FULL PAPER



Applied Organometallic Chemistry

Turn-on fluorescent probe for Zn²⁺ ions based on thiazolidine derivative

Hayriye Genç Bilgiçli¹ | Ahmet T. Bilgiçli¹ | Armağan Günsel¹ | Burak Tüzün² | Derya Ergön¹ | M. Nilüfer Yarasir¹ | Mustafa Zengin¹

¹Department of Chemistry, Sakarya University, 54050Sakarya, Turkey ²Department of Chemistry, Cumhuriyet University, Sivas, Turkey

Correspondence

Ahmet T. Bilgiçli, Sakarya University, Department of Chemistry, 54050. Sakarya, Turkey. Email: abilgicli@sakarya.edu.tr

Funding information Sakarya University, Grant/Award Number: 2018-3-12-195 In this study, simple on-off fluorescent/UV-visible (UV-Vis) probes were easily prepared using 2-(2-hydroxyphenyl)thiazolidine-4-carboxylic acid (Sen-1) and/or 2-(2-hydroxy-5-nitrophenyl)thiazolidine-4-carboxylic acid (Sen-2) for fast detection of Zn^{2+} ions. Their sensing properties towards common metal ions were investigated using UV-Vis and fluorescence spectroscopies. Sen-1 and Sen-2 displayed a significant change with the addition of Zn^{2+} ions in the UV-Vis spectra. The addition of Zn^{2+} ions induced a 104 nm bathochromic shift for **Sen-1**. The binding ratio towards Zn^{2+} metal ions was determined to be 1:1 by using Job plot analysis and fluorescence spectroscopy. The association constant and free energy (ΔG) of **Sen-1** and Sen-2 towards Zn^{2+} ions were calculated by the Benesi-Hildebrand equation. The limit of detection of Sen-1 towards Zn^{2+} ions is 3.73×10^{-8} M, which is about 1/100 of the value recommended by the World Health Organization for drinking water. Sen-1 was successfully applied to detect Zn²⁺ ions in water samples and the fluorescence test strip was prepared for visual detection of Zn^{2+} ions. Finally, the quantum chemical parameters of Sen-1 and Sen-2, such as highest occupied molecular orbital, lowest unoccupied molecular orbital, and chemical hardness, were investigated by the Becke, three-parameter, Lee-Yang-Parr, Hartree-Fock, and M062x methods.

KEYWORDS

quantum chemical calculation, test kit, thiazodiline, zinc fluorescence sensor

1 | INTRODUCTION

The synthesis of fluorescent chemosensors has received considerable attention in recent years.^[1–3] In particular, the investigation of specific sensors for ionic species is of great interest due to their significance for the environment and health.^[4–8] It is well known that metal ions are related to disease and human health, for example zinc, which is an essential trace element for all organisms. Zinc is the second most abundant metal ion in the human body and its

divalent zinc, Zn²⁺, is a trace nutrient critical for physiological function.^[9–11] Zinc deficiency is a major health risk. The daily zinc requirement is ~10–15 mg. Although zinc ions are very useful for human health, it is known that abnormal levels of free zinc ion concentration in cells is triggered by diseases such as Parkinson's disease,^[12] diabetes,^[13] prostate cancer,^[14,15] and Alzheimer's disease.^[16] It is therefore important to develop sensitive and selective compounds for fast detection of zinc ions.^[17,18] Some sensitive compounds can be used for the detection of zinc ions with UV-Vis and ² of 21 WILEY Applied Organometallic

fluorescence spectroscopy technics. Thus, some chemical compounds have been designed and synthesized for the detection of zinc ions in recent years. The heterocyclic compounds can be given as an example due to their usability in chemistry, biochemistry and medicine, etc. Among these heterocyclic compounds, especially thiazolidine and thiazole derivatives have been extensively investigated by scientists over the last decade .^[19]

In this study, we synthesized the thiazolidine derivatives 2-(2-hydroxyphenyl) thiazolidine-4-carboxylic and 2-(2-hydroxy-5-nitrophenyl) acid (Sen-1) thiazolidine-4-carboxylic acid (Sen-2) as simple on-off fluorescent/UV-Vis probes for fast detection of Zn²⁺ ions. Sen-1 and Sen-2 showed high selectivity and sensitivity towards Zn^{2+} ions in both the absence and presence of competitive metal ions. Sen-1 in particular demonstrated very fast response and excellent sensitivity to zinc ions in fluorescent measurements. The binding ratio of Sen-1 and Sen-2 towards Zn²⁺ metal ions was determined to be 1:1 using Job plot analysis. The association constant and free energy (ΔG) of **Sen-1** and Sen-2 towards Zn²⁺ ions were calculated by the Benesi-Hildebrand equation. The association constant is $3.59 \times 10^5 \text{ M}^{-1}$ for **Sen-1** and $4.00 \times 10^5 \text{ M}^{-1}$ for **Sen-2**. The free energy (ΔG) for Zn^{2+} ions was found to be -7.57 kcal M⁻¹ for **Sen-1** and -7.63 kcal M⁻¹ for **Sen-2**. The binding constant value for Zn^{2+} ions was determined by fluorescence spectroscopy as $2.0 \times 10^5 \text{ M}^{-1}$ for **Sen-1**. The limit of detection (LOD) of **Sen-1** for Zn^{2+} ions is 3.73×10^{-8} M, which is about 1/100 of the value recommended by the World Health Organization (WHO) for drinking water. The synthesized thiazolidine derivate **Sen-1** was successfully applied in the detection of Zn^{2+} ions in water samples and a fluorescence test strip was prepared for visual detection of Zn²⁺ ions. Finally, Sen-1 and Sen-2 were investigated by quantum chemical calculations. Their quantum chemical parameters, such as highest occupied molecular orbital (HOMO), lowest unoccupied molecular orbital (LUMO), and chemical hardness were calculated by the Becke, three-parameter, Lee-Yang-Parr (B3LYP), Hartree-Fock (HF), and M062x methods. The fourier transform infrared (FT-IR) spectroscopy, nuclear magnetic resonance (NMR), and UV-Vis spectra of Sen-1 and Sen-2 were further confirmed by density functional theory calculations.

2 | EXPERIMENTAL

2.1 | Materials

All solvents (dimethyl sulfoxide [DMSO], tetrahydrofuran [THF], ethanol [EtOH], methanol [MeOH], acetone) and metal salts of Ag⁺, Na⁺, K⁺, Cu²⁺, Zn²⁺, Pd²⁺, Cd²⁺, Fe²⁺, Hg²⁺, Pb²⁺, and Ni²⁺ were purchased from Sigma-Aldrich and Merck. FT-IR spectra were recorded on a Perkin Elmer Spectrum Two spectrophotometer. UV–Vis studies were performed on an Agilent Model 8453 diode array spectrophotometer. The fluorescent properties were recorded on a Hitachi F-7000 fluorescence spectrophotometer. ¹H and ¹³C NMR spectra were recorded on a Bruker 300 MHz spectrometer.

2.2 | General synthesis of thiazolidine-4-carboxylic acid derivatives^[20]

The benzaldehyde derivative (10 mmol) was dissolved in EtOH (10 ml). L-cysteine hydrochloride (1.57 g, 10 mmol) and NaOAc (0.98 g, 12 mmol) in water (10 ml) were added to this prepared solution. The reaction mixture was stirred for 24 hr at room temperature. The precipitate was then separated by filtration and washed several times with ethanol. The obtained thiazolidine-4-carboxylic acid derivatives were soluble in water, ethanol (hot), DMF, and DMSO (Scheme 1).

2.2.1 | (4R)-2-(2-hydroxyphenyl) thiazolidine-4-carboxylic acid (Sen-1)

¹H NMR (300 MHz, DMSO-d₆) δ : 3.05–2.94 (m, 2H), 3.21 (dd, 1H, *J* = 6.8, 10.2 Hz), 3.34 (dd, 1H, *J* = 6.9, 9.4 Hz), 3.83 (dd, 1H, *J* = 6.9, 8.9 Hz), 4.21 (dd, 1H, *J* = 5.2, 6.8 Hz), 5.65 (s, 1H), 5.84 (s, 1H), 6.73–6.83 (m, 4H), 7.06 (td, 1H, *J* = 7.6, 1.7 Hz), 7.13 (td,1H, *J* = 7.7, 1.7 Hz), 7.30 (d, 1 H, *J* = 7.7 Hz), 7.34 (dd, 1 H, *J* = 1.7, 7.7 Hz) 9.83 (s, 2H, -OH). ¹³C NMR (75 MHz, DMSO) δ : 173.6, 173.1, 155.8, 155.2, 129.7, 128.8, 128.6, 128.3, 126.7, 124.9, 119.7, 119.4, 116.3, 115.7, 68.3, 66.3, 65.9, 65.5, 38.8, 37.8.

