{2+} in CD_3CN.

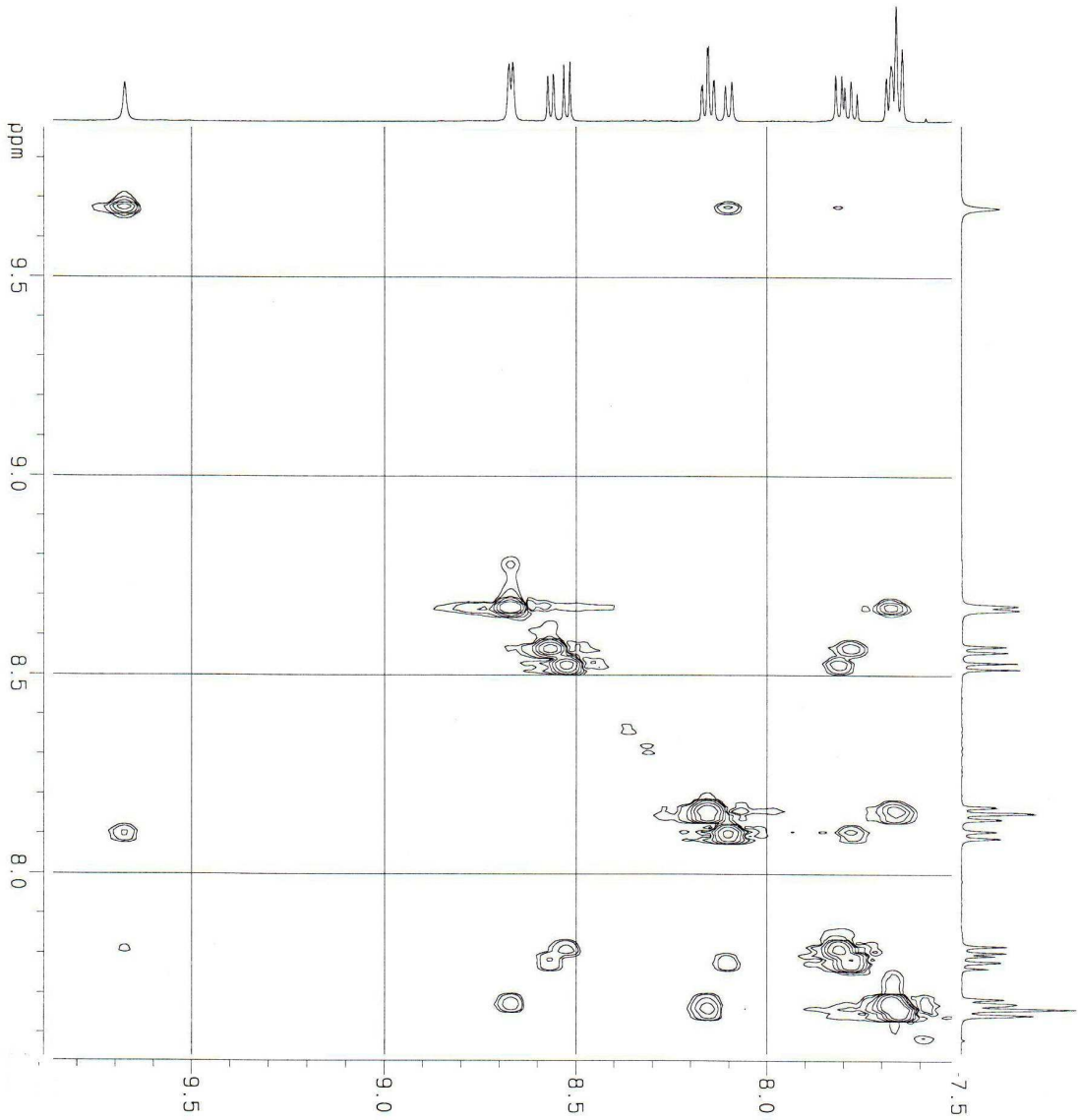

Figure S21. Partial 500 MHz ^{1}H-^{1}H NOESY spectrum of **ZTRS** with 1 eq. of Zn^{2+} in CD_3CN.

