Dalton Transactions

RSC Publishing

COMMUNICATION

View Article Online
View Journal

Cite this: DOI: 10.1039/c2dt32135a

Received 15th September 2012,
Accepted 24th October 2012

DOI: 10.1039/c2dt32135a

www.rsc.org/dalton

A novel, selective, and extremely responsive thienyl-based dual fluorogenic probe for tandem superoxide and Hg^{2+} chemosensing†

Atul P. Singh,[a] Dhiraj P. Murale,[a] Yonghwang Ha,[a] Hyunjeong Liew,[b] Kang Mun Lee,[a] Aviv Segev,[c] Yoo-Hun Suh[b] and David G. Churchill*[a]

Novel, high "*turn-on*" Hg^{2+} and O_2^- fluorescence behaviour (~25-fold) with probes bearing [$S_{thi}N_{py}$] and [$S_{thi}N_{py}N_{py}$] binding receptors, joined by oxidizable sulphides, may involve *S*-bound transient ROS species; such optical O_2^- behaviour operates moderately in neuroblastoma.

The development of highly selective and sensitive recognition for particularly harmful or biologically vital cations/anions/substrates is a fundamental goal in small molecule fluorescence chemosensing.[1] Analyte selectivity, sensitivity (low detection limit), and biocompatibility (solubility/non-toxicity) continue to be keen objectives in the field. Multi-input probes are important research foci as well, especially when considering various biorelevant inputs.[2] Certain systems, in which two or more inputs are detected, have been previously reported: external stimulants can be metal–metal,[3a–c] metal-irradiation,[3c] and water-irradiation.[3d] The recognition and quantification of reactive oxygen species (ROS) are also extremely important in biological research.[4] Oxidative stress, involving high concentrations of, *e.g.*, hydrogen peroxide (H_2O_2), superoxide (O_2^-), hydroxyl ($^{\cdot}OH$), singlet oxygen, and lipid hydroperoxides (ROOH), may be a contributing factor for diseases including cancer, neurodegeneration, and diabetes. Research into new modes of selective metal ion detection *in vivo* is also important.[5] The roles of such ions in biology cannot be understated. Heavy metal ions such as Hg^{2+} are lethal for living organisms;[6a] yet, this analyte is commonly acting as a molecular fluorescence quencher, problematic in sensor design.[6b] Reports of sensing Hg^{2+} and ROS *simultaneously* are not known in BODIPY-based and other fluorophore systems. Furthermore, *amino acid* sensors are also important synthetic targets because of the general difficulty faced by biologists or in biotech in accurately assessing the concentration of these free species.[7] Selectivity of amino acids may sometimes be achieved by considering carefully the coordination chemistry of donor atoms and their binding ability.

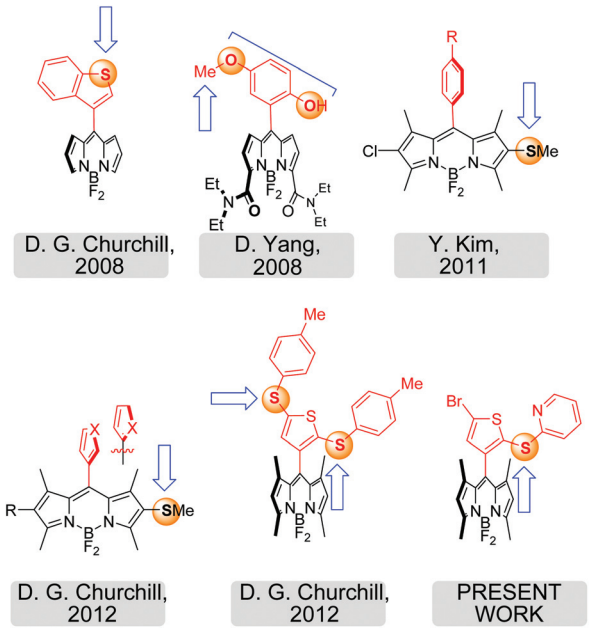
Our chemosensing strategy involves an interrogating 3-thienyl *S*-atom center flanked by Ar-sulfide groups[8,9] which constitutes a sensitive donor moiety of the donor–acceptor dyad. The 2-pyridyl-*S* arms allow for both (i) ROS oxidation and (ii) metal binding, and result in the formation of species that, upon analyte reaction/coordination, have greatly enhanced sterical rigidity of the *meso*-group. Here, we report the synthesis of novel BODIPY molecules (**3** and **4**) and their selective fluorescence cation and ROS responsiveness that leads to interpretation of "*AND*" logic gating (Scheme 1).

