

## A New Thiourea Compound as Potential Ionophore for Metal Ion Sensor

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### ABSTRACT

A new thiourea compound, 2,2-oxybis(ethyl)-4-(1-naphthyl)-3-thiourea **3** has been synthesized and characterized by using FTIR,  $^1\text{H-NMR}$ ,  $^{13}\text{C-NMR}$ , and MS spectroscopy. The binding properties with various cations were also carried out using 'naked eye', UV-vis and  $^1\text{H-NMR}$  titration experiments. This compound exhibited effective binding for  $\text{Hg}^{2+}$  in the presence of other cations, such as  $\text{Ag}^+$ ,  $\text{Ni}^{2+}$ ,  $\text{Sn}^{2+}$ ,  $\text{Zn}^{2+}$ ,  $\text{Fe}^{2+}$ ,  $\text{Cu}^{2+}$ , and  $\text{Pb}^{2+}$ . Continuous variation titration experiments were conducted in order to determine the binding behavior for  $\text{Hg}^{2+}$ . Stoichiometry of the host and guest binding interactions were also determined using continuous variation titration experiments and plotting molar-ratio curves. Pearson Product moment method was employed to calculate the correlation coefficient, and non-linear regression equation was used to calculate dissociation constant  $K_d$ . Molar-ratio and binding constant data substantiated the presence of binding sites for the compound **3**.

**Keywords:** thiourea; ionophore; sensor; mercury

### ABSTRAK

Senyawa tiourea baru, 2,2-oksibis(etil)-4-(1-naftil)-3-tiourea **3** telah disintesis dan dikarakterisasi dengan menggunakan FTIR,  $^1\text{H-NMR}$ ,  $^{13}\text{C-NMR}$ , dan spektroskopi MS. Sifat pengikatan dengan berbagai kation juga dipelajari dengan menggunakan eksperimen pengamatan mata, UV-vis dan titrasi  $^1\text{H-NMR}$ . Senyawa ini menunjukkan pengikatan efektif untuk  $\text{Hg}^{2+}$  dengan adanya kation lainnya, seperti  $\text{Ag}^+$ ,  $\text{Ni}^{2+}$ ,  $\text{Sn}^{2+}$ ,  $\text{Zn}^{2+}$ ,  $\text{Fe}^{2+}$ ,  $\text{Cu}^{2+}$  dan  $\text{Pb}^{2+}$ . Percobaan titrasi variasi kontinu dilakukan untuk menentukan perilaku pengikatan  $\text{Hg}^{2+}$ . Stoikiometri interaksi ikatan inang dan tamu juga ditentukan dengan menggunakan eksperimen titrasi variasi kontinu dan grafik rasio molar. Metode momen produk Pearson digunakan untuk menghitung koefisien korelasi, dan persamaan regresi non linier digunakan untuk menghitung konstanta disosiasi  $K_d$ . Rasio molar dan data konstanta ikatan membuktikan adanya situs ikatan pada senyawa **3**.

**Kata Kunci:** tiourea; ionofor; sensor; merkuri

### INTRODUCTION

Thiourea,  $\text{SC}(\text{NH}_2)_2$  is an organosulphur compound that has same analogue to urea,  $\text{CO}(\text{NH}_2)_2$  with replacement of oxygen atom in urea by sulphur atom and it has different properties compare to urea because of sulphur and oxygen atom [1-2]. The thiourea derivatives are very interesting and widely used in many fields including pharmaceutical and chemical industry due to their chemical and biological properties such as antifungi, anticancer, antibacterial, antioxidant and corrosion activity [3-5]. Despite of acting as ligand, thioureas also have high chemical and biological activity where they act as corrosion inhibitors and antioxidants and also are the component of polymers [4]. Thiourea is one of the chelating extractants that for separating metal ions. This is because of thiourea compounds have O, N and S atoms in the backbones of the ligands that can

bind with metal ions to be a stable complexes [6]. This is useful for supramolecular chemistry, redox sensing, magnetic materials, and so on [7].

