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Chemically reversible binding of H_2S to a zinc porphyrin: towards implementation of a reversible sensor via a "coordinative-based approach".

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Abstract

The use of a zinc porphyrin complex for monitoring hydrogen sulfide (H_2S) is explored by a coordinative-based approach. High-resolution MALDI Fourier transform ion cyclotron resonance mass spectrometry (HR MALDI-FT-ICR) and ^1H NMR experiments provide evidence that HS^- coordination occurs at the zinc centre. The coordination of HS^- occurs in a reversible manner and modulates fluorescence emission of tetra(N-methylpyridy1)porphine zinc complex (*TMPyPZn*). The results provide proof-of-principle that *TMPyPZn* represents a fast and simple H_2S sensor and opens the door to the implementation of a new family of devices for monitoring HS^- via a coordinative-based approach.

Introduction

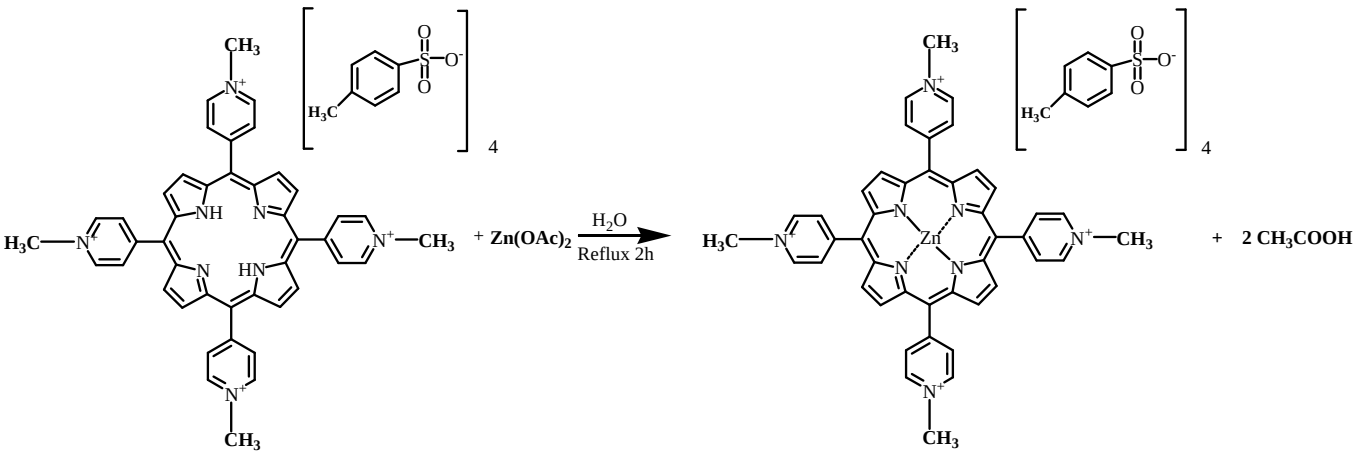
The traditional toxic effect of H_2S was firstly documented about 300 years ago. In more recent times a biological action of H_2S in both healthy and disease states has been established.[1-3] This finding triggered an upsurge of interest towards this molecule however the most part of its complex biological roles are still unknown.[4] It seems worth mentioning that intracellular H_2S levels generated in response to physiological stimuli are still controversial.[5;6] Thus it is clear the reason why several research groups focused on the design and implementation of new successful sensors for H_2S detection. In addition to the traditional approaches (e.g. colorimetry, electrochemistry and chromatography) a large number of H_2S fluorescent probes have been devised in the last years.[4;7-43] Implementation of improved H_2S fluorescence based probes is still considered a very challenging task and this simple and old molecule attracts lots of attention from several research groups in the world.[44;45]

A limitation of most of fluorescence-based probes developed so far is the irreversibility of the reaction by which H_2S recognition occurs, which renders the devices not reusable. On the other hand, a coordinative-based approach may ideally ensure a reversible binding process by removing H_2S from the metal center of the sensor,[42;46-50] a highly desiderable feature for practical applications allowing reusability of the sensing device.[51] By exploiting a coordinative-based approach in 2015, our research group reported a simple copper porphyrin complex as a ‘turn on’ fluorescent probe for the detection of H_2S in aqueous media.[50] Despite the selective 'turn on' of the fluorescence in the presence of H_2S against a wide range of possible competing species, the need of a basic aqueous medium to dissolve the sensor and the lack of reversibility for HS^- binding are a limitation for applications of the copper porphyrin system for real samples measurements.[50] Previously we had also proposed a metalloprotein, cobalt containing peptide deformylase (Co-PDF), as a FRET-based H_2S sensor by the same coordinative based approach, but also in the latter case we could not find the conditions for removing H_2S from the cobalt center.[48]

In this work, we devised to synthesize a zinc porphyrin featuring a water soluble porphyrin scaffold a condition necessary for potential application of a sensing device for measurements in biological samples. Our porphyrin of choice is tetra(N-methylpyridyl)porphine tetratosylate salt (TMPyP) which is commercially available, a further favorable condition for a quick and easy set up of a sensing device.

Results and discussion.