Synthetically, BODIPY conjugate formation involved the bromination (*N*-bromosuccinimide) of 3-thiophene carboxaldehyde in DMF to afford the 2,5-dibromo-3-thiophene carbaldehyde.[10] This aldehyde can then be functionalized to the disulfide (**1**) and monosulfide (**2**) versions through facile copper coupling;[11] these aldehydes can then undergo subsequent reaction with 2,4-dimethylpyrrole to give BODIPY dyes **3** and **4** in ~42 and ~46% yield, respectively (Scheme 2).[9,9b] Compound characterization was undertaken by ^{1}H-, ^{13}C-, and 2-D NMR spectroscopy and ESI† mass spectrometry (ESI†). Furthermore, compound **4** was structurally characterized by X-ray diffraction.

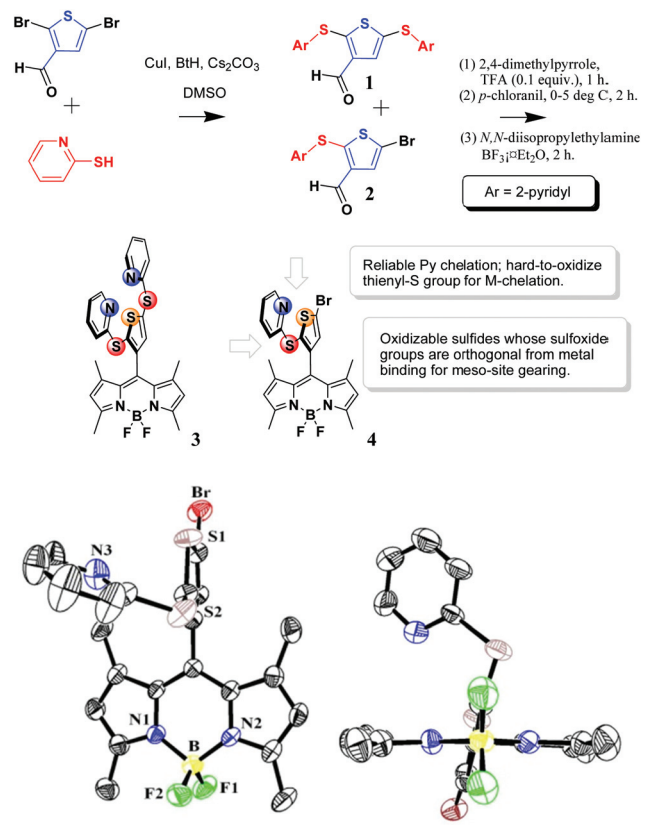
UV-vis and PL properties for **3** and **4** (Φ_F = 0.019 and 0.026, respectively) were also studied (Fig. 1 and 2) to understand the basic photophysical properties at play (water : acetonitrile, ≥30 : ≤70%). The initial small Φ_F values for **3** and **4** and other properties reveal that –Br substitution for -S-2-Py imparts a very minor difference in signal intensity to the fluorophore. In the absence of an aryl 8-substituent, extremely high

[a]*Molecular Logic Gate Laboratory, Department of Chemistry, Korea Advanced Institute of Science and Technology (KAIST), 373-1 Guseong-dong, Yuseong-gu, Daejeon 305-701, Republic of Korea. E-mail: dchurchill@kaist.ac.kr*
[b]*Department of Pharmacology, College of Medicine, National Creative Research Initiative Center for Alzheimer's Dementia and Neuroscience Research Institute, MRC, Seoul National University, Seoul 110-799, Republic of Korea*
[c]*"Know Lab" Department of Knowledge Service Engineering, KAIST, 373-1 Guseong-dong, Yuseong-gu, Daejeon 305-701, Republic of Korea*

†Electronic supplementary information (ESI) available: Experimental details, inline spectral data, reproductions of NMR spectra, HR MS spectra, crystallographic data, structural bond lengths and angles, *etc.* CCDC 877969. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c2dt32135a



Scheme 1 (*top*) Related ROS probes that bear sulfides and other BODIPY PET donor–acceptor motifs.