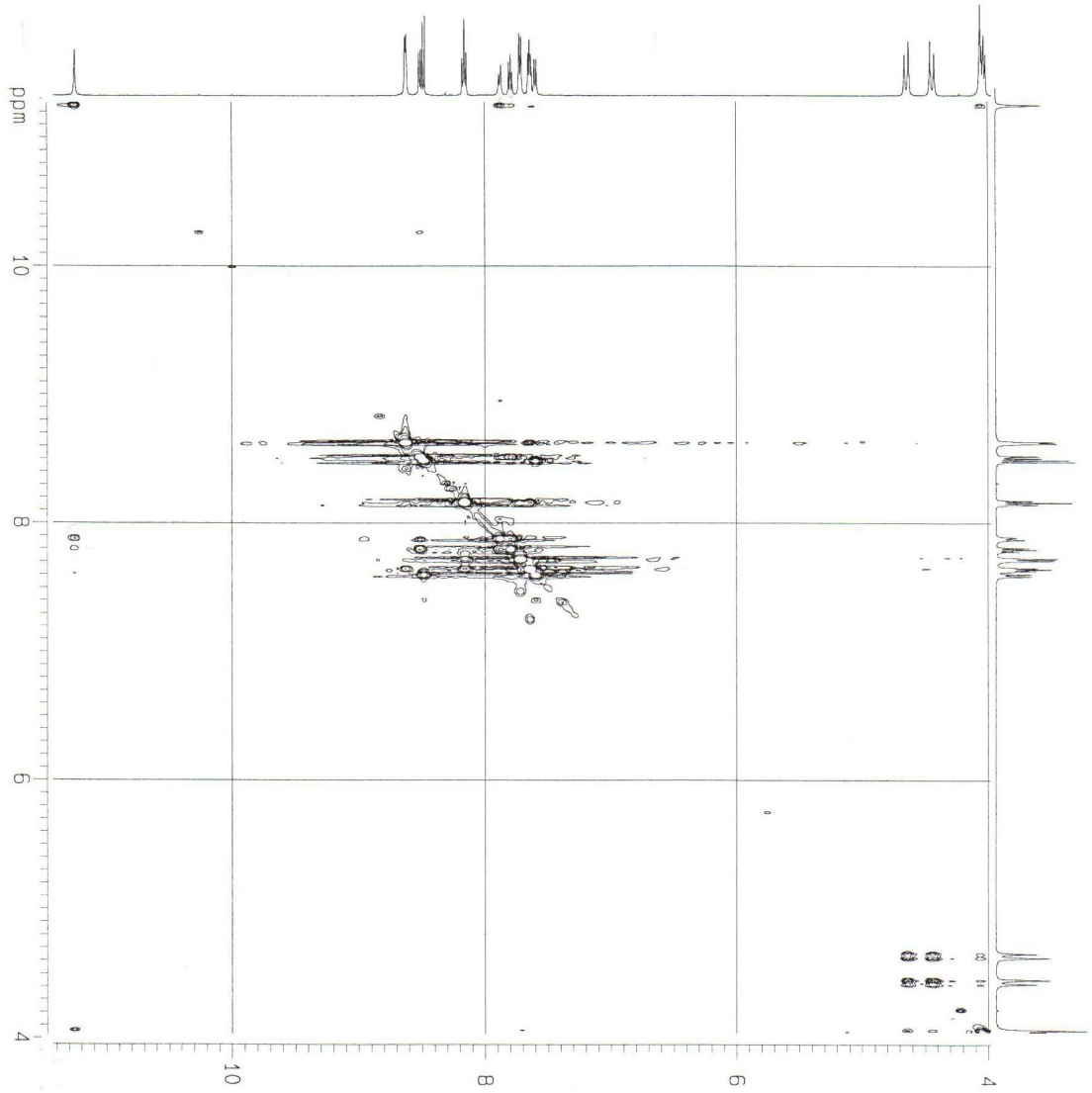

Figure S22. 500 MHz ^{1}H-^{1}H NOESY spectrum of **ZTRS** with 1 eq. of Zn^{2+} in DMSO-*d6*.