TMPyPZn was obtained in good yield by reacting an equimolar amount of TMPyP and $Zn(CH_3COO)_2$ in MilliQ water by following a slightly modified literature procedure (see Scheme 1).[52;53]



Scheme 1

The stoichiometry was confirmed by high-resolution MALDI Fourier transform ion cyclotron resonance mass spectrometry (HR MALDI-FT-ICR) where the major peak at 740.236 units corresponds to the mononuclear $[(TMPyPZn)]^+$ cation (figure S1 in the SI). No peaks ascribable to binuclear species in solution were found. *TMPyPZn* is fully soluble in dimethyl sulfoxide and in aqueous solutions of [4-(2-hydroxyethyl)-1-piperazineethanesulfonic acid (HEPES buffer) 25 mM at pH 7.4. The ^{1}H NMR spectrum of *TMPyPZn* in DMSO-d_6 consisted of sharp signals as expected for symmetric coordination of the ligand (figure S2 in the SI). Diagnostic resonances at 9.41 and 8.90 ppm for the aromatic protons on the pyridine groups together with a singlet at 4.69 ppm for the methyls on the pyridines were observed. The singlet at 9.05 ppm is ascribed to the pyrrolic protons whereas the signals at 7.43 and 7.07 ppm and that at 2.24 ppm to the aromatic protons and the methyls on the toluenesulfonate groups, respectively. These assignments were made on the basis of the spectra of similar porphyrin complexes reported in the literature.[54] The ^{1}H NMR pattern in D_2O closely resembles that observed in DMSO-d_6 (figure S4 in the SI). *TMPyPZn* was further characterized via Uv-vis and fluorescence spectroscopy. The electronic absorption spectra of the free ligand and of *TMPyPZn* were measured in hepes buffer 25 mM at physiological pH (figure S6 in the SI). The UV-vis spectrum of *TMPyPZn* (which is similar to those of similar metallo-porphyrin complexes)[52] features the B-band (Soret band) at 439 nm and the Q-band at 565 nm, both red shifted with respect to the free ligand.

The fluorescence spectra of TMPyP and of *TMPyPZn* are displayed in figure S7. *TMPyPZn* displays a fluorescence intensity higher than that of TMPyP with a more structured band whose major peak is centered at 630 nm.The capability of *TMPyPZn* to act as a recognition element for H_2S was first studied by ^1H NMR spectroscopy. Addition of NaSH to a D_2O solution of *TMPyPZn* resulted in a significant shift in the ^1H NMR spectrum of the complex although no new resonance ascribable to the hydrogenosulfide group bound to zinc was detected, likely owing to a fast SH/SD exchange in D_2O

(Figure 1).

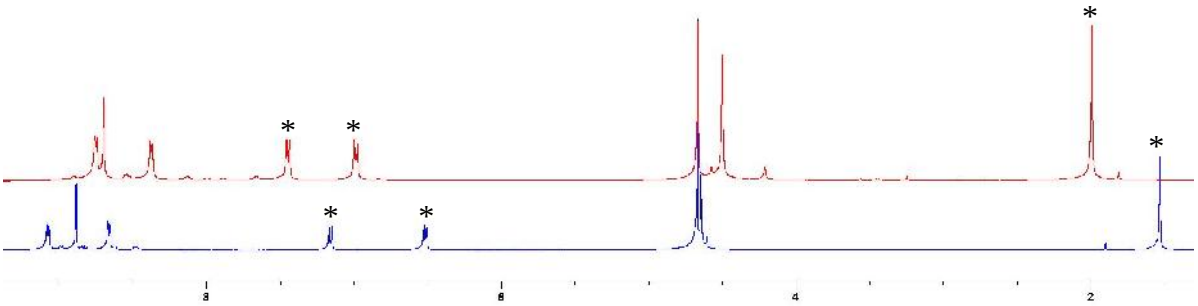


Figure 1 . ^1H NMR spectrum of TMPyPZn in D_2O (lower trace) and after addition of an excess of HS^- (upper trace). [TMPyPZn] = $7*10^{-3}$ M; [NaSH] = 0,35 M. Peaks denoted with a (*) correspond to the toluenesulfonate counterion.

In fact, addition of NaSH to a DMSO-d_6 solution of *TMPyPZn* resulted in a more pronounced shift of the proton resonances of the porphyrin moiety (Figure 2) and, most remarkably, in the appearance of a high field resonance at $\delta = -2.49$ ppm, ascribable to the SH group bound to the zinc center, in agreement with the spectra of hydrogenosulfido zinc complexes reported in the literature.[55;56]