Scheme 2 (*top*) Synthesis of probes **3** and **4**, and (*middle*) important points about rational probe design and role of receptor site heteroatoms. (*bottom*) Two views (from top and front) of the molecular structure of **4** (CCDC 877969). Hydrogen atoms omitted for clarity, percentage of thermal ellipsoids = 30%.

fluorescence is expected.[9a] Thus, the aryl group, as it exists for **3** or **4**, is most likely involved in a PET quenching phenomenon with the BODIPY fluorophore moiety. In compound **4**, which is the simpler of the two probes, the N_{py} and $S_{sulfide}$ groups participate in metal binding and ROS reactivity, and allow for PET mechanism quenching (Fig. 3). This allows for a concomitant fluorescence emission "turn-on" response (λ_{em} = 524 nm).[16]

The crystal structure of **4** was obtained. Its molecular geometry shows the expected BODIPY moiety bearing the requisite single 2-Py-S group attached at the 2-position of the thienyl group, as supported by various solution NMR spectroscopic data. A distal 5-position C–Br group is also shown which is the point of attachment for the second thioaryl group in compound **4**. In the molecular structure of compound **4**, the thienyl-BODIPY torsion angle is ~80°. This angle helps gauge the sterics of the system.‡ Furthermore, the Py group is found to be at a torsion angle of ~64° from the thienyl group. Attempts to crystallize metal complexes were not fruitful.

In solution, probes **3** and **4** were screened for responses with common metal ion species. Ions Cd^{2+}, Hg^{2+}, Fe^{2+}, Ca^{2+}, Cu^{2+}, Co^{2+}, Mn^{2+}, Mg^{2+}, Pb^{2+}, Zn^{2+} and Ag^{+} were used as their perchlorate salts in dissolved precalibrated forms. Colorimetric data of the probes with Hg^{2+} were obtained and metal chelation reversibility was studied with amino acids (Fig. 3a and b). Regarding absorption data, only Hg^{2+} affected the absorption band of **3** and **4** in solution: a light yellow initial solution led to a resulting orange-red solution response ($\lambda_{abs.max}$ = 506 → 532 nm). This quantifiable bathochromic shift (~25 nm) is enough to be observable with the "naked eye" at probe concentrations as low as 10^{-6} M (ESI†). Titrations of **3** and **4** with Hg^{2+} revealed the expected 1 : 1 stoichiometry (*vide infra*), confirmed by Job analysis (Fig. 3). Here, UV-vis responses could also be obtained in the presence of amino acid substrates; the amino acid is acting to displace the mercury atom from the probe chelation pocket and thus helps restore the colorimetric response. On studying **3**·Hg^{2+} + amino acid interactions for all amino acids, cysteine, histidine, arginine, and lysine were found to displace Hg^{2+} most completely from the probe chelation pocket under the same conditions (Fig. 3 and S40–S47†). The total Φ_F recovery occurs above 4.0 equiv. with these amino acids.

Emission spectra obtained from the solutions titrated above reveal quenching in the case of Hg^{2+} and slight quenching for Cu^{2+} (Fig. S17 and S25†); other metal ions did not affect the emission signal.[12] Fluorophore quenching is likely due to enhanced spin–orbit coupling through probe·Hg^{2+} binding (*vide infra*).[13] However, it is possible that the **4**·Hg^{2+} chelate bears a new absorption maximum different from the $\lambda_{abs.max}$ value of compound **4**.

Next, probes **3** and **4** were screened for responses with various reactive oxygen species. The sulfide group(s) in **3** and **4** become sulfoxide and sulfone groups upon treatment with ROS species. Probes **3** and **4** were titrated with *m*-CPBA, KO_2, H_2O_2, NaOCl, ^{t}BuOOH, $^{\cdot}$OH, $^{\cdot}$O^{t}Bu in MeCN/H_2O (70 : 30). Importantly, the photoluminescence data showed a selective

response for KO_2 (Fig. S19 and S27†), different from that for closely related systems.[9,14] Under the given conditions, this suggests sulfoxide/sulfone formation for this ROS species. When comparing the reaction of compounds **3** and **4** with KO_2, a greater emission enhancement was found for compound **3** (Fig. 1); in this case KO_2 gave a fluorescence increase of 150%; for *m*-CPBA an increase of only 25% was determined (Fig. 1).[12]