2.2.2 | (4R)-2-(2-hydroxy-4-nitrophenyl) thiazolidine-4-carboxylic acid (Sen-2)

¹H NMR (300 MHz, DMSO-d₆) δ : 8.41 (d, 1H, J = 2.7 Hz), 8.18 (d, 1H, J = 2.7 Hz), 8.10–7.96 (m, 1H,), 7.03–6.87 (m,



SCHEME 1 Synthesis of (4*R*)-2-(2-hydroxyphenyl) thiazolidine-4-carboxylic acid **(Sen-1)** and (4*R*)-2-(2-hydroxy-4-nitrophenyl)thiazolidine-4-carboxylic acid **(Sen-2**)

2H), 5.83 (s, 1H), 5.68 (s, 1H), 4.10 (td, 1H, J = 6.4, 1.8 Hz), 3.90 (ddd, 1H, J = 8.7, 6.5, 2.0 Hz), 3.29 (1H, ddd, J = 8.5, 6.7, 1.7 Hz), 3.20 (ddd, 1H, J = 8.2, 6.5, 1.7 Hz), 3.04–2.96 (m, 1H), 2.96–2.84 (m, 1H). ¹³C NMR (75 MHz, DMSO) & 173.39, 172.94, 162.42, 161.86, 140.74, 140.04, 131.06, 127.43, 125.94, 125.27, 124.72, 122.25, 116.43, 116.00, 66.17, 66.08, 65.53, 64.88, 37.98, 37.69.

2.3 | Job plot measurements

The binding ratio of **Sen-1** and **Sen-2** towards Zn^{2+} metal ions was determined using Job plot analysis. **Sen-1** and **Sen-2** (1×10^{-3} M) and metal ion solutions (1.0×10^{-3} M Zn²⁺ ions) were prepared in a 95% (v/v) water–DMSO mixture. First, solutions of **Sen-1** or **Sen-2** (100, 90, 80, 70, 60, 50, 40, 30, 20, 10, and 0 µl) were prepared. Then solutions of Zn²⁺ ions (0, 10, 20, 30, 40, 50, 60, 70, 80, 90, and 100 µl) were added to the previously prepared solutions of **Sen-1** or **Sen-2**, respectively. These mixtures were diluted to a total volume of 3.0 ml using 95% (v/v) water– DMSO solvent. The obtained mixture were recorded at room temperature by using UV–Vis spectroscopy.

2.4 | Determination of the association constants of Sen-1 and Sen-2 towards Zn²⁺ ions

2.4.1 | UV-Vis method

To determine the association constant (K_a) and free energy change (ΔG) due to the interaction between **Sen-1/Sen-2** and Zn²⁺ ions, the absorption spectra were further analyzed using the Benesi–Hildebrand relation. The association constants of **Sen-1** and **Sen-2** towards Zn²⁺ ions were calculated according to the titration curve using the following nonlinear least squares fitting:

$$C_{\text{metal}} = \frac{A_x - A_0 / A_{\text{max}} - A_0}{2 \times K_a \times C_{\text{sen}} \times (1 - (A_x - A_0 / A_{\text{max}} - A_0))^2} + \frac{(A_x - A_0 / A_{\text{max}} - A_0) \times K_a}{2}$$
(1)

where $K_{\rm a}$ is the association constant, $C_{\rm sen}$ is the concentration of the sensor probe, and $C_{\rm metal}$ is the concentration of metal ions.

2.4.2 | Fluorescence method

The binding constant value for **Sen-1** with Zn^{2+} ions was calculated by fluorescence spectroscopy according to the modified Benesi–Hildebrand equation:

$$\frac{1}{(F-F_0)} = \frac{1}{(F_{\max}-F_0)} + \frac{1}{K_{\rm a}[C]} \times \frac{1}{(F_{\max}-F_0)}$$
(2)

where F_0 is the emission intensity of **Sen-1** in the absence of Zn^{2+} ions, F is the emission intensity of **Sen-1** at the intermediate Zn^{2+} ion concentration, F_{max} is the emission intensity of **Sen-1** at the concentration of complete saturation, K_a is the binding constant, and [C] is the concentration of Zn^{2+} ions.

2.5 | Determination of limit of detection (LOD) of Sen-1 towards Zn²⁺ ions by fluorescence method

The LOD of **Sen-1** was calculated based on fluorescence emission during titration with Zn^{2+} ions. The change in fluorescence emission at $\lambda_{max} = 455$ nm was plotted against the concentration of Zn^{2+} ions and the LOD was calculated using the equation:

$$LOD = 3\sigma/k$$

where LOD, σ and k are limit of detection, the standard deviation of the response and theslope of the calibration curve respectively.

2.6 | Fluorescence quantum yield of Sen-1 towards Zn²⁺ ions

The fluorescence quantum yield $(\Phi_{\rm F})$ of the interaction of Sen-1 with Zn²⁺ ions (**Sen-1 + Zn**) was determined at room temperature by a comparative method using the equation

$$\Phi_F = \Phi_F(\text{std}) \frac{A_{\text{std}}}{A} \frac{F}{F_{\text{std}}} \frac{n^2}{n_{\text{std}}^2} \frac{D}{D_{\text{std}}}$$
(3)

where *F* and $F_{\rm std}$ are the areas under the fluorescence emission curves of the sample and the standard, respectively. *A* and $A_{\rm std}$ are the respective absorbances of the sample and standard at the excitation wavelengths, respectively. n^2 and $n^2_{\rm std}$ are the refractive indices of the solvents used for the sample and standard. *D* and $D_{\rm std}$ are the dilution factors of the sample and reference, respectively. 9-anthracene carboxylic acid was used as the standard owing to its appropriate emission peak area. The quantum yield of 9-anthracene carboxylic acid is 0.86 at 3.0×10^{-4} M concentration in ethanol.^[21] 4 of 21 WILEY Organometallic

2.7 | Calculation method

Theoretical studies are one of the most important tools used to compare the activities of molecules. Many programs and methods are used to make theoretical calculations. These programs can work in great harmony with each other. The GaussView 5.0.8, Gaussian09 AS64L-G09RevD.01, ChemDraw Professional 15.1, and Chemcraft V1.8 packages were used.^[22-26] The studied molecules were analyzed using the HF^[26] and B3LYP,^[26,27] M06-2X^[28] methods with the 3-21G, 6-31G, and sdd basis sets. The HOMO and LUMO values of the molecules were used to explain the molecular activity. The chemical reactivity parameters of the molecules, such as Energy of the Highest Occupied Molecular Orbital (E_{HOMO}) , Energy of the Lowest Unoccupied Molecular Orbital (E_{LUMO}), ΔE (HOMO – LUMO energy gap), electronegativity (γ) , chemical potential (μ) , chemical hardness (η), electrophilicity (ω), nucleophilicity (ε), global softness (σ), and proton affinity (PA) were used to obtain information about the activities of the molecules^[29-38]:

$$\mu = -\chi = \left(\frac{\partial E}{\partial N}\right)_{v(r)} \tag{4}$$

$$\eta = \frac{1}{2} \left(\frac{\partial^2 E}{\partial N^2} \right)_{\nu(r)} = \frac{1}{2} \left(\frac{\partial \mu}{\partial N} \right)$$
(5)

The ionization energy (I) and electron affinity (A) of the Sen-1, Sen-2 and their zinc complexes were calculated with HOMO and LUMO energies. I and A values are related to electronegativity, global softness and chemical hardness, which were obtained using the following equations^[39]:

$$\chi = -\mu = \left(\frac{I+A}{2}\right) \tag{6}$$

$$\eta = \frac{I - A}{2} \tag{7}$$

It is well known that global softness is defined as the inverse of chemical hardness:

$$\sigma = 1/\eta \tag{8}$$

$$\chi = -\mu = \left(\frac{-E_{\rm HOMO} - E_{\rm LUMO}}{2}\right) \tag{9}$$

$$\eta = \left(\frac{E_{\rm LUMO} - E_{\rm HOMO}}{2}\right) \tag{10}$$

The global electrophilicity index^[40] (ω), investigated by Parr *et al.*, is the inverse of nucleophilicity:

$$\omega = \mu^2 / 2\eta = \chi^2 / 2\eta \tag{11}$$

Electrophilicity and nucleophilicity are used to predict organic and inorganic reaction mechanisms. Nucleophilicity (ε) is defined as the inverse of electrophilicity:

$$\varepsilon = 1/\omega$$
 (12)