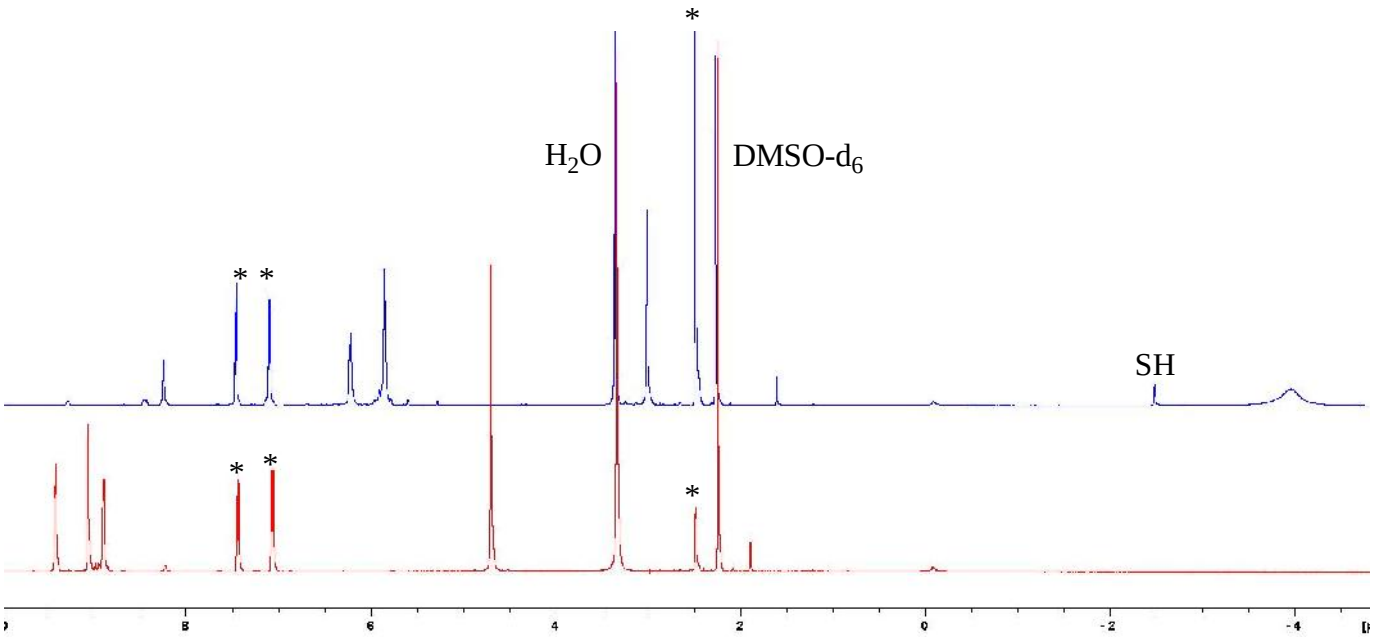


Figure 2. ^{1}H NMR spectrum of TMPyPZn in DMSO-d_6 (lower trace) and after addition of an excess of HS^- (upper trace). [TMPyPZn] = $7*10^{-3}$ M; [NaSH] = 0,14 M. Peaks denoted with a (*) correspond to the toluenesulfonate counterion.

A blank experiment performed adding NaSH to the free TMPyP ligand in D_2O resulted in a completely different spectrum (see figure S9), displaying only the peaks belonging to the toluenesulfonate groups, suggesting precipitation of the porphyrin ligand.

The system was then studied via fluorescence spectroscopy. In the presence of an excess of NaSH a significant quenching of the fluorescence emission was observed (see figure 3); a concomitant and immediate color change (visible to the naked eye) from dark brown to dark green occurred.

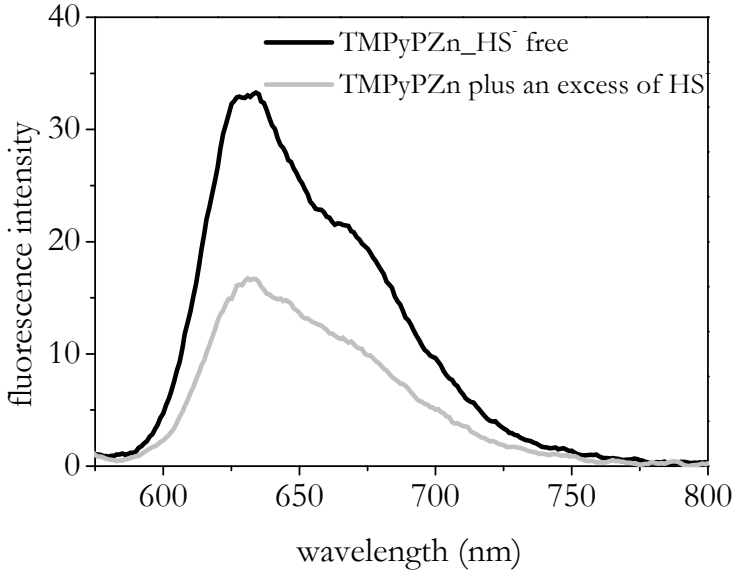


Figure 3. Emission spectra of *TMPyPZn* free (λ_{ex} = 563 nm; λ_{em} = 630 nm) and upon addition of an excess of NaSH (rt, hepes buffer 25 mM, pH = 7.4). [TMPyPZn] = $5*10^{-6}$ M; [NaSH] = $7*10^{-4}$ M.

To assess whether the amount of the fluorescence quenching of TMPyPZn depends on the concentration of HS^-, the fluorescence intensity of the system was monitored after the addition of increasing amounts of NaSH. The response for a series of NaSH concentrations is shown in figure S10 (A). The fluorescence intensity of the system versus the HS^- concentration exhibits a linear correlation which can be used as a calibration line (figure S10 (B)).

The interaction of HS^- with the *TMPyPZn* complex was further investigated by HR MALDI-FT-ICR in aqueous solution, ionizing the product of the reaction in the negative ion mode and comparing the spectrum with that of HS^--free *TMPyPZn* (under the same experimental conditions). An additional peak at 771.108 *m/z* units was visible in the spectrum of the hydrogen sulfido adduct (see figure S11). The isotope pattern of this peak is consistent with the $[TMPyPZnHS\text{-}H]^-$ species ($C_{44}H_{35}N_8ZnS$), thus suggesting analyte binding to the zinc complex. This finding corroborates the hypotheses put forward on the basis of ^1H NMR experiments.