A study of both analytes together was then undertaken. Upon dual addition, whether in the order (i) **3** + Hg^{2+} + O_2^- or (ii) **3** + O_2^- + Hg^{2+}, a strong "turn-on" fluorescence response resulted after the addition of the third component; this is especially interesting because of this being achieved at low concentrations (Fig. S33 and S35†). The relative inactivity with just one analyte (superoxide or Hg^{2+}) underscores the profound change at the fluorophore. Important geometrical changes occur at the receptor site where two donor atom sets [$NS_{thi}N$] and [$S_{sulfide}S_{sulfide}$] exist, the first set acts to cradle the metal ion; and the second one, orthogonal to the first, allows reactions with ROS species. This rationally designed motif is important to allow for small molecule probes to have multi-input properties. Compounds **3** and **4** can be designated as having "*AND*" logic gating under the given analyte conditions (ESI†). A truth table and a bar graph for the "*AND*" logic gate are provided in Fig. 1. Sequence-independent optical changes also suggest a versatility created by the *o*-Py nitrogen group when compared to the previously reported *p*-Tol groups.[9,15] Stern–Volmer plot data were obtained (in triplicate) at variable [Hg^{2+}] and [*probe*] concentrations where [KO_2] was fixed at 20 equiv. (Fig. 1). Saturative behavior for compound **3** was observed at higher concentrations (ESI†). Artificial neural networking was used in optimizing optical outputting and analyte sensing performance (ESI†).

Cellular neurobiological studies were then undertaken. The sensing pattern found in cuvette research translates to the matrixes of live cell assays in which neuroblastomas were used. Moderate responses for superoxide were obtained in which there was the presence of probe + ROS only (not Hg^{2+}). Furthermore, extremely low cell toxicity is also evident with this new class of probe.

Since the titrations showed strong "turn-on" responses with KO_2 that were strongly suspected to arise from the formation of the sulfoxide/sulfone species, authentic samples of the mono- and dioxidized forms of **4** were prepared. Compound **4**

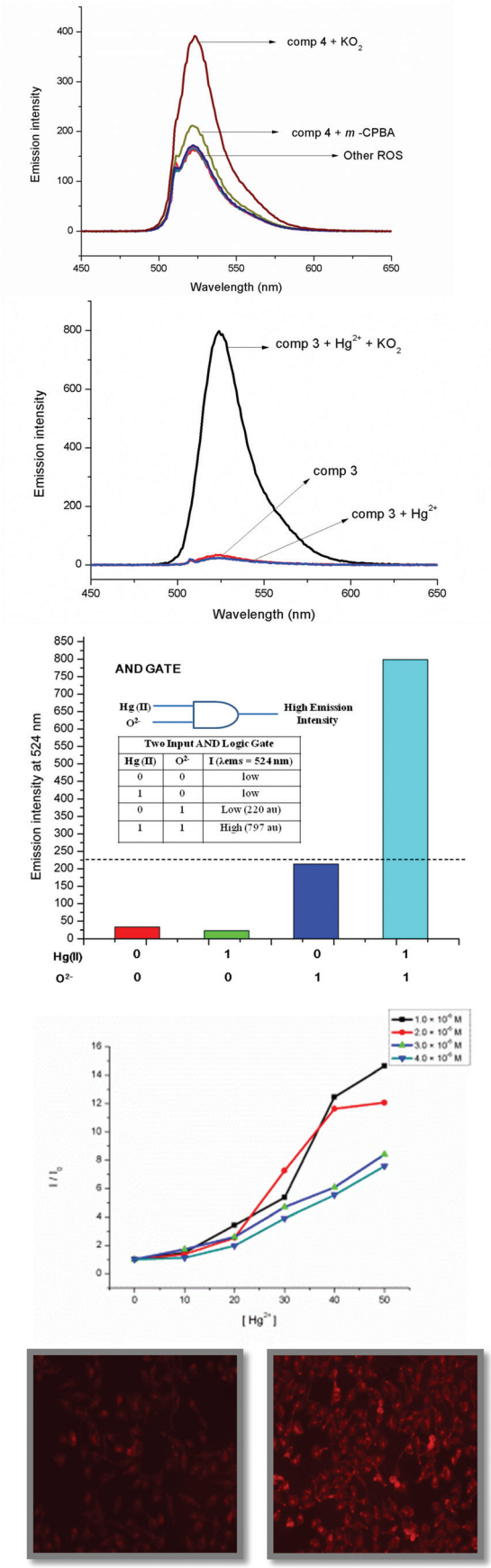


Fig. 1 (*top*) Emission spectra of compound **3** (1.0×10^{-6} M, 3.0 mL) with *m*-CPBA, KO_2, H_2O_2, NaOCl, ^{t}BuOOH, $^{\cdot}$OH, $^{\cdot}O^t$Bu (1.0×10^{-2} M, 50 μL, ~18 equiv.) showing selectivity of **3** for KO_2. (*top*) "Turn-on" response with superoxide (150% increase, $\lambda_{exc} = \lambda_{abs}$ = 506 nm) in MeCN : H_2O (70 : 30). (*second from top*) Emission spectra of **3** (1.0×10^{-6} M, 3.0 mL) with dual inputs, KO_2 (1.0×10^{-2} M, 50 μL, ~18 equiv.) and Hg^{2+} (1.0×10^{-2} M, 50 μL, ~18 equiv.) in acetonitrile–water (70/30). (*middle*) "*AND*" logic gate truth table and bar chart for probe **3**. (*second from bottom*) Stern–Volmer diagrams obtained at variable [Hg^{2+}] and [**4**] with [KO_2] = 20 equiv. (in triplicate). (*bottom*) "Proof-of-concept" in neurological milieu: (*bottom left*) just probe **3** and (*bottom right*) probe + KO_2 showing a moderate response (ESI†).