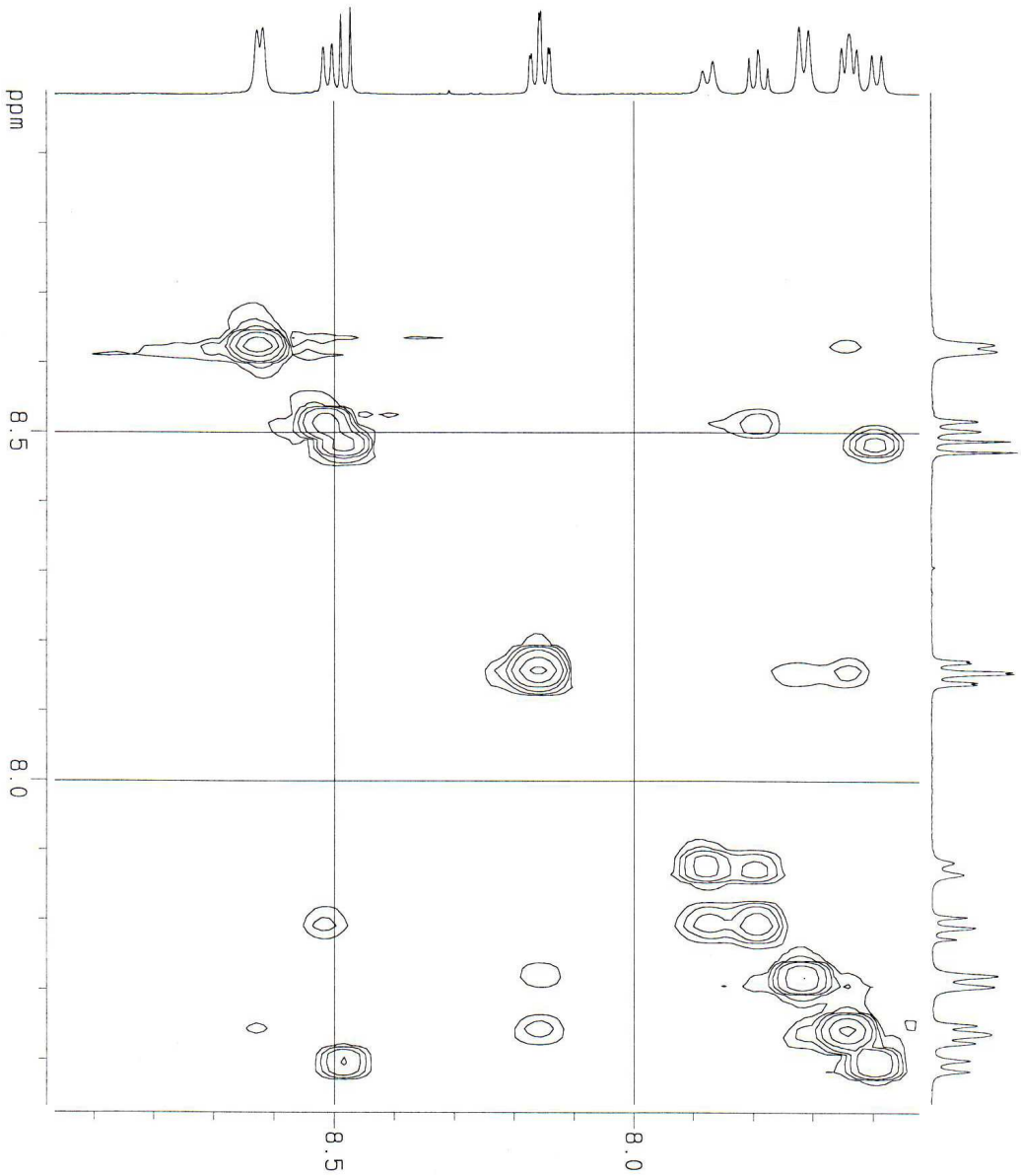

Figure S23. Partial ^{1}H-^{1}H 500 MHz NOESY spectrum of **ZTRS** with 1 eq. of Zn^{2+} in DMSO-*d6*.