We reasoned that HS^- coordination should be acid-labile, thus resulting in chemically reversible coordination of HS^- by the addition of a suitable proton source. Reversibility of HS^- binding to zinc phthalocyanines promoted by acetic acid had been already observed by Pluth et al.[57] To test our hypothesis, we prepared the *TMPyPZn*-HS species *in situ* by adding 100 equiv of NaSH to the complex in water followed by an excess of acetic acid. As expected, the initial fluorescence intensity of *TMPyPZn*, which quenches upon addition of HS^-, was restored when acetic acid was added. Figure 4 shows a typical time trace of a solution containing 5 µM of *TMPyPZn* when excited either at 322 nm or at 563 nm. These two different wavelengths correspond to absorption maxima of *TMPyPZn*. As it is clearly visible from figure 4, very similar fluorescence trends were observed when exciting the system either at 322 nm or at 563 nm.

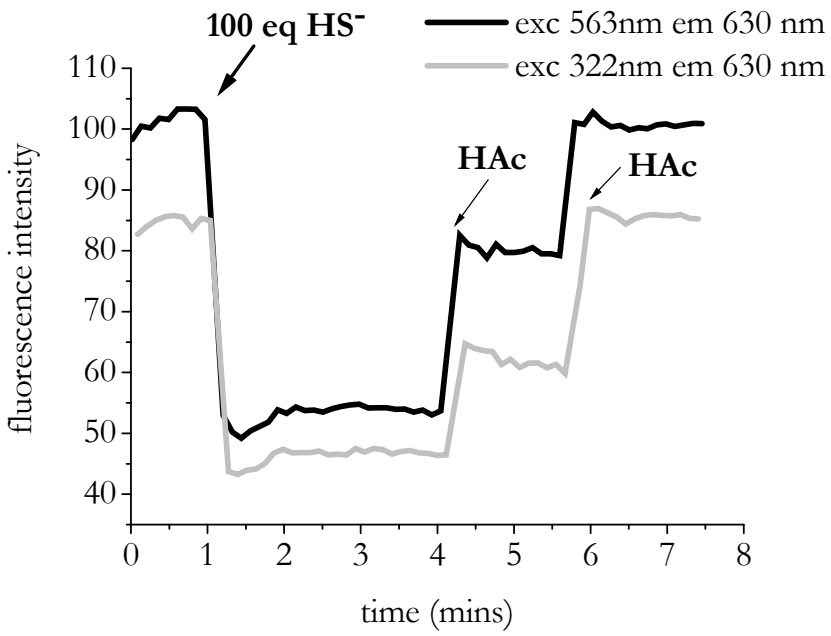


Figure 4. Emission spectra of *TMPyPZn* free (λ_{ex} = 322nm (grey trace) and 563 nm (black trace); λ_{em} = 630 nm) and upon addition of an excess of NaSH (rt). [TMPyPZn] = $5*10^{-6}$ M; [NaSH] = $5*10^{-4}$ M.

The cycle could be repeated various times. Concomitant color changes (visible to the naked eye) from dark brown to dark green and back to dark brown occur when subsequently adding NaSH/ HAc/ NaSH.

The minimum and maximum fluorescence levels slowly decrease when the number of cycles increases likely due to partial decomposition of *TMPyPZn*.

This fluorescence trend suggests that the HS^- binding process is reversible, which is crucial for practical sensing applications.

To obtain an indication of the selectivity of the system we monitored the fluorescence intensity of the system in the presence of biologically relevant and potentially competing thiols [e.g. glutathione (GSH) and L-cysteine (L-Cys) or in the presence of a range of anions, aminoacids, common oxidants]. No significant changes of the initial fluorescence intensity were observed (for details on this experiment please see the experimental section in the paragraph titled “selectivity experiments”).

Conclusions

A fast and selective HS^- sensor in buffered solutions at physiological pH was devised. HR MALDI-FT-ICR and ^1H NMR experiments provide evidence that HS^- coordination occurs at the zinc center. Reversibility of HS^- coordination was proven by fluorescence experiments.

The system constitutes the first example of a reversible HS^- sensor working via a coordinative-based approach. Future work will address its possible application for HS^- measurements in real samples as well as design and testing of related complexes.

Experimental Section

Materials: All chemicals used for the synthetic work were obtained from Sigma-Aldrich or Strem Chemicals and were of reagent grade. They were used without further purification.

General. Elemental analyses were performed with a PERKIN-Elmer 240-C. HR MALDI mass spectra were recorded using a Bruker solariX XR Fourier transform ion cyclotron resonance (FT-ICR) mass spectrometer (Bruker Daltonik GmbH, Bremen, Germany) equipped with a 7 T refrigerated actively-shielded superconducting magnet (Bruker Biospin, Wissembourg, France). The samples were ionized in positive or negative ion mode using the MALDI ion source. The mass range was set to *m/z* 150 – 2000. The laser power was 15% and 15 laser shots were used for each scan. Mass spectra were calibrated externally using a mix of peptide clusters in MALDI ionization positive ion mode. A linear calibration was applied. To improve the mass accuracy, the sample spectra were recalibrated internally by matrix ionization (2,5-DHB).