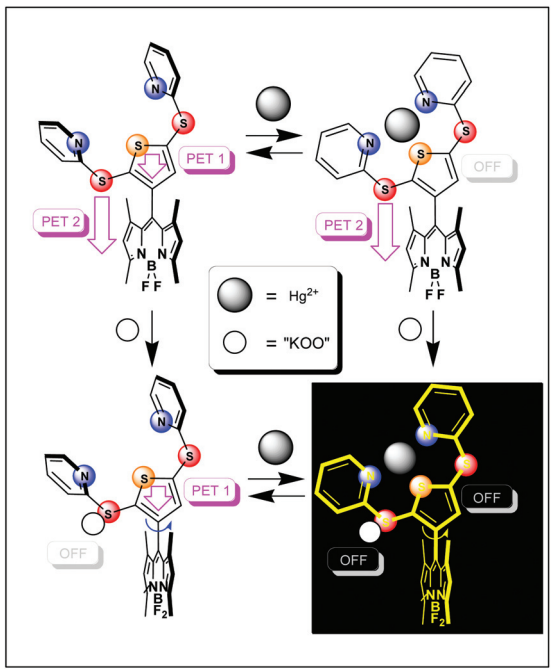


Fig. 2 Proposed dual PET pathways for OFF–ON on inputs of O_2^- and Hg^{2+} with dye **3**.

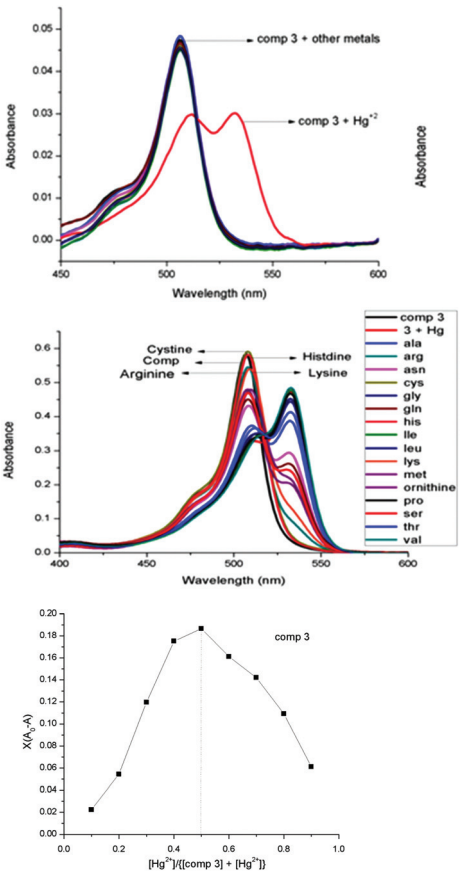


Fig. 3 (*top*) Absorption spectra for compound **3** (1.0×10^{-6} M, 3.0 (*middle*) amino acid competition studies with **3**. (*bottom*) Job plot analysis.

was used, which is a simpler system where mono- and di-oxidation can occur at the proximal sulfide site only. A separate reaction was performed to characterize the products of **4** with KO_2 in acetonitrile–H_2O. Unfortunately, decomposition occurred during the work-up step as the reaction solvent was being concentrated. To circumvent this synthetic problem, the *fluorescent mono-* (**5**) and *di*-oxidized (**6**) forms of compound **4** were prepared with *m*-CPBA (in CH_2Cl_2) (Φ_F = 0.87 and 0.77, respectively). Surprisingly, upon titration with Hg^{2+}, no emission or absorption changes were found (Fig. S48–51†). When **3** or **4** are titrated with KO_2, they do *not* generate respective compounds **5** and **6**, as found for closely related studies in which tolylsulfide groups are oxidized with *m*-CPBA to give straightforward sulfoxide and sulfone formation (Fig. 1).[9a] For compounds **3** or **4**, a long-lasting oxidized species giving a signal from the superoxide is *neither* the sulfoxide nor the sulfone; a transient $S_{sulfide}$···OOK-type species or BODIPY···OOK-type species is instead proposed. Prior to Hg^{2+}-binding these proposed species account for only a given moderate increase in fluorescence (Fig. 1, top) unlike the fluorescence seen for **5** and **6**. The proposed $S_{sulfide}$···OOK-like intermediate loses its solution fluorescence easily (MeCN–H_2O) and is not isolable, whereas the fluorescence for **5** and **6** persists and these species are isolable.