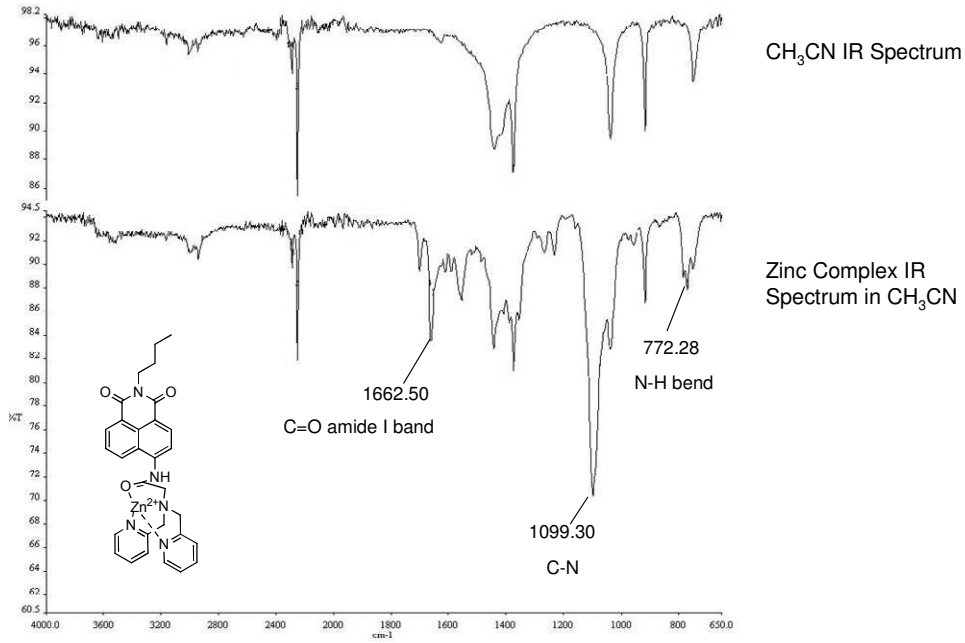

Figure S24. IR spectrum of **ZTRS** /Zn^{2+} (1:1) complex in CH_3CN.

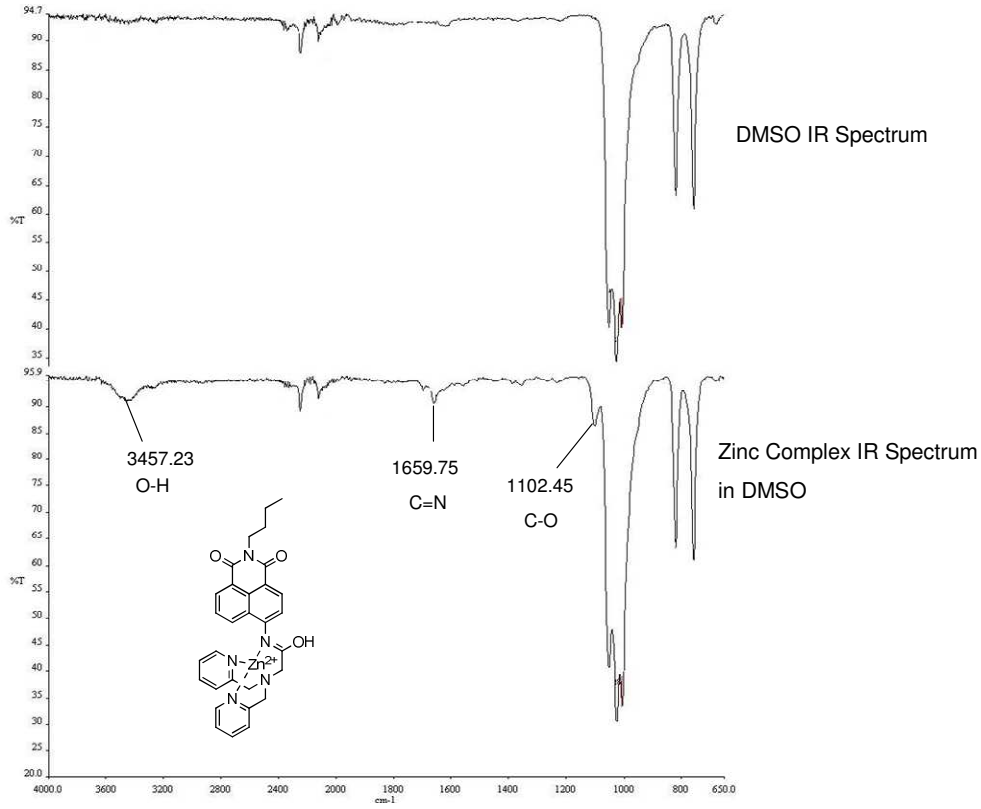

Figure S25. IR spectrum of **ZTRS** /Zn^{2+} (1:1) complex in DMSO.