The samples were dissolved in Milliq water at a concentration of 1 mg/mL. For the *in situ* experiments between *TMPyPZn* and NaSH the reaction was performed in MilliQ water in a 1:10 molar ratio. The matrix used was 2,5-DHB acid and was dissolved in H_2O/CH_3CN (50:50) with 0.1% formic acid at a concentration of 30 mg/mL. Solutions of matrix and sample were mixed in a volume ratio of 1:1. The mixed solution was spotted onto a stainless steel MALDI target and left to dryness. Room temperature NMR spectra were recorded on a Bruker AVANCE 400 NMR instrument (^1H, 400.13 MHz; ^{13}C, 100.62 MHz) using 5 mm o.d. NMR tubes. The chemical shifts were reported in ∂ (ppm) referenced to $SiMe_4$. Typically, 5 mg of the complex in 0.5 mL of solvent were used for each experiment.

Synthesis of TMPyPZn: 0.25 g (0.18 mmol) of 5,10,15,20-Tetrakis(1-methyl-4-pyridinio)porphyrin tetra(*p*-toluenesulfonate) [known also as *meso*-Tetra(*N*-methyl-4-pyridyl)porphine tetratosylate salt, TMPyP] in 20 ml of MilliQ water is refluxed with 0.04 g (0.18

mmol) of zinc(II) acetate. The solution is left under stirring and at reflux for 2 hours. After conversion to the Zn(II)-porphyrin is complete, as indicated by the absence of free porphyrin absorption bands in a visual spectroscope, the solution is evaporated to dryness under vacuum to yield the purple-brown solid. Yield: 84%. C72H64ZnN8O12S4: calcd C 60.60, H 4.52, N 7.85; found C 60.62, H 4.55, N 7.82. MS (MALDI FT-ICR water): m/z (%) 740.236 (100) $[TMPyPZn]^+$. ^{1}H NMR [400 MHz, DMSO-d_6]: δ =9.41 (d, 8H, pyridinio-*H*), 9.05 (s, 8H, pyrrole-*H*), 8.90 (d, 8H, pyridinio-*H*) 7.43 (d, 8H, toluenesulfonate-*H*), 7.07 (d, 8H, toluenesulfonate-*H*), 4.70 (s, 12H, pyridinio-CH_3), 2.24 (s, 12 H, toluenesulfonate-CH_3) ppm; ^{1}H NMR [400 MHz, D_2O] : δ =9.21 (d, 8H, pyridinio-*H*), 9.01 (s, 8H, pyrrole-*H*), 8.80 (d, 8H, pyridinio-*H*), 7.30 (d, 8H, toluenesulfonate-*H*), 6.66 (d, 8H, toluenesulfonate-*H*), 4.77 (s, 12H, pyridinio-CH_3), 1.66 (s, 12 H, toluenesulfonate-CH_3) ppm. ^{13}C NMR [100 MHz, DMSO-d_6] : δ = 20.74, 47.77, 116.20, 125.46, 128.01, 132.02, 132.78, 137.53, 143.78, 145.78, 148.42, 157,75; ^{13}C NMR [100 MHz, D_2O] : δ = 19.784, 47.874, 115.684, 124.746, 128.370, 132.374, 132.901, 138.942, 141.358, 143.171, 148.608, 159,028.

Absorbance and fluorescence measurements. Absorption spectra were recorded on a Cary-50 Spectrophotometer, using a 1 cm quartz cuvette (Hellma Benelux bv, Rijswijk, Netherlands) and a slit-width equivalent to a bandwidth of 5 nm. Fluorescence spectra were measured on a Cary Eclipse Spectrophotometer in a 10 × 10mm^2 airtight quartz fluorescence cuvette (Hellma Benelux bv, Rijswijk, Netherlands) with an emission band-pass of 10 nm and an excitation band-pass of 5 nm. Both absorption and fluorescence measurements were performed in hepes buffer 25 mM pH 7.4 at room temperature. Fluorescence emission spectra were registered by exciting the samples either at 563 nm or at 322 nm (as specified in the figure captions). H_2S titration experiments were performed as follows: the cuvette was filled with sample solutions in hepes buffer 25 mM pH 7.4. Then µL amounts of NaSH (a commonly employed HS^- donor) solutions in MilliQ water (to the end concentrations specified in the figure captions) were injected via gas-tight syringe at intervals of 1 min between subsequent additions. The experiment ended when no changes in the fluorescence intensities could be detected upon H_2S addition.

NMR characterization of the TMPyPZnHS adduct. The NMR tube was charged with *TMPyPZn* solutions either in D_2O or in DMSO-d_6 then NaSH solid (to the end concentrations specified in the figure captions) was added and the spectra registered.

^{1}H NMR [400 MHz, D_2O] : δ =8.75 (d, 8H, pyridinio-*H*), 8.69 (s, 8H, pyrrole-*H*), 8.38 (d, 8H, pyridinio-*H*), 7.45 (d, 8H, toluenesulfonate-*H*), 6.99 (d, 8H, toluenesulfonate-*H*), 4.49 (s, 12H, pyridinio-CH_3), 1.99 (s, 12 H, toluenesulfonate-CH_3) ppm.^{1}H NMR [400 MHz, DMSO-d_6]: δ =7.45 (d, 8H, toluenesulfonate-*H*), 7.12 (d, 8H, toluenesulfonate-*H*), 6.21 (d, 8H, pyrrole-*H*), 5.86 (s, 16H, pyridinio-*H*), 3.00 (s, 12H, pyridinio-CH_3), 2.27 (s, 12H, toluenesulfonate-CH_3), -2.49 (s, 1H, SH) ppm; ^{13}C NMR [100 MHz, DMSO-d_6] : δ = 21.11, 97.25, 106.24, 109.80, 125.93, 128.43, 129.08, 130.15, 131.75, 133.29, 138.04, 145,81.

