An Ir(III) complex chemosensor for the detection of thiols

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In this study, we report the use of a cyclometalated luminescent iridium(III) complex for the visualization of thiols. The detection of glutathione (GSH) by complex 1 is achieved through the reduction of its phendione N=N donor, which influences the metal-to-ligand charge-transfer (MLCT) of the complex. Complex 1 produced a maximum threefold luminescence enhancement at 587 nm in response to GSH. The linear detection range of 1 for GSH is between 0.2 and 2 M equivalents of GSH, with a detection limit of 1.67 μM. Complex 1 also displays good selectivity for thiols over other amino acids.

**KEYWORDS**

iridium(iii) complex; chemosensor; thiols

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**ABSTRACT**

In this study, we report the use of a cyclometalated luminescent iridium(III) complex for the visualization of thiols. The detection of glutathione (GSH) by complex 1 is achieved through the reduction of its phendione N=N donor, which influences the metal-to-ligand charge-transfer (MLCT) of the complex. Complex 1 produced a maximum threefold luminescence enhancement at 587 nm in response to GSH. The linear detection range of 1 for GSH is between 0.2 and 2 M equivalents of GSH, with a detection limit of 1.67 μM. Complex 1 also displays good selectivity for thiols over other amino acids.

**1. Introduction**

Biological thiols play essential roles in cell function and maintenance. In particular, glutathione (GSH) is critically involved in redox homeostasis in cellulo. The dysregulation of GSH activity has been linked to diseases such as cancer, cystic fibrosis and neurodegenerative diseases.[1] Therefore, the development of sensitive detection methods for biothiols has recently been an active area of research.

Typical instrumental detection methods for biothiols include liquid chromatography,[2,3] capillary electrophoresis,[4] voltammetry [5] and flow injection.[6] However, those techniques require relatively complex sample preparation protocols and sophisticated instrumentation. Meanwhile, a number of chemosensors have been employed for the detection of thiols based on the thiol addition reaction, reviewed in [7,8]. However, thiol chemosensors are based on organic molecules, [9–17] and only a few examples of transition metal complexes as thiol chemosensors have been reported.

Compared with organic molecules, transition metal complexes are generally relatively easy to synthesize and modify, exhibit large Stokes shifts, and offer long-lived luminescence that could allow them to be potentially used in autofluorescent biological matrices.[18–24] Several iridium(III) complex chemosensors have been reported for thiol detection. Che and co-workers reported a FRET-based luminescent iridium(III) probe for the detection of cysteine (Cys) and homocysteine.[31] Later on some iridium(III) complexes were reported for thiol detection in cellulo. [32,33] Li, Huang, Yi and co-workers have demonstrated iridium(III) complex chemosensors for selectively detecting homocysteine [34] or both homocysteine and cysteine,[35–38] and have employed these for the visualization of thiol in the cell. While Chao’s group
3. Results and discussion

3.1. Design and synthesis of a thiols chemosensor

The photophysical properties of iridium(III) complex are sensitive to both the solvent environment and the nature of their C^N or N^N donor ligands. Phenanthrene-9,10-quinone, which has been associated with the production of reactive oxygen species (ROS), can be reduced back to catechol in futile redox cycles both enzymatically and nonenzymatically. On the other hand, GSH, as the most abundant non-protein thiol, is a major reductant in internal cellular compartments. As a consequence, we chose the structurally related 1,10-phenanthroline-5,6-dione (phendione) moiety as the N^N donor for the iridium(III) complex, thereby allowing the complex to function as a luminescent chemosensor for thiols detection.

2. Experimental details

2.1. Synthesis of [Ir(ppy)2(phendione)](PF6) 1

Complex 1 was reported in previous literature. A suspension of [Ir(ppy)]2Cl2 (ppy = 2-phenylpyridine) (0.2 mmol) and 1,10-phenanthroline-5,6-dione (phendione) (0.42 mmol) in a mixture of CH2Cl2:MeOH (1:1, 20 ml) was refluxed overnight under N2. The product mixture was then allowed to cool down to 25°C, and was filtered to remove unreacted dimer. To the filtrate, excess amount of NH4PF6 was added and the filtrate was reduced in volume by evaporation until precipitation of the crude product was observed. The precipitate was then filtered and washed by 40 ml water twice followed by 40 ml diethyl ether twice. The product was recrystallized by acetone: diethyl ether vapor diffusion to yield the titled compound as a brown solid.

![Figure 1](image1.jpg)

Figure 1. Mechanism of GSH detection by iridium(iii) complex 1 while GSSG is oxidized by glutathione.

![Figure 2](image2.jpg)

Figure 2. (A) Luminescence spectra of 1 (20 μM) with increasing concentration of GSH (0–3.75 eq.) in DMSO:HEPES 9:1 (10 mM, pH 7.0). (B) The relationship between luminescence intensity and GSH concentration.
their emission to be identified from a strongly autofluorescent background signal by utilizing time-resolved luminescence spectroscopy. Moreover, 1 exhibited a maximum emission wavelength at 587 nm upon excitation at 350 nm. The Stokes shift is approximately 237 nm, which is much higher than those typically exhibited by organic chemosensors.

3.3. Signal response of 1 to GSH

We next examined the emission response of 1 towards GSH. In the absence of GSH, the luminescence intensity of 1 is weak in a 9:1 mixture of dimethyl sulfoxide and 4-(2-hydroxyethyl)-1-piperazineethanesulfonic acid (DMSO:HEPES, 10 mM, pH 7.0). However, upon addition of GSH, a significant enhancement in the luminescence intensity of 1 was recorded. The luminescence of...
GSH and Cys was significantly stronger than that of 1 M equivalent of other amino acids while the luminescence enhancement of GSH is twofold higher than that of Cys. This is presumably due to the different oxidizing ability. These results demonstrate the selectivity of the chemosensor for thiols over amino acids. We also performed a competition experiment to investigate the response of 1 towards GSH and (1 M equivalent) in the presence of a mixture of all interfering amino acids (1 M equivalent each). Encouragingly, the luminescence intensity of 1 was not significantly affected upon the addition of different interfering amino acids, indicating that 1 could possibly be utilized to detect thiols in a real sample matrix in the presence of other amino acids.

4. Conclusions

In conclusion, we have employed the iridium(III) complex 1 for the detection of thiols. We postulate that the reduction of the phendione N^N donor by thiols may influence the MLCT state of complex 1, thereby enabling 1 to function as a luminescent chemosensor for thiols. The proposed mechanism of the chemosensor was supported by NMR and high-resolution mass spectrometry analysis. Complex 1 produced a maximum threefold luminescence enhancement at 583 nm in response to GSH. The linear detection range of 1 for GSH is 0.2‒2 M equivalents of GSH, with a detection limit of 1.67 μM. Complex 1 also displays good selectivity for GSH and Cys over common amino acids. Compared with common organic chemosensors, 1 displays a large Stokes shift and a long-lived luminescence that may favor its use in strongly autofluorescent biological samples.

Disclosure statement

No potential conflict of interest was reported by the authors.

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References


[31] Shiu H-Y, Wong M-K, Che C-M. "Turn-on" FRET-based luminescent iridium(III) probes for the detection...