3 | RESULTS AND DISCUSSIONS

3.1 | Absorption studies

The UV–Vis properties of **Sen-1** and **Sen-2** were investigated by experimental and calculated methods. The absorbance and molar absorptivity values of **Sen-1** and **Sen-2** are given in **table S1** in the absence/presence of metal ions. The calculated and experimental data of **Sen-1** and **Sen-2** agree with each other. A main band at 280 nm and a small shoulder peak at around 328 nm were observed for **Sen-1** in the experimental absorption spectrum in 95% (v/v) water–DMSO mixture (Figure 1). Although the experimental results are closer to the visible region by ~100 nm. Similarly, two bands were observed at 249 nm and 327 nm for **Sen-2** in the UV–Vis spectrum (Figure 2).

3.1.1 | Metal ion binding titration studies

The metal ion sensing properties of Sen-1 and Sen-2 were investigated by UV-Vis spectroscopy in the presence of metal ions K⁺, Ag⁺, Ca²⁺, Mg²⁺, Mn²⁺, Mg²⁺, Pb²⁺, Zn²⁺, Fe²⁺, Hg²⁺, Pd²⁺ Ni²⁺, and Cu²⁺. The concentration of the metal salts was chosen to be 10^{-3} mol/L to eliminate absorption decreases due to dilution. Before the titration experiment, the aggregation behaviors of Sen-1 and Sen-2 were investigated. UV-Vis electronic absorption spectra of thiazolidine derivatives were recorded at different concentrations. The UV-Vis spectra for Sen-1 and Sen-2 at different concentrations in a 95% (v/v) water-DMSO mixture are shown in Supporting Information Figures S1 and S2, respectively. As the concentrations of Sen-1 and Sen-2 increased, the main band intensities at 280 nm for Sen-1 and at 327 nm for Sen-2 also increased. New band formation due to aggregation was not observed. These results show that there are monomeric species in the solution in the absence of metal ions. UV-Vis electronic absorption changes for Sen-1 and Sen-2 were recorded during the titration in the presence of metal ions K⁺, Ag⁺, Ca²⁺, Mg²⁺, Mn²⁺,

calculated UV-Vis spectra of Sen-1

FIGURE 1 Experimental (in DMSO) and

10000

600



FIGURE 2 Experimental (in DMSO) and calculated UV–Vis spectra of **Sen-2**



0.2

0.0

100

200

300

Wavelength (nm)

During the titration of **Sen-1** with Pd²⁺ ions, the main band at 279 nm in the electronic spectrum slightly increased and a new band was observed at 321 nm due to the interaction of **Sen-1** with Pd²⁺ ions (Supporting Information **Figure S3**). During the titration of **Sen-2** with Pd²⁺ ions, the main band at 327 nm in the electronic spectrum did not change, but new bands appeared at 268 and 377 nm due to interaction with the Pd^{2+} ions (Supporting Information **Figure S4**). The Cu²⁺ ion is optically sensitive to **Sen-1** and **Sen-2**. Similar titration experiments were made for Cu²⁺ions. During the titration of **Sen-1** with Cu²⁺ ions, the main band at 279 nm slightly increased and a new peak at 360 nm appeared due to the interaction of **Sen-1** with Cu²⁺ ions (Supporting Information **Figure S5**). During the titration of **Sen-2** with Cu²⁺ ions, the main band at 327 nm in the electronic spectrum did not change, but new bands were observed at 261 and 370 nm due to interaction with the Cu²⁺ ions, similar to the titration with Pd²⁺ ions (Supporting Information **Figure S6**). The significant changes in the absorption spectra demonstrated the selectivity of **Sen-1** and **Sen-2** against Pd²⁺ and Cu²⁺ ions. In

400

500

6 of 21 WILEY Organometallic

addition, the color change observed by even the naked eye from colorless to yellow/green also may be indicative of the interaction of **Sen-1** and **Sen-2** with Pd^{2+} and Cu^{2+} ions during the titration.

Sen-1 and **Sen-2** are highly sensitive to Zn^{2+} ions. During the titrations of **Sen-1** and **Sen-2** with Zn^{2+} ions, new bands were observed at 370 and 385 nm, respectively (Figure 3 for **Sen-1** and Figure 4 for **Sen-2**). This red shift obtained by titration implies that **Sen-1** and **Sen-2** are optically sensitive to Zn^{2+} ions. Some experiments were carried out to determine whether **Sen-1** and **Sen-2** were more selective against Pd^{2+} , Cu^{2+} , and Zn^{2+} ions. After **Sen-1** and **Sen-2** were saturated with Pd^{2+} or Cu^{2+} ions, Zn^{2+} ions were added to the solution. On the addition of



FIGURE 3 UV–Vis spectra of **Sen-1** during titration with Zn^{2+} ions. Inset: plot of absorbance versus added Zn^{2+} ions



FIGURE 4 UV–Vis spectra of **Sen-2** during titration with Zn^{2+} ions. Inset: plot of absorbance versus added Zn^{2+} ions

 Zn^{2+} ions, **Sen-1** and **Sen-2** reacted immediately and were selective to these ions (Figure 5 was given as an example). After the titration of **Sen-1** and **Sen-2** with Pd^{2+} , Zn^{2+} ions were added to the solution. After addition of Zn^{2+} ions, new bands were observed at ~370 nm for **Sen-1** and 385 nm for **Sen-2**. These results indicate that the sensor compounds prefer Zn^{2+} ions to Pd^{2+} ions.

The effect of pH on UV–Vis sensing properties was also investigated. After compounds **Sen-1** and **Sen-2** were saturated with Zn^{2+} , Pd^{2+} , or Cu^{2+} ions, the pH was adjusted to an acidic value of 5 or 6. When the pH fell below 6, **Sen-1** and **Sen-2** did not show sensor behavior towards Zn^{2+} , Pd^{2+} , or Cu^{2+} ions. When the pH was adjusted to 6, the peak of 380 nm for the interaction of Zn^{2+} with **Sen-1** started to decrease. When the pH reached 5, the spectrum reverted to its original state (Figure 6). The same results were obtained for **Sen-2** with a small difference: when the pH was 6, the spectrum reverted to its original state (Figure 7). In summary, when the pH is greater than 5, **Sen-1** and **Sen-2** act as optical sensors towards Zn^{2+} , Pd^{2+} , or Cu^{2+} ions.

The stoichiometry and association constants of Sen-1 and **Sen-2** towards Zn^{2+} ions were calculated from the UV-Vis spectral data. The binding ratio between Sen-1 or **Sen-2** and Zn^{2+} metal ions was determined by using Job plot analysis. As shown in Figure 8 for Sen-1 and Figure 9 for Sen-2, the Job plots for Sen-1 and Sen-2 with Zn²⁺ metal ions exhibited 1:1 stoichiometry. A picture of **Sen-1** was taken under a UV lamp after the addition of Zn²⁺ ion solution (0, 10, 20, 30, 40, 50, 60, 70, 80, 90, and 100 µl) (Figure 8 inset). With increasing concentration of Zn²⁺ ions, the color change under the UV lamp (seen by the naked eve) may be indicative of the 1:1 binding ratio. The association constant of Sen-1 and Sen-2 towards Zn^{2+} ions was calculated from the titration data by using the Benesi-Hildebrand equation. The association constants of Sen-1 and Sen-2 were found to be $3.59 \times 10^6 \text{ M}^{-1}$ (Supporting Information Figure S7) and 4.0×10^5 M⁻¹ (Supporting Information Figure S8), respectively.