Reversibility experiments. Each cycle was started by adding NaSH to an end concentration of 500 µM (i.e., in considerable excess over the *TMPyPZn* concentration) and completed by adding acetic acid to the sample solution for the complete removal of HS^- from the zinc complex. The emission was followed at 630 nm.

Selectivity experiments. Fluorescence emission at 630 nm (λ_{ex}= 563 nm) of TMPyPZn (5 µM) was monitored in the presence of KOH, Glutathione (GSH), L-Cysteine, L-alanine, L-leucine, CH_3COONa, NaSCN, $Na_2S_2O_3$, Na_3(citrate)* 2 H_2O, H_2O_2 (end concentration = 1.2 mM) in hepes buffer 25 mM at pH 7.4 and no significant changes were observed.

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Reference List

(1) Li, L.; Moore, P. K. *Biochem.Soc.Trans.*, 2007, **35**, 1138-1141.

(2) Wang, R. *Physiol Rev*, 2012, **92**, 791-896.

(3) Lin, V. S.; Lippert, A. R.; Chang, C. J. *Proc.Natl.Acad.Sci.U.S.A*, 2013, **110**, 7131-7135.

(4) Yu, C. M.; Li, X. Z.; Zeng, F.; Zheng, F. Y.; Wu, S. Z. *Chem. Commun.*, 2013, **49**, 403-405.

(5) Yang, G. D.; Wu, L. Y.; Jiang, B.; Yang, W.; Qi, J. S.; Cao, K.; Meng, Q. H.; Mustafa, A. K.; Mu, W. T.; Zhang, S. M.; Snyder, S. H.; Wang, R. *Science*, 2008, **322**, 587-590.

(6) Papapetropoulos, A.; Pyriochou, A.; Altaany, Z.; Yang, G.; Marazioti, A.; Zhou, Z.; Jeschke, M. G.; Branski, L. K.; Herndon, D. N.; Wang, R.; Szabo, C. *Proc.Natl.Acad.Sci.U.S.A*, 2009, **106**, 21972-21977.

(7) Liu, J.; Sun, Y. Q.; Zhang, J.; Yang, T.; Cao, J.; Zhang, L.; Guo, W. *Chem. Eur. J.*, 2013, **19**, 4717-4722.

(8) Kumar, N.; Bhalla, V.; Kumar, M. *Coord. Chem. Rev.*, 2013, **257**, 2335-2347.

(9) Strianese, M.; Pellecchia, C. *Coord. Chem. Rev.*, 2016, **318**, 16-28.

(10) Guo, Z.; Chen, G. Q.; Zeng, G. M.; Li, Z. W.; Chen, A. W.; Wang, J. J.; Jiang, L. B. *Analyst*, 2015, **140**, 1772-1786.

(11) Lin, V. S.; Lippert, A. R.; Chang, C. J. *Proc.Natl.Acad.Sci.U.S.A*, 2013, **110**, 7131-7135.

(12) Wang, X.; Sun, J.; Zhang, W.; Ma, X.; Lv, J.; Tang, B. *Chem.Sci.*, 2013, **4**, 2551-2556.

(13) Zhou, G.; Wang, H.; Ma, Y.; Chen, X. *Tetrahedron*, 2013, **69**, 867-870.

(14) Chen, S.; Chen, Z. J.; Ren, W.; Ai, H. W. *J.Am.Chem Soc.*, 2012, **134**, 9589-9592.

(15) Chen, T.; Zheng, Y.; Xu, Z.; Zhao, M.; Xu, Y.; Cui, J. *Tetrahedron Lett.*, 2013, **54**, 2980-2982.

(16) Mao, G. J.; Wei, T. T.; Wang, X. X.; Huan, S. Y.; Lu, D. Q.; Zhang, J.; Zhang, X. B.; Tan, W.; Shen, G. L.; Yu, R. Q. *Anal.Chem*, 2013, **85**, 7875-7881.

(17) Quek, Y. L.; Tan, C. H.; Bian, J.; Huang, D. *Inorg.Chem*, 2011, **50**, 7379-7381.

(18) Tropiano, M.; Faulkner, S. *Chem Commun.)*, 2014, **50**, 4696-4698.

(19) Takashima, I.; Kinoshita, M.; Kawagoe, R.; Nakagawa, S.; Sugimoto, M.; Hamachi, I.; Ojida, A. *Chem. Eur. J.*, 2014, **20**, 2184-2192.

(20) Lin, V. S.; Chang, C. J. *Curr.Opin.Chem Biol*, 2012, **16**, 595-601.

(21) Lippert, A. R.; New, E. J.; Chang, C. J. *J.Am.Chem Soc.*, 2011, **133**, 10078-10080.

(22) Peng, H.; Cheng, Y.; Dai, C.; King, A. L.; Predmore, B. L.; Lefer, D. J.; Wang, B. *Angew.Chem Int.Ed Engl.*, 2011, **50**, 9672-9675.