Nowadays, one of problem issues to environment was heavy metals because it is toxic. Due to the industrial development, many studies were focusing on the treatment of industrial waste. One of heavy metals from industrial waste was mercury [8]. They are not biodegradable and it is harmful to human body organs [9]. It can cause cancer, brain damage and also motion disorder because it can pass through biological membranes [10]. The high concentrations of heavy metal in environment can give serious effect to living organisms such as animals and also human [11]. Thiourea compound was be selected to this research because thiourea derivatives have interesting and versatile structure [12] that can make a stable complex with metal ions due to its sulphur atom which is a good

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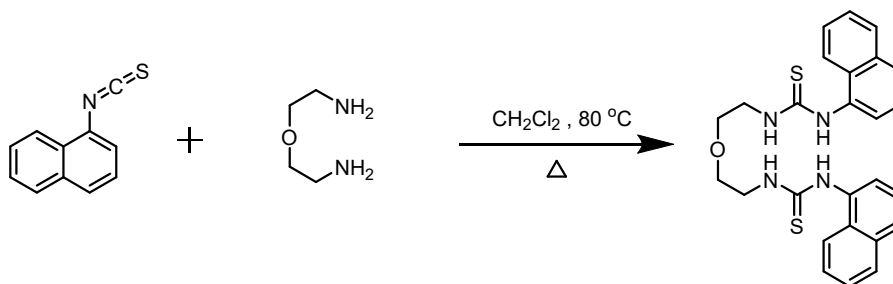


Fig 1. Reaction scheme of compound 3

donor atom [13]. In this study, newly synthesized thiourea compound, **3** was used as potential ionophore for detection of  $\text{Hg}^{2+}$ . The behavior of this compound was investigated by using UV-vis, FTIR, and  $^1\text{H-NMR}$  spectroscopies.

## EXPERIMENTAL SECTION

### Physical Measurement

All reactions were performed under reflux method. Chemicals and solvents were purchased from Sigma Aldrich and Acros and used directly without further purification. The compound was analyzed using FTIR Perkin Elmer Model Spectrum GX in the range 400–4000  $\text{cm}^{-1}$  using KBr and ATR method,  $^1\text{H}$  and  $^{13}\text{C-NMR}$  spectrometer model Bruker Advance 400 MHz, Liquid Chromatography Mass Spectroscopy model Dionex/Bruker MicroToF Q and Ultraviolet visible (UV-vis) CARY Agilent 100.

### Synthesis of 2,2-Oxybis(ethyl)-4-(1-naphthyl)-3-thiourea (**3**)

A solution of 1-naphthyl isothiocyanate (6.00 mmol, 1.111 g) and 2,2-oxybis(ethylamine) (3.00 mmol, 0.313 g) in 15 mL dichloromethane (DCM) was refluxed for 23 h. The white precipitate was filtered out and compound **3** was obtained in 87% (1.243 g). Mp: 175.8–179.0 °C. FTIR (KBr pellet)  $\nu$  ( $\text{cm}^{-1}$ ): 3298, 3181, 3056, 2998, 1530, 1503, 1343, 1198, 1090, 1272.  $^1\text{H-NMR}$  (DMSO- $d_6$ , 400 MHz)  $\delta$  (ppm): 9.69 (s, 1H, NH), 7.93 (t, 2H, J = 3.2 and 3.6 Hz, NH), 7.86 (d, 4H, J = 6.8 Hz, Ar-H), 7.51 (m, 10H, J = 3.2, 5.2 and 12.4 Hz, Ar-H), 3.59 (s, 4H,  $\text{CH}_2$ ), 3.51 (s, 4H,  $\text{CH}_2$ ).  $^{13}\text{C-NMR}$  (DMSO- $d_6$ , 100 MHz)  $\delta$  (ppm): 182.4 (C=S), 134.6, 134.3, 130.1 (6 Ar-C), 128.6, 127.3, 126.8, 126.7, 126.2, 125.6, 123.1 (14 Ar-CH), 68.8 (O- $\text{CH}_2$ ), 44.2 (N- $\text{CH}_2$ ). LCMS (ESI) m/z: calculated for  $\text{C}_{26}\text{H}_{26}\text{N}_4\text{S}_2$  (474.64), found  $[\text{M}+\text{H}]^+$  (475.1516).

### Binding Behaviors of Compound 3 towards Some Selected Metal Salts

Cation binding experiments were carried out by using naked-eyes method, UV-vis titration and  $^1\text{H-NMR}$  titration. For naked-eyes sensor detection of metal ions ( $\text{Fe}^{2+}$ ,  $\text{Pb}^{2+}$ ,  $\text{Hg}^{2+}$ ,  $\text{Ni}^{2+}$ ,  $\text{Zn}^{2+}$ ,  $\text{Ag}^+$ ,  $\text{Cu}^{2+}$ , and  $\text{Sn}^{2+}$ ) ( $1 \times 10^{-3}$  M) and compound **3** ( $1 \times 10^{-3}$  M) in DMSO were added together in vials and shaken well. The color changes were observed by naked-eyes and the data were collected [14].