3.2 | NMR titration studies

The interaction properties of Zn^{2+} ions and the thiazolidine compounds **Sen-1** and **Sen-2** were investigated by ¹H NMR titration experiments. After taking the ¹H NMR of the pure molecule in DMSO-d⁶, Zn^{2+} ions in DMSO-d⁶ solution were added into the tube and the changes in the ¹H MR spectra after the addition of Zn^{2+} ions were observed (Figures 10 and 11). It was expected that the phenolic OH group would disappear as the Zn^{2+}



FIGURE 5 The effect of Zn^{2+} ions on absorption spectra of **Sen-1** (a) and **Sen-2** (b) after saturation with Pd^{2+} ions



FIGURE 6 The effect of pH on absorption spectra of **Sen-1** after saturation with Zn^{2+} ions

ratio increased and therefore the oxygen of hydroxyl group must be interacting with Zn^{2+} . While this effect is seen in the hydroxyphenyl derivative, it is not seen in the 2-hydroxy-5-nitrophenyl derivative because the hydroxyl peak shrinks as a result of the electron-withdrawing effect of the nitro group. The hydrogen atom peaks for the second carbon in the heterocyclic ring are shifted to 5.80 ppm (for (2R,4R)-(2-hydroxyphenyl)thiazolidine-4-carboxylic acid) and 5.62 ppm (for (2S,4R)-(2-hydroxyphenyl)thiazolidine-4-carboxylic acid). Since the proton in the (2S,4R) isomer is in the same plane as the carboxylic acid group, it is shifted further downfield (5.80 ppm). Similarly, in the (2R,4R) isomer, the proton and carboxylic acid groups are on different planes and their magnetic fields are not affected by each other. Hence, this proton is shifted more upfield (5.62 ppm). As Zn^{2+} is added, the proton peak in the (2S,4R) isomer becomes broader and lies to the more upfield. This effect,



FIGURE 7 The effect of pH on absorption spectra of **Sen-2** after saturation with Zn^{2+} ions

which is not seen in the other (2R,4R) isomer, is a result of the configurations of the stereoisomer described above. Since the groups interacting with Zn^{2+} are in the reverse plane, this proton remains under the influence of the magnetic field of Zn^{2+} (Scheme 2). This result is also seen in the ¹H NMR spectra of the 2-hydroxy-5-nitrophenyl derivative. For the proton affected by the magnetic field of the metal, the relaxation time is extended and the peaks become broader. As the amount of Zn^{2+} increases, it can be seen that the splits in the aromatic ring peaks lose their sharpness because the presence of the metal disrupts the ¹H NMR resolution.^[41,42] Because a constant resolution cannot be achieved, the cleavage intensity of the peaks changes and the cleavages lose their clarity.



8 of 21

FIGURE 8 Job plot diagram of **Sen-1** for Zn²⁺ ions. Inset: photograph of the mixtures under UV light



FIGURE 9 Job plot diagram of **Sen-2** for Zn²⁺ ions. Inset: photograph of the mixtures under UV light

3.3 Fluorescence studies

3.3.1 | Fluorescence spectra of the synthesized thiazolidine derivatives

The fluorescence behaviors of Sen-1 and Sen-2 were investigated in a 95% (v/v) water-DMSO mixture at room temperature. Sen-1 and Sen-2 exhibited emission peaks at 351 and 369 nm, respectively, when excited at 279 nm (Figure 12 for Sen-1 and Figure 13 for Sen-2). The fluorescence spectra were found to be mirror images of the absorption spectra for Sen-1 and Sen-2. Before interaction with Zn²⁺ ions, the Stokes shift values of Sen-1 and Sen-2 were 71 and 42 nm, respectively (Supporting Information Table S1). Generally, Stokes shifts of some common dyes such as fluorescein and rhodamine are less than 25 nm. Stokes shifts less than 25 nm may cause self-quenching and measurement errors.^[43,44] The low Stokes shifts are a disadvantage for quantitative analysis and bioimaging applications. The obtained Stokes shift values for Sen-1 and Sen-2 are promising for quantitative analysis and bioimaging applications.

Because Sen-1 and Sen-2 have high selectivity to zinc ions, the emission spectra and Stokes shifts of Sen-1 and Sen-2 were compared before and after interaction with Zn^{2+} ions. The emission peaks of **Sen-1 + Zn** and **Sen-**2 + Zn appeared at 455 and ~488 nm, respectively, after interaction with Zn^{2+} . The interaction of **Sen-1** with Zn²⁺ caused a 104 nm red shift in addition to a 71 nm Stokes shift in the fluorescence emission spectrum (Supporting Information Table S1). Recently, many fluorescent sensors have been developed to detect zinc ions. Some of them cause fluorescence enhancement in emission intensity and some cause fluorescence quenching in emission intensity after interaction with zinc ions. In this work, Sen-1 showed a significant increase in fluorescence emission intensity with 104 nm red shift when compared to other Zn²⁺ fluorescence sensors in the literature.

3.3.2 | The effect of metal ions on fluorescence properties

The metal ion sensing behaviors of the synthesized thiazolidine derivatives Sen-1 and Sen-2 were investigated by fluorescence emission spectroscopy in the presence of the metal ions K⁺, Ag⁺, Ca²⁺, Mg²⁺, Mn²⁺, Mg²⁺, Pb²⁺, Zn²⁺, Fe²⁺, Hg²⁺, Pd²⁺ Ni²⁺, and Cu²⁺. The fluorescence emission spectra of Sen-1 and Sen-2 with the metal ions in 95% (v/v) water-DMSO mixture were recorded at room temperature. Fluorescence emission changes of Sen-1 and Sen-2 were investigated with the addition of metal ions at the increasing concentrations. According to the results, Zn²⁺ ions caused only significant fluorescence enhancement for Sen-1. The other metal ions did not cause any fluorescence enhancement. On the contrary, some of them caused fluorescence quenching, while some showed no effect. Figures 14 and 15 show the color changes in Sen-1 and Sen-2 under daylight and UV light in the presence of different metal ions. Sen-1 showed fluorescence enhancement towards Zn²⁺ ions under a UV lamp. This observed fluorescence enhancement can be easily detected by the naked eye.

Supporting Information Figure S9 shows the fluorescence changes for **Sen-1** during titration with Fe²⁺, Ni²⁺, Cu²⁺, Ag⁺, Pd²⁺, and Pb²⁺ ions. The **Sen-1** fluorescence



FIGURE 10 ¹H NMR spectra of Sen-1 during the titration with Zn²⁺ ions



FIGURE 11 ¹H NMR spectra of Sen-2 during the titration with Zn²⁺ ions

spectra did not show any significant change during the addition of these metal ions. Although the titration of **Sen-1** with Fe^{2+} ions gives a fluorescence peak at around 450 nm, its intensity is negligible. The color changes under UV light were not seen in the presence of Fe2+ ions. Supporting Information Figure S10 shows

9 of 21



SCHEME 2 Estimated interaction of thiazolidine-4-carboxylic acid diastereomers with $Zn (R = H \text{ or } NO_2)$



FIGURE 12 Absorption and emission spectra of Sen-1 and Sen-1 + Zn complex: _____, absorption (Sen-1); _____, emission (Sen-1); _____, emission (Sen-1 + Zn)

fluorescence changes for **Sen-2** during titration with Pd^{2+} , Fe^{2+} , Ni^{2+} , and Cu^{2+} ions. The addition of these metal ions caused fluorescence quenching in **Sen-2**. A new emission band due to fluorescence did not appear. The **Sen-2** fluorescence spectra did not show any significant change during the addition of the other metal ions.



The addition of Zn^{2+} ions caused a new fluorescence emission band at 459 nm for **Sen-1**. This indicates strong complex formation of Zn^{2+} ions with **Sen-1**. In addition, the observed color change under UV light from colorless to bright turquoise may be indicative of interaction with Zn^{2+} ions for **Sen-1** (Figure 16). Similarly, the addition of Zn^{2+} ions caused a new broad fluorescence emission band at ~500 nm for **Sen-2**. However, it did not show strong fluorescence, unlike the **Sen-1** band, and there was no visible change under UV light because the presence of a nitro group in a benzene ring is known to lead to fluorescence quenching (Supporting Information **Figure S11**).^[45-47]

Selectivity is an important parameter when testing the performance of fluorescent probes. Thus, the fluorescence behavior of **Sen-1** in the presence of metal ions $(Fe^{2+}, Cu^{2+}, Hg^{2+}, Ca^{2+}, Pb^{2+}, Pd^{2+}, Zn^{2+}, Mg^{2+}, Cu^{2+}, Cd^{2+}, Al^{3+}, K^+, Na^+, Mn^{2+}, Ag^+)$ was also investigated in 95% (v/v) water–DMSO mixture at room temperature. As shown in Figure 17, the addition of Zn²⁺ ions in the presence of other metal ions caused significant fluorescence enhancement at 459 nm for **Sen-1**. This indicates that **Sen-1** has a high selectivity for Zn²⁺ ions in the presence of other metal ions.