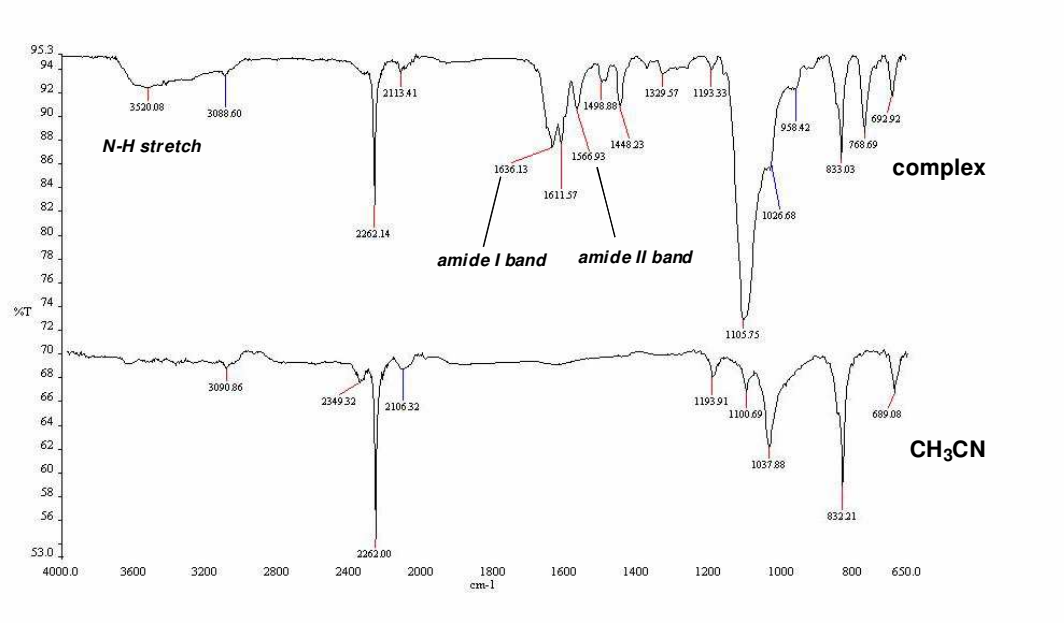

Figure S26. IR spectrum of **ZTF**/Zn^{2+} (1:1) complex in CD_3CN.

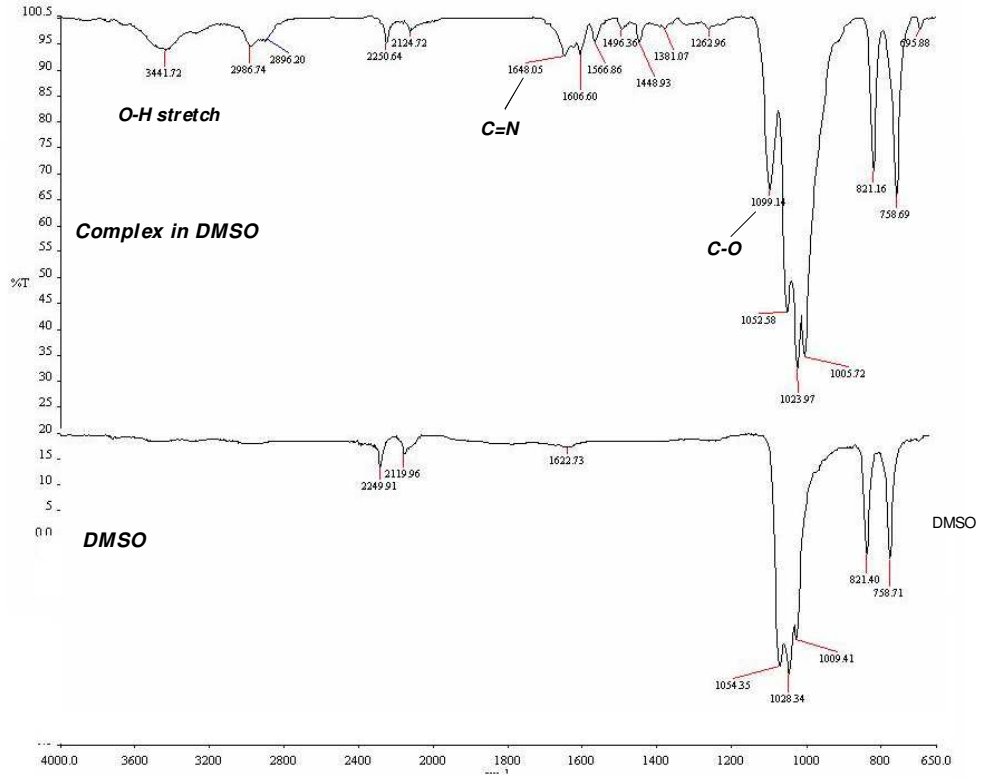

Figure S27. IR spectrum of **ZTF**/Zn^{2+} (1:1) complex in DMSO.