(23) Yu, F.; Li, P.; Song, P.; Wang, B.; Zhao, J.; Han, K. *Chem Commun.*, 2012, **48**, 2852-2854.

(24) Das, S. K.; Lim, C. S.; Yang, S. Y.; Han, J. H.; Cho, B. R. *Chem Commun.*, 2012, **48**, 8395-8397.

(25) Montoya, L. A.; Pluth, M. D. *Chem Commun.*, 2012, **48**, 4767-4769.

(26) Zheng, K.; Lin, W.; Tan, L. *Org.Biomol.Chem*, 2012, **10**, 9683-9688.

(27) Wu, Z.; Li, Z.; Yang, L.; Han, J.; Han, S. *Chem Commun.*, 2012, **48**, 10120-10122.

(28) Qian, Y.; Karpus, J.; Kabil, O.; Zhang, S. Y.; Zhu, H. L.; Banerjee, R.; Zhao, J.; He, C. *Nat.Commun.*, 2011, **2**, 495.

(29) Liu, C.; Pan, J.; Li, S.; Zhao, Y.; Wu, L. Y.; Berkman, C. E.; Whorton, A. R.; Xian, M. *Angew.Chem Int.Ed Engl.*, 2011, **50**, 10327-10329.

(30) Liu, C.; Peng, B.; Li, S.; Park, C. M.; Whorton, A. R.; Xian, M. *Org.Lett.*, 2012, **14**, 2184-2187.

(31) Zhao, Y.; Zhu, X.; Kan, H.; Wang, W.; Zhu, B.; Du, B.; Zhang, X. *Analyst*, 2012, **137**, 5576-5580.

(32) Sasakura, K.; Hanaoka, K.; Shibuya, N.; Mikami, Y.; Kimura, Y.; Komatsu, T.; Ueno, T.; Terai, T.; Kimura, H.; Nagano, T. *J.Am.Chem Soc.*, 2011, **133**, 18003-18005.

(33) Choi, M. G.; Cha, S.; Lee, H.; Jeon, H. L.; Chang, S. K. *Chem Commun.*, 2009, 7390-7392.

(34) Hou, F.; Huang, L.; Xi, P.; Cheng, J.; Zhao, X.; Xie, G.; Shi, Y.; Cheng, F.; Yao, X.; Bai, D.; Zeng, Z. *Inorg.Chem*, 2012, **51**, 2454-2460.

(35) Wang, M. Q.; Li, K.; Hou, J. T.; Wu, M. Y.; Huang, Z.; Yu, X. Q. *J.Org.Chem.*, 2012, **77**, 8350-8354.

(36) Cao, X.; Lin, W.; He, L. *Org.Lett.*, 2011, **13**, 4716-4719.

(37) Wu, M. Y.; Li, K.; Hou, J. T.; Huang, Z.; Yu, X. Q. *Org.Biomol.Chem*, 2012, **10**, 8342-8347.

(38) Xuan, W.; Pan, R.; Cao, Y.; Liu, K.; Wang, W. *Chem Commun.*, 2012, **48**, 10669-10671.

(39) Zhang, D.; Jin, W. *Spectrochim.Acta A Mol.Biomol.Spectrosc.*, 2012, **90**, 35-39.

(40) Santos-Figueroa, L. E.; de la Torre, C.; El Sayed, S.; Sancenon, F.; Martinez-Manez, R.; Costero, A. M.; Gil, S.; Parra, M. *Eur. J. Inorg. Chem.*, 2014, **2014**, 41-45.

(41) Ye, Z.; An, X.; Song, B.; Zhang, W.; Dai, Z.; Yuan, J. *Dalton Trans.*, 2014, **43**, 13055-13060.

(42) Strianese, M.; Milione, S.; Bertolasi, V.; Pellecchia, C.; Grassi, A. *Inorg.Chem.*, 2011, **50**, 900-910.

(43) Liu, Z. P.; He, W. J.; Guo, Z. J. *Chem. Soc. Rev.*, 2013, **42**, 1568-1600.

(44) Chen, W.; Pacheco, A.; Takano, Y.; Day, J. J.; Hanaoka, K.; Xian, M. *Angew.Chem.Int.Ed.*, 2016, **55**, 9993-9996.

(45) Hartle, M. D.; Delgado, M.; Gilbertson, J. D.; Pluth, M. D. *Chem.Commun.*, 2016, **52**, 7680-7682.

(46) Galardon, E.; Tomas, A.; Roussel, P.; Artaud, I. *Dalton Trans.*, 2009, 9126-9130.

(47) Strianese, M.; De, M. F.; Pellecchia, C.; Ruggiero, G.; D'Auria, S. *Protein Pept.Lett.*, 2011, **18**, 282-286.

(48) Strianese, M.; Palm, G. J.; Milione, S.; Kuhl, O.; Hinrichs, W.; Pellecchia, C. *Inorg.Chem*, 2012, **51**, 11220-11222.

(49) Strianese, M.; Mirra, S.; Bertolasi, V.; Milione, S.; Pellecchia, C. *New J.Chem.*, 2015, **39**, 4093-4099.

(50) Mirra, S.; Milione, S.; Strianese, M.; Pellecchia, C. *Eur. J. Inorg. Chem.*, 2015, 2272-2276.

(51) Quang, D. T.; Kim, J. S. *Chem.Rev.*, 2010, **110**, 6280-6301.