Hg^{2+} and superoxide binding can be tentatively assigned to be at the *meso* group, considering the available donor atoms found there. One Hg^{2+} ion is expected to interact per one probe molecule, based on Job analysis (*vide supra*); this metal ion binding will be proximal to the $S_{sulfide}$···OOK-type species. Thus, an Hg^{2+} S_{thi},N_{py}-bound system with an additional $S_{sulfide}$···OOK interaction is expected to lead easily to *PET deactivation* by giving a significant electronic change proximal to the fluorophore. "Gearing" may occur with this enhanced steric group which slows aryl rotation and further helps fluorescence recovery. Pathways other than sulfur oxidation by superoxide have less support from the data: (i) probe self-oxidation that gives dimerization would most likely lead to a species that is greatly red-shifted ($\gg\lambda_{abs.max}$) and that is assumed to be in no better position to undergo a "turn-on" response with Hg^{2+}. (ii) N_{pyr}-Oxide formation is not likely because of Hg^{2+}; when Hg^{2+} is added in excess *prior* to superoxide addition, the fluorophore retains a "turn-on" response. (iii) Lastly, a BODIPY that is oxidized at the dyad acceptor 2- or 6-positions results from electrophilic addition typically and is not thought to lead to greater fluorescence. Furthermore, such a substituted species is not likely to account for the observed brightness when in the presence of Hg^{2+}.

In summary, herein, we have pursued the synthesis of systems that may be able to determine, simultaneously, cations, anions, and substrates closely together at the same chelation pocket. We have prepared two novel bifunctional organic-based probes for novel chemosensing. "*AND*" logic gating is demonstrated for the two different types of species: superoxide and the mercuric ion. These species were able to be selectively detected by probes **3** and **4** from respective sets of ROS and metal ions. As shown in emission spectra,

~25-fold fluorescence "*turn-on*" enhancement was demonstrated; separate responses for the superoxide anion and Hg^{2+} with dye **3** reveal only moderate changes in emission profiles. The novel molecular probes (**3** and **4**) involve novel and versatile 2,5-bis(2-pyridylsulfido)- and 5-2-pyridylsulfido-substituted *meso*-thienyl groups.[9,17] The chelating sites bearing *N*- and *S*-atoms are versatile, as compared to the activity for related systems.[9a] The responses to these data were improved when Stern–Volmer plot data were processed by artificial neural network modelling. In attempting to elucidate a binding/reaction mechanism that is consistent with the two inputs and the optical output, the oxygenated monopyridyl species **5** and **6** were separately prepared and characterized. Importantly, these do *not* give a fluorescence change with [Hg^{2+}], suggesting that *neither the sulfoxide nor sulfone is on the reaction pathway to giving the excellent turn-on signal in the presence of both analytes*. This work is interesting because few, if any, chemical systems can selectively detect superoxide and mercuric ions at the same time. Neuronal cells were also studied; clear responses were shown with superoxide. Lastly, colorimetric sensing behaviour was observed with Hg^{2+} (light yellow → red; 25 nm red-shift) and reverted back to the unbound species through the competitive chelation action of certain amino acids. Hypsochromic shifting is effective with **3**·Hg^{2+} in the presence of histidine, arginine, lysine, and cysteine. Such a probe class can be further explored in sensor chemical and molecular neurodegenerative disease research.

The Molecular Logic Gate Laboratory operated by D.G.C. acknowledges research support from the National Research Foundation (NRF) (Grant # 2009-0070330 & 2010-0013660, 2011-0017280). Mr. Hack Soo Shin and Prof. Youngkyu Do are gratefully acknowledged, respectively, for facilitating the acquisition of NMR spectroscopic and crystallographic data. These data greatly enhance our work. The research support staff at KAIST facilitated the acquisition of our MS data. We thank Deposition Coordinator Kamila Nowakowska (CCDC).