Reversibility studies of **Sen-1** and **Sen-2** towards Zn^{2+} ions were also performed. After interaction of **Sen-1** and **Sen-2** with Zn^{2+} ions, ethylene diamine tetra acetic acid (EDTA) was added to the solution. The addition of EDTA caused a reduction in fluorescence intensity at 459 nm for **Sen-1** and ~500 nm for **Sen-2**. At the same time, the main fluorescence intensities at ~351 nm for **Sen-1** and ~369 nm for **Sen-2** were observed at the original intensities (Figure 18 for **Sen-1** and Figure 19 for **Sen-2**).

The binding constant value of **Sen-1** with Zn^{2+} ions was also calculated by fluorescence spectroscopy according to the modified Benesi–Hildebrand equation.

FIGURE 13 Absorption and emission spectra of Sen-2 and Sen-2 + Zn complex: ______, absorption (Sen-2); _____, emission (Sen-2); _____, emission (Sen-2 + Zn)



FIGURE 14 Color change of Sen-1 under daylight (a) and UV light (b) in the presence of different metal ions



FIGURE 15 Color change of Sen-2 under daylight (a) and UV light (b) in the presence of different metal ions

The association constant for **Sen-1** towards Zn^{2+} ions is $K_a = 2.0 \times 10^5 \text{ M}^{-1}$ according to the fluorescence experiment (Supporting Information **Figure S12**). The detection limit of the sensor is a significant parameter for real sample applications. Thus, the LOD of **Sen-1** was calculated based on the fluorescence emission during titration with Zn^{2+} ions (Supporting Information **Figure S13**). The LOD of **Sen-1** towards Zn^{2+} ions calculated to be 0.37 nM, which is about 1/100 of the value recommended by the WHO for drinking water. **Sen-1**, with LOD = 0.37 nM, can be used as a selective sensor for the analysis of Zn^{2+} ions in real environmental water samples.

The turn on-off fluorescence behavior of **Sen-1** on sequential addition of Zn^{2+} ions and EDTA is shown in

Figure 20. The addition of Zn^{2+} ions caused a fluorescence enhancement for **Sen-1**, and the addition of EDTA to this solution caused fluorescence quenching. This procedure was repeated five times and the same results were obtained each time. The turn on-off fluorescence behavior of **Sen-1** after interaction with Zn^{2+} ions might be explained by considering the strong binding affinity of EDTA to Zn^{2+} ions. According to these results, **Sen-1** and **Sen-2** may be recyclable through treatment with suitable reagents such as EDTA.

The fluorescence is electron transfer or energy transfer between the sensor probes and metal ions, therefore the metal ion sensing behavior of the sensor probe can lead to a change in the electronic structure. The electron transfer or energy transfer between the sensor probes and metal



FIGURE 16 Fluorescence spectra of **Sen-1** during titration with Zn^{2+} ions



FIGURE 17 Fluorescence spectra of Sen-1 in the presence of metal ions

ions can result in fluorescence enhancement or quenching. In the emission studies, **Sen-1** and **Sen-2** exhibited weak fluorescence at 351 and 369 nm, respectively, when excited at 279 nm. This observed weak fluorescence for **Sen-1** and **Sen-2** is due to the free electrons of the –NH group in the thiazolidine (Scheme 3). After the addition of Zn^{2+} ions, **Sen-1** displayed a significant enhancement in fluorescence emission intensity. The interaction of metal ions with oxygen atoms in

the benzene ring and nitrogen atom in the thiazolidine group changes their electron-withdrawing properties. The possible reasons may be the formation of deprotonated **Sen-1** and also prevention of photo-induced electron transfer processing by the addition of Zn^{2+} ions.^[48–50]

The fluorescence quantum yield ($\Phi_{\rm F}$) of **Sen-1** after saturation with Zn²⁺ ions was determined at room temperature by the comparative method in water (Supporting Information **Figure S14**). The $\Phi_{\rm F}$ value of



FIGURE 18 Changes in the fluorescence spectrum of **Sen-1** with addition of Zn^{2+} ions and EDTA. Inset: fluorescence changes from 300 to 400 nm



FIGURE 19 Changes in the fluorescence spectrum of **Sen-2** with addition of Zn^{2+} ions and EDTA. Inset: fluorescence changes from 300 to 400 nm

Sen-1 + Zn was found to be 0.52 (Supporting Information **Table S1**).

3.4 | Interference studies

Many fluorescent sensors have been developed to detect Zn^{2+} ions,^[51-53] but most of them suffer from interference from other transition metal ions. In particular, it is difficult for fluorescent sensors to distinguish Zn^{2+} and Cd^{2+} ions due to their similar chemical properties. In this study, the interference effect of Cd^{2+} and Fe^{3+} ions on **Sen-1** and **Sen-2** was investigated by UV–Vis and



FIGURE 20 Reversible fluorescence intensity at 455 nm of **Sen-1** on sequential addition of Zn²⁺ions and EDTA

fluorescence spectroscopy. During the titration of **Sen-1** and **Sen-2** with Cd^{2+} ions, no significant changes in the UV–Vis spectra were observed, but the addition of Zn^{2+} ions after saturation with Cd^{2+} ions caused a significant optical change in the UV–Vis spectra (Figure 21 for **Sen-1** and Supporting Information **Figure S15** for **Sen-2**). Contrary to the situation with Cd^{2+} ions, the titration of Fe³⁺ ions caused some spectral changes in the UV–Vis spectra, but as soon as Zn^{2+} ions were added, **Sen-1** and **Sen-2** released Fe³⁺ ions and showed optical sensitivity towards the Zn^{2+} ions (Figure 22 for **Sen-1** and Supporting Information **Figure S16** for **Sen-2**).

The interference effect of Cd^{2+} and Fe^{3+} ions on **Sen-1** was also investigated by fluorescence spectroscopy. The addition of Fe^{3+} ions caused fluorescence quenching, while not significant changes were observed during the titration Cd^{2+} ions. The addition of Zn^{2+} ions to these saturated solutions of Cd^{2+} or Fe^{3+} ions caused high fluorescence enhancement (Figures 23 and 24). From the UV–Vis and florescence results, **Sen-1** may be suitable for use as a fluorescence sensor for the determination of Zn^{2+} ions.

3.5 | Application

3.5.1 | Determination of Zn²⁺ions in water samples

Zinc is one of the most important elements for humans. The deficiency and excess of Zn^{2+} ions have many negative effects on health, therefore, according to the WHO, the concentration of zinc in drinking water should be below 3 µg/m,^[54] and a higher rate of zinc than this is undesirable. Thus, it is important to know the amount of







SCHEME 3 Plausible mechanism of a new probe for the fluorescent detection of Zn^{2+} ions

FIGURE 21 The interference effect of Cd^{2+} ions on the absorption spectra of **Sen-1**

zinc in drinking water. **Sen-1** was successfully used to detect Zn^{2+} ions in water samples (Sapanca Lake water and laboratory tap water). The fluorescence intensity of **Sen-1** was recorded before and after the addition of 10 μl of Zn^{2+} ion solution. We examined the effect of deionized water on the fluorescence change and found no enhancing effect (Supporting Information **Figure S17**). After addition of 10 μl of Zn^{2+} ion solution, the fluorescence intensity of **Sen-1** was significantly enhanced. A fluorescence peak appeared around 455 nm when tap water or lake water was used instead of deionized water (Supporting Information **Figure S18**). The experiments were repeated five times under the same conditions and the results are shown in Table 1. The average amounts of Zn^{2+} ions in the five samples were 0.15 and 0.11 μg/ml in

lake water and tap water, respectively. **Sen-1** can therefore be successfully used to detect Zn^{2+} ions in water samples without any interference from other metal ions.

3.5.2 | Fluorescence test strip for visual detection of Zn^{2+} ions

A fluorescence test strip for visual detection of Zn^{2+} ions was prepared. A solution of **Sen-1** was prepared in a 95% (v/v) water–DMSO mixture and immobilized onto a silica gel plate. Solutions containing zinc at different concentrations were added as spots onto the silica gel plate. The picture of plate was taken under the UV lamp. The



FIGURE 23 The fluorescence spectra of Sen-1 during the addition of Zn²⁺ions following saturation with Cd²⁺ ions

initially blue fluorescence spots changed to bright turquoise as the concentration Zn²⁺ ions increased (Figure 25).