For UV-vis analysis, stock solution of compound **3** ( $1 \times 10^{-3}$  M) and some selected metal salts,  $\text{Fe}^{2+}$ ,  $\text{Pb}^{2+}$ ,  $\text{Hg}^{2+}$ ,  $\text{Ni}^{2+}$ ,  $\text{Zn}^{2+}$ ,  $\text{Ag}^+$ ,  $\text{Cu}^{2+}$ , and  $\text{Sn}^{2+}$  ( $1 \times 10^{-3}$  M) were prepared in DMSO solvent. The screening on UV-vis spectrophotometer was done on these mixtures. Then, 100  $\mu\text{L}$  of compound **3** and 0–600  $\mu\text{L}$  of mercury salt solution were titrated and directly analyzed by using UV-vis spectrophotometer [15].

For the  $^1\text{H-NMR}$  titrations analysis, stock solution of mercury salt (0–0.06 M) was added into stock solution of compound **3** (0.03 M) was prepared in DMSO- $d_6$  and titrated. Then, the titration solutions were analyzed by using  $^1\text{H-NMR}$  spectroscopy [16].

The FTIR spectroscopy analysis was prepared by using 0.03 M of compound **3** and  $\text{HgI}_2$  salt respectively, in DMSO solvent.

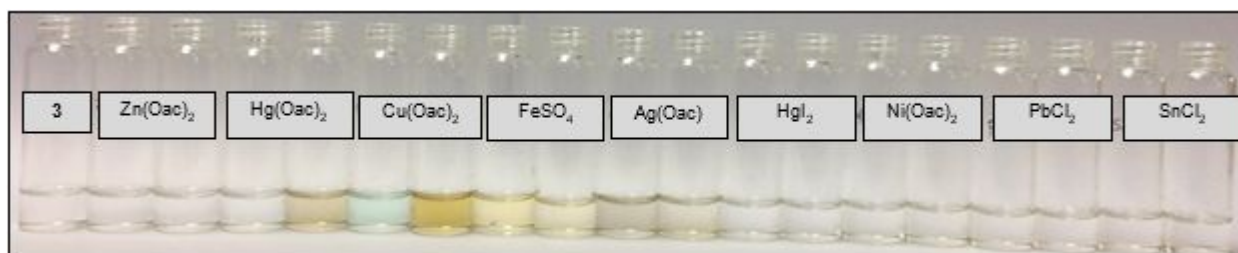
## RESULT AND DISCUSSION

### Chemical Analysis and Spectroscopies Study

Compound **3** was synthesized from the reaction of 1-naphthyl isothiocyanate **1** with 2,2-oxybis(ethylamine) as shown in Fig. 1.

### Binding Behaviors for compound 3 towards Some Selected Metal Salts

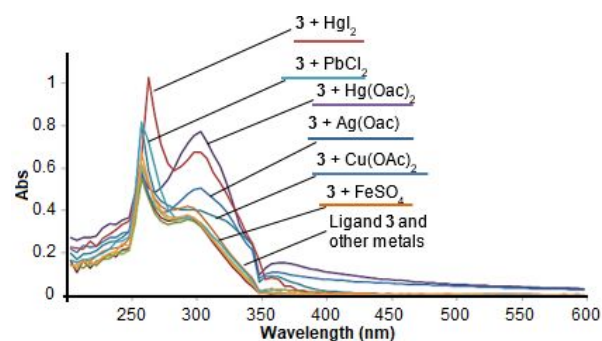
For naked-eyes observation, the most remarkable



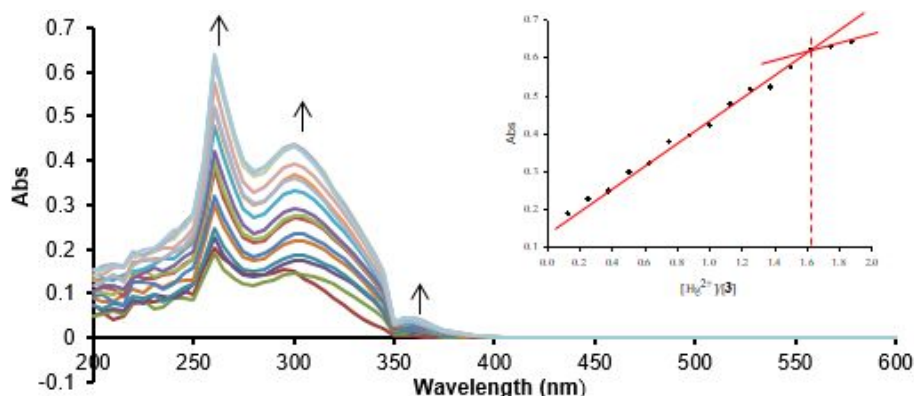
**Fig 2.** Color changes for naked-eyes sensor of compound **3** ( $1 \times 10^{-3}$  M) towards selected metals ( $1 \times 10^{-3}$  M)