Notes and references

‡Crystallographic data: Compound **4** (CCDC 877969): $C_{22}H_{19}BBrF_2N_3S_2$, F.W.: 518.24. Monoclinic, $P2(1)/n$, $Z = 4$, $a = 7.5392(14)$ Å, $b = 11.289(2)$ Å, $c = 27.479(5)$ Å, $\beta = 95.937(8)°$, $V = 2326.2(7)$ Å^3, $T = 296(2)$ K, No. of reflections = 8225, no. of independent reflections = 5946 [$R_{(int)} = 0.1663$], $R_1 = 0.0724$, w$R_2 = 0.1907$, abs. coeff. (mm^{-1}) = 1.977, largest diff. peak and hole = 0.628 and 0.496 e Å^{-3}.

1 (*a*) A. P. de Silva, H. Q. N. Gunaratne, T. Gunnalugsson, A. J. M. Huxley, C. P. McCoy, J. T. Rademacher and T. E. Rice, *Chem. Rev.*, 1997, **97**, 1515–1566; (*b*) A. P. de Silva, D. B. Fox and A. J. M. Huxley, *Coord. Chem. Rev.*, 2000, **205**, 41–57.

2 (*a*) A. P. de Silva, T. P. Vance, M. E. S. West and G. D. Wright, *Org. Biomol. Chem.*, 2008, **6**, 2468–2480; (*b*) H. Tian, B. Quin, R. X. Yao, X. L. Zhao and S. J. Yang, *Adv. Mater.*, 2003, **15**, 2104–2107; (*c*) H. M. Wang, D. Q. Zhang, X. F. Guo, L. Y. Zhu, Z. G. Shuai and D. B. Zhu, *Chem. Commun.*, 2004, 670–671; (*d*) Y. Liu, W. Jiang, H. Y. Zhang and C. J. Li, *J. Phys. Chem. B*, 2006, **110**, 14231–14235; (*e*) N. Kaur, N. Singh, D. Cairns and J. F. Callan, *Org. Lett.*, 2009, **11**, 2229–2232.

3 (*a*) O. A. Bozdemir, R. Guliyev, O. Buyukcakir, S. Selcuk, S. Kolemen, G. Gulseren, T. Nalbantoglu, H. Boyaci and E. U. Akkaya, *J. Am. Chem. Soc.*, 2010, **132**, 8029–8036; (*b*) M. Yuan, W. Zhou, X. Liu, M. Zhu, J. Li, X. Yin, H. Zheng, Z. Zuo, C. Ouyang, H. Liu, Y. Li and D. Zhu, *J. Org. Chem.*, 2008, **73**, 5008–5014; (*c*) R. Guliyev, S. Ozturk, Z. Kostereli and E. U. Akkaya, *Angew. Chem., Int. Ed.*, 2011, **50**, 9826–9831; (*d*) S. Chen, W. Chen, W. Shi and H. Ma, *Chem.–Eur. J.*, 2012, **18**, 925–930.

4 (*a*) B. C. Dickinson and C. J. Chang, *Nat. Chem. Biol.*, 2011, **7**, 504–511; (*b*) M. Schaeferling, D. B. M. Groegel and S. Schreml, *Microchim. Acta*, 2011, **174**, 1–18; (*c*) C. J. Chang, *Cur. Opin. Chem. Biol.*, 2010, **14**, 50–56; (*d*) C. C. Winterbourn, *Nat. Chem. Biol.*, 2008, **4**, 278–286; (*e*) B. Halliwell and J. M. C. Gutteridge, *Free Radicals in Bology and Medicine*, Oxford University Press, Oxford, 4th edn, 2007; (*f*) P. Wardman, *Free Radical Biol. Med.*, 2007, **43**, 995–1022; (*g*) N. Soh, *Anal. Bioanal. Chem.*, 2006, **386**, 532–543.

5 (*a*) E. L. Que and C. J. Chang, *Chem. Soc. Rev.*, 2010, **39**, 51–60; (*b*) J. F. Zhang, Y. Zhou, J. Yoon and J. S. Kim, *Chem. Soc. Rev.*, 2011, **40**, 3416–3429; (*c*) Z. Ma, F. E. Jacobsen and D. P. Giedroc, *Chem. Rev.*, 2009, **109**, 4644–4681; (*d*) L. Fabbrizzi and A. Poggi, *Chem. Soc. Rev.*, 1995, **39**, 197–202.

6 (*a*) H. N. Kim, W. X. Ren, J. S. Kim and J. Yoon, *Chem. Soc. Rev.*, 2012, **41**, 3210–3244; (*b*) H. Masuhara, H. Shioyama, T. Saito, K. Hamada, S. Yasoshima and N. Mataga, *J. Phys. Chem.*, 1984, **88**, 5868–5873.