Calculation results 3.6

A good way to learn about the activities of molecules and the thermodynamics of the reactions is to use quantum chemical calculations to determine parameters related to molecules. The parameters obtained from the quantum chemical calculations give informations about molecules. Quantum chemical parameters such as E_{HOMO} , E_{LUMO} , and ΔE (HOMO – LUMO energy gap) can be used to compare the activities of molecules.[30-32]

FIGURE 24 The fluorescence spectra of Sen-1 during the addition of Zn²⁺ions following saturation with Fe³⁺ ions

Applied

15 of 21

The most important parameter in comparing the activities of molecules is the HOMO energy parameter. The HOMO energy parameter is the Highest Occupied Molecular Orbital (HOMO) indicating the electron donating ability of studied molecules. The HOMO structures of the molecules are shown in Figure 26. It can be seen from this figure where the molecules will give electrons to metal atoms.^[55] The activity of a molecule increases when HOMO energy value increases. In the light of previous explanations, the activity of the studied molecules were found to be Sen-1 > Sen-2 in all basis set in Table 2.

On the other hand, the LUMO energy parameter indicates that electron accepting abilities of molecules from metal atoms. The LUMO structures of Sen-1 and Sen-2 are shown in Figure 26. It can be seen from this figure

Sample	Added	Found value of Zn ²⁺ ions	Total sample number	SSD	RSD (%)
Deionized water	_	_	5	-	-
	10 µl	0.21 μg/ml		0.014	7.00
Lake water	-	0.15 μg/ml	5	0.019	12.65
	10 µl	0.39 μg/ml		0.026	6.50
Tap water	-	0.15 μg/ml	5	0.015	10.54
	10 µl	0.35 μg/ml		0.022	6.39

TABLE 1 The determination of Zn^{2+} ions in water samples

16 of 21

Note. RSD, relative standard deviation; SSD, sample standard deviation.



FIGURE 25 Images of **Sen-1** without the addition of zinc solution under UV light (a) and after the addition of zinc solution at different concentrations under UV light (b)

where the molecules will accept electrons from metal atoms.^[56]

The energy gap (ΔE) is also important parameter when comparing the activities of molecules. If a molecule has a small energy gap, it is the most active molecule.^[57]

Because the energy gap value shows the electron transfer values between the transition metal atoms and the ligand molecules. A molecule with a low energy gap is more active.

It is thought that Sen-1 and Sen-2 form two different complexes with Zn metal in 95% (v/v) water-DMSO solution. First, the molecule forms a complex with DMSO and Zn metal (Supporting Information Figures S19 and S20). Second, the molecule forms a complex with the water molecule (H₂O) and Zn metal (Supporting Information Figure S19 and S20). These two complexes were studied in three different phases and the effect of dielectric constant in the complexes was investigated. The values obtained from the theoretical studies were compared with the experimental results obtained in DMSO media. The complexes were optimized to comment about them. The Gibbs free energy values were calculated and compared using the energies of these optimized structures.

The Gibbs free energy (ΔG) was calculated using equation:





TABLE 2 The calculated quantum chemical parameters in different basis sets

	E _{HOMO}	$E_{\rm LUMO}$	I	A	ΔE	η	σ	χ	Рİ	ω	ε	Dipol	Energy
B3LYP	/3-21g leve	1											
Sen-1	-6.306	-0.781	6.306	0.781	5.525	2.762	0.362	3.543	-3.543	2.273	0.440	6.032	-28857.733
Sen-2	-6.588	-2.869	6.588	2.869	3.719	1.860	0.538	4.728	-4.728	6.011	0.166	7.255	-34391.244
B3LYP	/6-31g leve	1											
Sen-1	-6.237	-0.724	6.237	0.724	5.513	2.756	0.363	3.481	-3.481	2.198	0.455	6.941	-29005.219
Sen-2	-6.584	-3.075	6.584	3.075	3.509	1.754	0.570	4.829	-4.829	6.646	0.150	5.382	-34567.836
B3LYP	/sdd level												
Sen-1	-6.336	-1.026	6.336	1.026	5.310	2.655	0.377	3.681	-3.681	2.552	0.392	7.266	-29008.117
Sen-2	-6.671	-3.423	6.671	3.423	3.248	1.624	0.616	5.047	-5.047	7.841	0.128	4.933	-34572.194
HF/3-2	1g level												
Sen-1	-8.952	3.151	8.952	-3.151	12.104	6.052	0.165	2.900	-2.900	0.695	1.439	6.663	-28730.297
Sen-2	-9.748	0.951	9.748	-0.951	10.699	5.350	0.187	4.398	-4.398	1.808	0.553	8.694	-34235.050
HF/6-3	1g level												
Sen-1	-9.205	3.089	9.205	-3.089	12.294	6.147	0.163	3.058	-3.058	0.761	1.315	7.623	-28875.483
Sen-2	-9.832	0.633	9.832	-0.633	10.465	5.233	0.191	4.600	-4.600	2.022	0.495	7.891	-34408.973
HF/sde	d level												
Sen-1	-9.333	2.655	9.333	-2.655	11.988	5.994	0.167	3.339	-3.339	0.930	1.075	7.772	-28878.056
Sen-2	-10.019	0.411	10.019	-0.411	10.430	5.215	0.192	4.804	-4.804	2.213	0.452	5.775	-34412.950
M062X	/3-21g leve	1											
Sen-1	-7.706	0.212	7.706	-0.212	7.918	3.959	0.253	3.747	-3.747	1.773	0.564	8.434	-28849.513
Sen-2	-8.189	-1.838	8.189	1.838	6.352	3.176	0.315	5.013	-5.013	3.957	0.253	7.699	-34380.379
M062X/6-31g level													
Sen-1	-7.774	0.084	7.774	-0.084	7.857	3.929	0.255	3.845	-3.845	1.882	0.531	8.670	-28997.008
Sen-2	-8.298	-2.061	8.298	2.061	6.237	3.118	0.321	5.179	-5.179	4.301	0.233	7.921	-34557.372
M062X/sdd level													
Sen-1	-7.913	-0.221	7.913	0.221	7.692	3.846	0.260	4.067	-4.067	2.150	0.465	9.019	-29000.331
Sen-2	-8.427	-2.434	8427	2.434	5.994	2.997	0.334	5.430	-5.430	4.920	0.203	8.275	-34562.174

$$\Delta G = E_{\rm M-L_{complex}} - \left(E_{\rm M^{2+}} + \sum E_{\rm ligand} + E_{\rm water or DMSO} \right)$$
(13)

where $E_{\rm M-L_{complex}}$ is the sum of the electronic and thermal free energies of the metal complex, $E_{\rm ligand}$ is the sum of the electronic and thermal free energies of the ligand, and $E_{\rm M^{2+}}$ is the sum of the electronic and thermal free energies of the metal ion.^[56–61]

When we look at the calculations in Table 3, we can see that four different complexes were obtained for **Sen-1** and **Sen-2** in three different phases. The **Sen-2** complexes are more stable than the **Sen-1** complexes in all three phases. When looking at the four different complexes, it was found that the Gibbs free energy values of the Zn-Sen-2-DMSO were higher (Table 4). If we examine the complexes formed in more detail, it can be seen that the complexes formed with DMSO are more stable

TABLE 3 Energy values of studied molecules (eV)

	Gas phase	Aqueous phase	DMSO phase
Sen-1	-28875.4832	-28876.2263	-28876.2183
Sen-2	-34408.9727	-34410.0156	-34410.0053
DMSO	-15048.6752	-15049.1016	-15049.0969
Water	-2078.5102	-2078.7651	-2078.7628
Zn metal	-1759.0174	-1777.7412	-17775782

Applied Organometallic_WILEY Chemistry

17 of 21

than the complexes formed with water (H_2O) or in the gas phase.