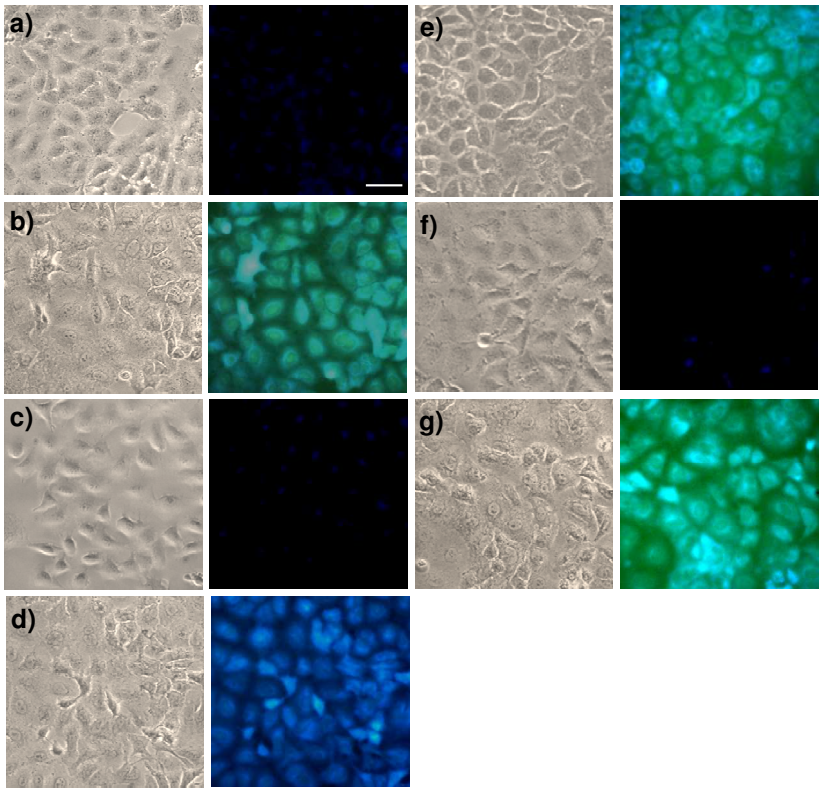

Figure S28. Fluorescence images of A549 cells incubated with 5 μM **ZTRS** and ions. Cells treated with **ZTRS** a) in the absence and b) presence of 1 μM of external zinc ions, and c) after treatment with **ZTRS** and 1 μM $ZnCl_2$ and subsequent treatment of the cells with 25 μM TPEN. d) Cells treated with **ZTRS** and 5 μM $CdCl_2$ and e) after treatment with **ZTRS** and 5 μM $CdCl_2$ and subsequent treatment of the cells with 1 μM $ZnCl_2$. f) Cells treated with **ZTRS** and 5 μM $Fe(ClO_4)_2$ and g) after treatment with **ZTRS** and 5 μM $Fe(ClO_4)_2$ and subsequent treatment of the cells with 1 μM $ZnCl_2$ (bar = 50 μm) (left: bright field images, right: fluorescence images).

Table 1. Crystal data and structure refinement for **ZTF**-Zn^{2+}

Empirical formula	$C_{22}H_{25}Cl_2N_5O_{10}Zn$	
Formula weight	655.74	
Temperature	180(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	C2/c	
Unit cell dimensions	a = 21.3422(3) Å	$\alpha = 90^o$.
	b = 13.3525(2) Å	$\beta = 102.279(1)^o$.
	c = 19.5085(3) Å	$\gamma = 90^o$.
Volume	5432.19(14) $Å^3$	
Z	8	
Density (calculated)	1.604 Mg/m^3	
Absorption coefficient	1.165 mm^{-1}	
F(000)	2688	
Crystal size	0.28 × 0.23 × 0.12 mm3	
Theta range for data collection	3.58 to 33.76°.	
Index ranges	-33<=h<=33, -20<=k<=20, -30<=l<=30	
Reflections collected	22556	
Independent reflections	10755 [R(int) = 0.0333]	
Completeness to theta = 33.76°	98.9%	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.958 and 0.858	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	10755 / 0 / 368	

Goodness-of-fit on F^2	1.039
Final R indices [I>2sigma(I)]	R1 = 0.0438, wR2 = 0.1009
R indices (all data)	R1 = 0.0621, wR2 = 0.1120
Largest diff. peak and hole	0.558 and -0.510 e.Å-3