**Table 1.** Color changes before and after adding the metal salts solution into the compound **3** solution

Metal salts	Compound <b>3</b> (colorless)
Zn(OAc) <sub>2</sub> (colorless)	Unchanged
Hg(OAc) <sub>2</sub> (colorless)	Light brown
Cu(OAc) <sub>2</sub> (blue)	Yellow-brownish
FeSO <sub>4</sub> (yellowish)	Light yellow
Ag(OAc) (light grey)	Light brown
HgI <sub>2</sub> (colorless)	Unchanged
Ni(OAc) <sub>2</sub> (colorless)	Unchanged
PbCl <sub>2</sub> (colorless)	Unchanged
SnCl <sub>2</sub> (colorless)	Unchanged



**Fig 3.** UV-vis spectra of compound **3** ( $1 \times 10^{-3}$  M) with all metal ions ( $1 \times 10^{-3}$  M) in DMSO solvent

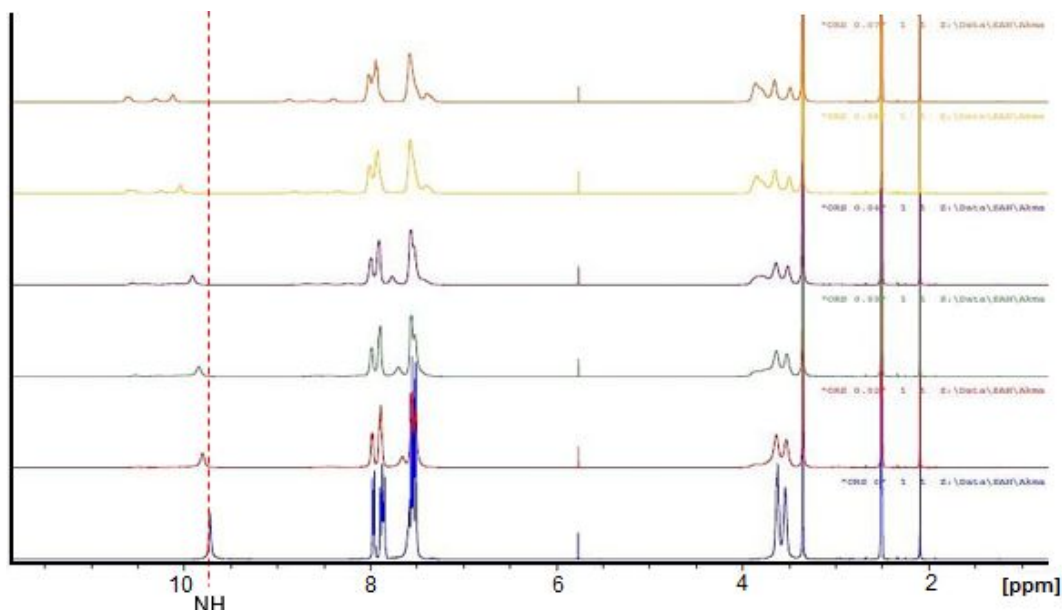


**Fig 4.** Changes in absorption spectra of compound **3** ( $1 \times 10^{-3}$  M) with increasing amount of  $\text{Hg}^{2+}$  ions ( $\text{HgI}_2$ ) ( $1 \times 10^{-3}$  M) in DMSO solvent. (Inset: Variation of absorbance at 260 nm versus  $[\text{Hg}^{2+}]/[\mathbf{3}]$ )