7 (*a*) M. Martínez-Máñez and F. Sancenón, *Chem. Rev.*, 2003, **103**, 4419–4476; (*b*) A. Buryak and K. Severin, *Angew. Chem., Int. Ed.*, 2005, **44**, 7935–7938; (*c*) A. Buryak and K. Severin, *J. Am. Chem. Soc.*, 2005, **127**, 3700–3701; (*d*) H. Aït-Haddou, S. L. Wiskur, V. M. Lynch and E. V. Anslyn, *J. Am. Chem. Soc.*, 2001, **123**, 11296–11297; (*e*) M. A. Hortalá, L. Fabbrizzi, N. Marcotte, F. Stomeo and A. Taglietti, *J. Am. Chem. Soc.*, 2003, **125**, 20–21; (*f*) Y. Zhou, J. Won, J. Y. Lee and J. Yoon, *Chem. Commun.*, 2011, 1997–1999.

8 (*a*) S. H. Choi, K. Kim, J. Jeon, B. Meka, D. Bucella, K. Pang, S. Khatua, J. Lee and D. G. Churchill, *Inorg. Chem.*, 2008, **47**, 11071–11083; (*b*) S. H. Choi, K. Kim, J. Lee, Y. Do and D. G. Churchill, *J. Chem. Crystallogr.*, 2007, **37**, 315; (*c*) K. Kim, C. Jo, S. Easwaramoorthi, J. Sung, D. H. Kim and D. G. Churchill, *Inorg. Chem.*, 2010, **49**, 4881; (*d*) S. H. Choi, K. Pang, K. Kim and D. G. Churchill, *Inorg. Chem.*, 2007, **46**, 10564; (*e*) E. Peña-Cabrera, A. Aguilar-Aguilar, M. Gonzalez-Dominguez, E. Lager, R. Zamudio-Vazquez, J. Godoy-Vargas and F. Villanueva-Garcia, *Org. Lett.*, 2007, **9**, 3985.

9 (*a*) A. P. Singh, K. M. Lee, D. P. Murale, T. Jun, H. Liew, Y.-H. Suh and D. G. Churchill, *Chem. Commun.*, 2012, **48**, 7298–7300; (*b*) *Note*: compounds were designed to contain mixed soft/hard donor atoms: *N*,(*S*),S_{thi},(*S*),*N* (for **3**) and

N,(*S*),*S* (for **4**). Divalent sulfide sulfurs may change to +4 and +6 upon addition of consecutive oxygen atoms. The thienyl-S with its 1–2 lone pairs is a pivotal site for coordination and organic chemistry considerations.

10 K.-H. Lee, K. Morino, A. Sudo and T. Endo, *J. Polym. Sci., Part A: Polym. Chem.*, 2011, **49**, 1190–1194.

11 A. K. Verma, J. Singh and R. Chaudhary, *Tetrahedron Lett.*, 2007, **48**, 7199–7202.

12 J. H. Chang, Y. Jeong and Y.-K. Shin, *Bull. Korean Chem. Soc.*, 2003, **24**, 119–122.

13 (*a*) D. S. McClure, *J. Chem. Phys.*, 1952, **20**, 682; (*b*) X. Qi, S. K. Kim, E. J. Jun, L. Xu, S. -J. Kim and J. Yoon, *Bull. Korean Chem. Soc.*, 2007, **28**, 2231–2234.

14 T.-I. Kim, S. Park, Y. Choi and Y. Kim, *Chem.–Asian J.*, 2011, **6**, 1358–1361.

15 (*a*) A. P. de Silva, H. Q. N. Gunaratne and C. P. McCoy, *Nature*, 1993, **364**, 42–44; (*b*) A. P. de Silva, H. Q. N. Gunaratne and C. P. McCoy, *J. Am. Chem. Soc.*, 1997, **119**, 7891–7892.

16 (*a*) M. Yuan, Y. Li, J. Li, C. Li, X. Liu, J. Lv, J. Xu, H. Liu, S. Wang and D. Zhu, *Org. Lett.*, 2007, **9**, 2313–2316; (*b*) J. Fan, K. Guo, X. Peng, J. Du, J. Wang, S. Sun and H. Li, *Sens. Actuators, B*, 2009, **142**, 191–196.

17 (*a*) H. Tian and S. Wang, *Chem. Commun.*, 2007, 781–792; (*b*) P. Kaur, S. Kaur and K. Singh, *Org. Biomol. Chem.*, 2012, **10**, 1497–1501.