(52) Pasternack, R. F.; Francesconi, L.; Raff, D.; Spiro, E. *Inorg.Chem.*, 1973, **12**, 2606-2611.

(53) Adler, A. D.; Longo, F. R.; Kampas, F.; Kim, J. *J Inorg. Nucl. Chem.*, 1970, **32**, 2443-2445.

(54) Maeda, C.; Taniguchi, T.; Ogawa, K.; Ema, T. *Angew.Chem.Int.Ed.*, 2015, **54**, 134-138.

(55) Rombach, M.; Vahrenkamp, H. *Inorg.Chem.*, 2001, **40**, 6144-6150.

(56) Galardon, E.; Tomas, A.; Selkti, M.; Roussel, P.; Artaud, I. *Inorg.Chem.*, 2009, **48**, 5921-5927.

(57) Hartle, M. D.; Sommer, S. K.; Dietrich, S. R.; Pluth, M. D. *Inorg.Chem*, 2014, **53**, 7800-7802.

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Chemically reversible binding of H_2S to a zinc porphyrin: towards implementation of a reversible sensor via a "coordinative-based approach".

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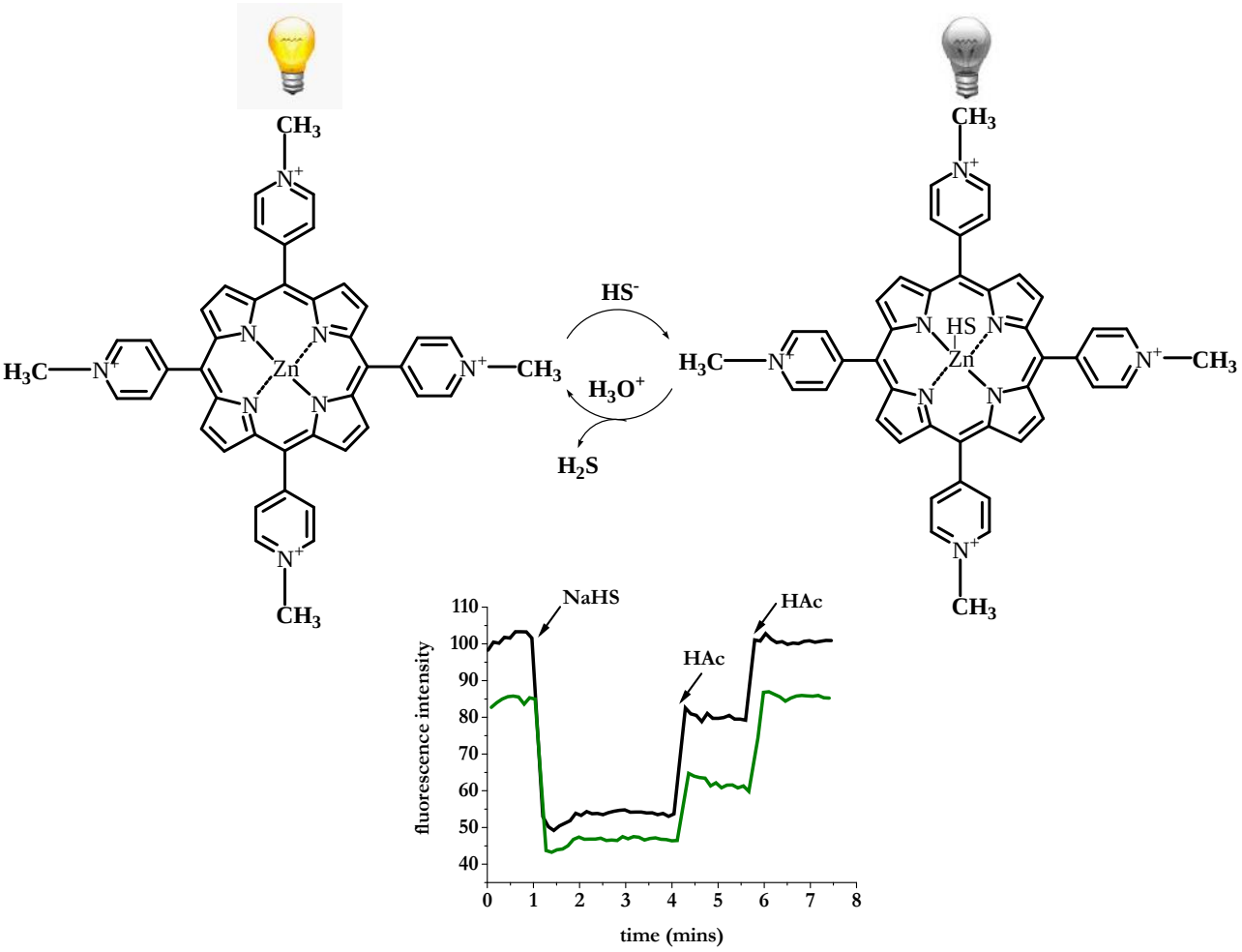

SYNOPSIS TOC.

Proof-of-principle results that *TMPyPZn* can be successfully implemented as a fluorescence-based sensing system for H_2S in buffered solutions and at physiological pH are reported. By HR MALDI-FT-ICR and ^1H NMR experiments we provide evidence that HS^- coordination occurs at the zinc centre. We believe *TMPyPZn* opens the door to a new family of devices for monitoring HS^- via a coordinative-based approach.

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