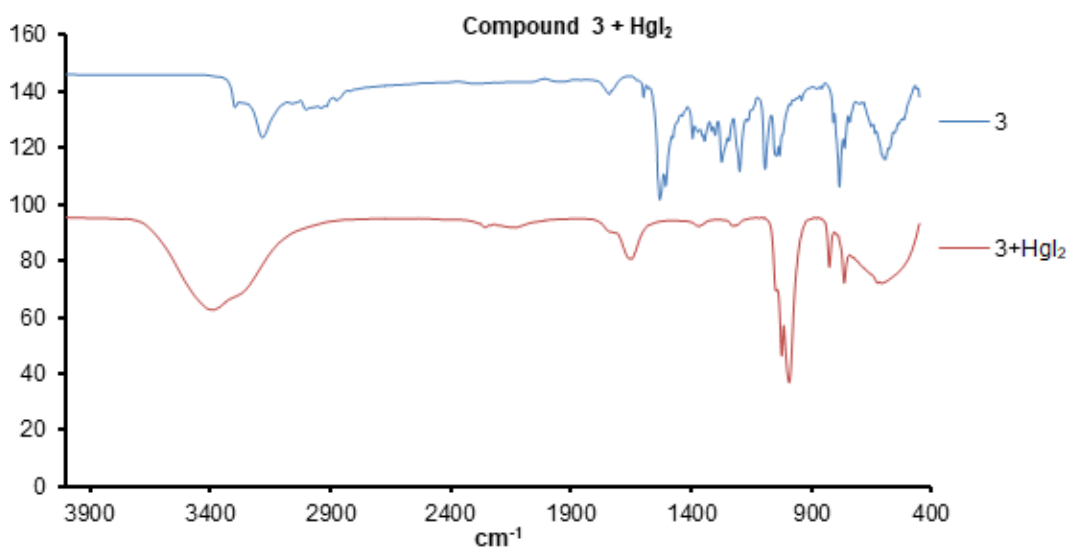
effect can be observed in the presence of  $\text{Hg}^{2+}$ ,  $\text{Cu}^{2+}$ ,  $\text{Fe}^{2+}$ , and  $\text{Ag}^+$  ion. Fig. 2 and Table 1 showed the color changes before and after adding the metal salts solution into the compound **3** solution. The screening of compound **3** with some selected metal salts was carried out in order to determine the change of absorption of the compound-metal mixture (Fig. 3). Based on the screening test, metal salts,  $\text{HgI}_2$  was found to give highest absorption at 260 nm and therefore was chosen for further analysis using FTIR, UV-Vis and  $^1\text{H-NMR}$  titrations.

Titration analysis of compound **3** with  $\text{Hg}^{2+}$  ions were performed in 10 mL of volumetric flask in DMSO solvent using iodide ( $\text{I}^-$ ) as counter anion. Fig. 4 showed an increasing amount of  $\text{Hg}^{2+}$  (0–500  $\mu\text{L}$ ) to the ligand solution (200  $\mu\text{L}$ ), an absorption bands at 260 nm was

increasing. The absorbance maxima increased linearly with the concentration of  $[\text{Hg}^{2+}]/[\mathbf{3}]$  in a range of (0–1.6) with a correlation coefficient of 0.9940 (Inset in Fig. 4) after 14 readings. Then, a new shoulder peak was appeared at 345 nm that was referring to the intramolecular charge transfer (ICT) on thiourea moiety. Then, the band at 370 nm also was increasing (hyperchromic effect) with the increasing amount of  $\text{Hg}^{2+}$  ion. In this region, deprotonation of NH was occurred because of the iodide as counter anion in mercury salt. The interaction of **3**-Hg in the solution was occurred. We got binding ratio 1:2 for the compound **3**-Hg. The binding constant ( $K_d$ ) value can be calculated by nonlinear regression equation in the Sigma Plot 12.0 software. The  $K_{d1}$  and  $K_{d2}$  values of compound **3**-Hg were  $5.853 \times 10^{-18}$  M and 12.605 M.



**Fig 5.**  $^1\text{H-NMR}$  titration of compound **3** showing changes in the NH chemical shift of the compound **3** (0.03M) with increasing amount of  $\text{Hg}^{2+}$  (0–0.06 M) in  $\text{DMSO-}d_6$



**Fig 6.** FTIR spectrum of compound **3** with  $\text{HgI}_2$  solution

To further study the binding behavior,  $^1\text{H-NMR}$  titrations were performed and showed in the Fig. 5. Protons of NH of the ligand were observed at 9.69 ppm. The integral of the peaks were 2.00. After adding the  $\text{Hg}^{2+}$  solution (0–0.06 M), the integration and intensity of the peaks were decreasing. This was due to the interaction between ligand **3** and the  $\text{Hg}^{2+}$  ion in thiourea moiety.

Next, FTIR spectrum in Fig. 6 showed that the decreasing intensity of CN and C=S groups and new peak appeared at  $998\text{ cm}^{-1}$  after adding the  $\text{HgI}_2$  salt solution. These peaks are referring to binding peak between Hg and thiourea moiety [17]. The region of NH

group also showed some shifted in frequency. As we conclude, some intramolecular charge transfer may occur at thiourea moiety because the changes also happened at the region of NH group besides CN and C=S group.

## CONCLUSION

The thiourea compound, **3** was successful synthesized by using heating conventional method in high yield and characterized by the spectroscopies analysis. Naked eye method, UV-vis titration, FTIR, and  $^1\text{H-NMR}$  titration showed that the binding behavior

of the compound **3** towards mercury (Hg) with 1:2 binding ratio. This compound can be used for the fabrication of chemical sensor to selective detection of mercury.

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