The energy difference between the HOMO and LUMO is termed the HOMO–LUMO gap. HOMO and LUMO are sometimes called frontier orbitals. Thus, the frontier molecular orbital diagrams of the complexes formed by **Sen-1** and **Sen-2** molecules with Zn²⁺ metal were investigated. The frontier molecular orbital

	Gas phase	Aqueous phase	DMSO phase
Zn-Sen-1-water	-32853.1067	-32853.8143	-32853.8042
Zn-Sen-1-DMSO	-45825.3443	-45826.3425	-45826.3318
Zn-Sen-2-water	-38416.0500	-38418.0364	-38417.9955
Zn-Sen-2-DMSO	-51388.0285	-51388.6363	-51388.5635
ΔG for Sen-1-water	-140.0959	-121.0816	-121.2450
ΔG for Sen-1-DMSO	-142.1685	-123.2734	-123.4385
ΔG for Sen-2-water	-169.5497	-151.5144	-151.6493
ΔG for Sen-2-DMSO	-171.3632	-151.7779	-151.8832

TABLE 5Calculated ¹³C NMR and ¹H NMR results for Sen-1 and Sen-2

Sen-1				Sen-2			
	Theoretic	al	Experimental		Theoretica	վ	Experimental
	Gas	DMSO	DMSO		Gas	DMSO	DMSO
C1	119.39	118.97	124.9	C1	136.34	136.14	140.74
C2	132.47	131.70	128.3	C2	127.48	128.86	131.06
C3	122.11	121.22	119.4	C3	130.59	129.47	125.27
C4	153.71	153.80	155.2	C4	158.60	160.67	162.42
C5	111.21	112.71	115.7	C5	109.31	110.82	116.43
C6	132.76	133.63	128.8	C6	131.60	133.07	125.94
C13	62.88	64.34	65.5	C12	57.89	58.77	65.53
C15	36.51	36.65	37.8	C14	33.91	34.13	37.98
C16	57.71	58.29	66.3	C15	58.93	59.48	66.17
C23	173.13	177.65	173.1	C22	173.13	178.32	173.39
H7	7.30	7.42	6.83	H7	9.04	9.22	8.18
H8	8.41	8.38	7.13	H8	6.76	7.21	7.03
H9	6.94	7.35	6.83	H9	9.06	9.20	8.10
H10	7.74	7.96	7.34	H11	4.88	5.81	-
H12	4.26	5.06	9.83	H13	5.69	5.86	5.83
H14	5.38	5.41	5.84	H16	3.27	3.11	3.29
H17	3.71	3.50	3.34	H17	2.86	3.18	3.04
H18	2.98	3.33	3.00	H18	3.92	4.32	4.10
H19	3.56	4.06	4.21	H20	1.07	1.82	-
H21	1.47	2.12	-	H24	9.27	10.12	-
H25	9.80	10.37	9.83				

diagrams of the zinc complexes formed with **Sen-1** or **Sen-2** are shown in Supporting Information **Figures S21** and **S22**, respectively. In the HF/6-31g basis set, HOMO and LUMO shapes were calculated for the ground and the excited states of the **Sen-1** and **Sen-2** Zn complexes. The HOMO energy value of the **Sen-1** and **Sen-2** molecules is lower than the HOMO energy value of the Zn complex. However, the LUMO energy value of the **Sen-1** and **Sen-2** molecules is higher than the HOMO energy

value of the Zn complex. Consequently, the energy gap values of the Zn complexes are lower than those of the **Sen-1** and **Sen-2** molecules. The most important reason is that the rearrangement of the electron distiribution of Sen-1 and Sen-2 after the interaction with Zn^{2+} ions. Because of changes in the energy level causing by electron redistribution, the interaction of **Sen-1** and **Sen-2** with zinc ions is expected to lead to fluorescence enhancement. When the experimental results and

TABLE 6Selected frequencies of ligand at the HF/6-31g level

Compounds	Band	Frequency (cm ⁻¹)	Vibration mode ^a
Sen-1	1	3406	STRE (aromatic CH)
	2	3318	STRE (aliphatic CH)
	3	1946	STRE (C=O)
	4	1794	STRE (C=C)
	5	1687	BEND (H-C=C)
	6	1458	BEND (H-O-C)
	7	1418	BEND (H-C-S)
	8	1208	BEND (C-C-C)
	9	882	TORS (H-C=C=C)
	10	818	TORS (H-O-C-C)
	11	698	STRE (S-C)
Sen-2	1	3438	STRE (aromatic CH)
	2	3331	STRE (aliphatic CH)
	3	1948	STRE (C=O)
	4	1797	STRE (C=C)
	5	1631	BEND (H-C=C)
	6	1563	STRE (O-N)
	7	1444	STRE (C-C)
	8	1321	BEND (H-O-C)
	9	1203	BEND (H-O-C)
	10	974	TORS (H-C=C=C)
	11	818	TORS (H-O-C-C)
	12	695	STRE (S-C)

Note. BENDİNG (BEND), ; STRENGTH (STRE), ; TORSİON (TORS).

theoretical calculations were evaluated together, the interaction of **Sen-1** with Zn^{2+} ions caused fluorescence enhancement, but the same effect was not seen for **Sen-2** due to the fluorescence quenching properties of the nitro groups in benzen ring.

3.6.1 | NMR spectra

Chemical shift values are important to determine the structure of molecules. The chemical shift values for the hydrogen and carbon atoms of **Sen-1** and **Sen-2** were calculated at the HF/6-31++g level by using the gauge including atomic orbital method. The chemical shift values were calculated by subtracting the theoretical values of tetramethylsilane.^[57]

The calculated ¹³C NMR and ¹H NMR chemical shift values for **Sen-1** and **Sen-2** are shown in Table 5. In NMR spectra, the atomic labeling of the optimized structures for **Sen-1** and **Sen-2** are shown in **Figures S23 and S24**. From Table 5, we can see that the aromatic carbon

atoms of **Sen-1** and **Sen-2** have calculated chemical shifts between 111 and 173 ppm, and the aliphatic carbon atoms have calculated chemical shifts between 33 and 62 ppm. The aliphatic hydrogen atoms of these molecules have calculated chemical shifts between 1 and 5 ppm, and the aromatic hydrogen atoms have calculated chemical shifts between 5 and 9 ppm.^[56–61]

The calculated chemical shift values can be compared to the experimental values. The calculated chemical shift values were investigated by drawing correlation graphs (Supporting Information **Figures S25** and **S26**). Compared with experimental observations, the correlation values were found to be very close to 1. ^[58–61] Theoretical calculations were done in two phases: the gas phase and DMSO. Experimental procedures were performed in DMSO solvent. For both phases, the correlation values obtained were 0.99, which shows that the calculations were correct.

3.6.2 | FT-IR spectra

The FT-IR spectra used to identify functional groups and molecular structure are calculated at the HF/6-31g(d,p) level. A detailed study of the optimized structures of the ligands was calculated in the VEDA program.^[57–61]

The FT-IR spectra of **Sen-1** and **Sen-2** are shown in Supporting Information **Figures S27** and **S28**. The main peaks in the obtained spectra are listed in Table 6, which shows the numerical value of the theoretical frequencies of the functional groups in the ligands. In general, when the FT-IR spectra of **Sen-1** and **Sen-2** are examined, the aliphatic carbons in **Sen-1** and **Sen-2** vibrate in the range 3331–3318 cm⁻¹, while the aromatic carbons vibrate between 3406 and 3438 cm⁻¹. The vibration frequency of the C=O bond is ~1950 cm⁻¹ and that of the C–S bond is ~695 cm.^[57–61]

3.6.3 | UV-Vis spectra

UV/Vis spectroscopy is used in chemistry for the quantitative/qualitative analysis of many different compounds, such a stransition metal ions, conjugated organic compounds, complexes and biological macromolecules, which can absorb UV or visible wavelengths. An absorption spectrum consists of several absorption bands that show the structure of the molecule. This spectrum provides information about the electronic transitions that may occur in the molecule. The UV–Vis spectra of the **Sen-1** and **Sen-2** were calculated basis set in chloroform ($\varepsilon = 4.711$), methanol ($\varepsilon = 32.613$), DMSO ($\varepsilon = 46.826$), water ($\varepsilon = 78.355$), and *n*-methyl formamide mixture ($\varepsilon = 181.56$) at HF/6-31++g.^[62] The UV-Vis spectra of Zn complexes of **Sen-1** and **Sen-2** were calculated at HF/6-31++g in the gas, water and DMSO phases. The results of the calculations show that there is one basic peak for **Sen-1** (Supporting Information **Figure S29**), which shows that an electronic transition has occurred. This electronic transition is called the $n \to \pi^*$ transition. When UV-Vis spectrum of **Sen-2** is examined, two basic peaks are seen, which shows there are two electronic transitions (Supporting Information **Figure S30**). These electronic transitions are the $n \to \pi^*$ and $\pi \to \pi^*$ transitions.^[62]

The UV–Vis spectra of the complexes obtained from experimental procedures were compared with the theoretical results in three estimated forms containing water, DMSO and in the gas phase. When the spectra were examined, the maximum peaks for the **Sen-1** complexes were seen at 172, 186, and 162 nm and the maximum peaks for the **Sen-2** complexes were at 170, 178, and 17 nm.

4 | CONCLUSION

The thiazolidine derivatives Sen-1 and Sen-2 were synthesized and characterized by common spectroscopic techniques. The experimental results and the theoretical calculations for the UV-Vis, FT-IR, ¹H NMR, and ¹³C NMR spectra of Sen-1 and Sen-2 are in agreement. In the theoretical calculations, the energy values of the complexes formed between Sen-1 or Sen-2 and Zn metal were compared in gas, aqua and DMSO phases. The complex formed between Sen-2 and zinc metal in DMSO was found to be more stable than the gas phase complex because its Gibbs free energy value is lower. Sen-1 and Sen-2 exhibited optical selectivity for Pd²⁺, Cu²⁺, and Zn^{2+} ions, and have more selectivity for Zn^{2+} ions than Pd²⁺and Cu²⁺ ions. In particular, the selectivity of Sen-1 for Zn^{2+} ions is excellent, with large Stokes shifts, low detection limits, and a color change from colorless to bright turquoise that can be monitored by the naked eye under UV light. The binding ratio of Sen-1 and Sen-2 with Zn^{2+} metal ions was determined to be 1:1 using Job plot analysis. The association constants are $3.59 \times 10^5 \text{ M}^{-1}$ for **Sen-1** and $4.00 \times 10^5 \text{ M}^{-1}$ for **Sen-2**. The Gibbs free energies (ΔG) of **Sen-1** and **Sen-2** towards Zn^{2+} ions were found to be -7.57 kcal M⁻¹ and -7.63 kcal M⁻¹, respectively. The excited state binding constant for Sen-1 with Zn²⁺ ions was determined by fluorescence spectroscopy to be 2.0×10^5 M⁻¹. The LOD of **Sen-1** towards Zn^{2+} ions is 3.73×10^{-8} M, which is about 1/100 of the value recommended by the WHO for drinking water. The reversible fluorescence behavior of **Sen-1** and **Sen-2** was determined on sequential addition of Zn^{2+} ions and EDTA. **Sen-1** was successfully used for detection of Zn^{2+} ions in water samples and a fluorescence test strip was successfully prepared for visual detection of Zn^{2+} ions. The results indicate that **Sen-1** can be used in a simple and effective method for visual and fast detection of Zn^{2+} ions.

ACKNOWLEDGMENTS

This research was made possible by Tubitak Ulakbim, High Performance and Grid Computing Center (TR-Grid e-Infrastructure) and supported by the Research Fund of Sakarya University (Project Number: 2018-3-12-195).

ORCID

Hayriye Genç Bilgiçli ¹⁰ https://orcid.org/0000-0001-6909-316X

Ahmet T. Bilgiçli D https://orcid.org/0000-0002-4144-7357 Armağan Günsel D https://orcid.org/0000-0003-1965-1017

Burak Tüzün ^b https://orcid.org/0000-0002-0420-2043 *M. Nilüfer Yarasir* ^b https://orcid.org/0000-0002-7327-7137

Mustafa Zengin ^b https://orcid.org/0000-0002-0243-1432

REFERENCES

- [1] R. Martínez-Máñez, F. Sancenón, Chem. Rev. 2003, 103, 4419.
- [2] A. N. Kursunlu, E. Guler, H. I. Ucan, R. W. Boyle, *Dyes Pigm.* 2012, 94, 496.
- [3] J. S. Kim, D. T. Quang, Chem. Rev. 2007, 107, 3780.
- [4] S. Anbu, R. Ravishankaran, M. Fátima, C. G. da Silva, A. A. Karande, A. J. L. Pombeiro, *Inorg. Chem.* 2014, 53, 6655.
- [5] T. A. Khan, M. Sheoran, M. Venkata Nikhil Raj, S. Jain, D. Gupta, S. G. Naik, *Spectrochim. Acta, Part a* **2018**, *189*, 176.
- [6] J. M. Jung, S. Y. Lee, E. Nam, M. H. Lim, C. Kim, Sens Actuators B 2017, 244, 1045.
- [7] E. M. Nolan, S. J. Lippard, Chem. Rev. 2008, 108, 3443.
- [8] K. Komatsu, Y. Urano, H. Kojima, T. Nagano, J. Am. Chem. Soc. 2007, 129, 13447.
- [9] T. Fukada, S. Yamasaki, K. Nishida, M. Murakami, T. Hirano, JBIC, J. Biol. Inorg. Chem. 2011, 16, 1123.
- [10] D. Beyersmann, H. Haase, BioMetals 2001, 14, 331.
- [11] W. Maret, *BioMetals* **2009**, *22*, 149.
- [12] M. P. Cuajungco, G. J. Leesa, Brain Res Rev 1997, 23, 219.
- [13] P. Chabosseau, G. A. Rutter, Arch. Biochem. Biophys. 2016, 611, 79.
- [14] L. C. Costello, R. B. Franklin, Oncology 2000, 59, 269.
- [15] L. C. Costello, R. B. Franklin, Mol Cancer 2006, 5, 17.
- [16] J. H. Weiss, S. L. Sensi, J. Y. Koh, *Trends Pharmacol. Sci.* 2000, 21, 395.
- [17] H. Kim, G. R. You, G. J. Park, J. Y. Choi, I. Noh, Y. Kim, S. J. Kim, C. Kim, R. G. Harrison, *Dyes Pigm.* **2015**, *113*, 723.
- [18] S. S. Mati, S. Chall, S. Konar, S. Rakshit, S. C. Bhattacharya, *Sens Actuators B* 2014, 201, 204.
- [19] Z. C. Song, G. Y. Ma, P. C. Lv, H. Q. Li, Z. P. Xiao, H. L. Zhu, *Eur. J. Med. Chem.* **2009**, 44(10), 3903.

- [20] Y. M. Ha, Y. J. Park, J. Y. Lee, D. Park, Y. J. Choi, E. K. Lee, J. M. Kim, J. A. Kim, J. Y. Park, H. J. Lee, H. R. Moon, H. Y. Chung, *Biochimie* **2012**, *94*, 533.
- [21] N. Ghoneim, D. Scherrer, P. Suppan, J. Lumin. 1993, 55, 271.
- [22] R. Dennington, T. Keith, J. Millam, GaussView, Version 6, Semichem Inc., Shawnee Mission, KS 2016.
- [23] M. J. Frisch, G. W. Trucks, H. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G. A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H. P. Hratchian, A. F. Izmaylov, J. Bloino, G. Zheng, J. L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, J. A. Montgomery Jr., J. E. Peralta, F. Ogliaro, M. Bearpark, J. J. Heyd, E. Brothers, K. N. Kudin, V. N. Staroverov, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, N. Rega, J. M. Millam, M. Klene, J. E. Knox, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, R. L. Martin, K. Morokuma, V. G. Zakrzewski, G. A. Voth, P. Salvador, J. J. Dannenberg, S. Dapprich, A. D. Daniels, O. Farkas, J. B. Foresman, J. V. Ortiz, J. Cioslowski, D. J. Fox, Gaussian 09, Revision D.01, Gaussian, Inc., Wallingford, CT 2009.
- [24] PerkinElmer, ChemBioDraw Ultra Version (13.0.0.3015), CambridgeSoft Waltham, MA, USA 2012.
- [25] Chemissan Version 4.43 package (2016)
- [26] A. D. Becke, J Chem Phys 1993, 98, 5648.
- [27] K. B. Wiberg, J. Comput. Chem. 2004, 25, 1342.
- [28] E. G. Hohenstein, S. T. Chill, C. D. Sherrill, J. Chem. Theory Comput. 2008, 4, 1996.
- [29] B. Tüzün, J New Results Sci 2014, 3, 67.
- [30] S. Kaya, B. Tüzün, Curr Phys Chem 2017, 7, 147.
- [31] S. Kaya, B. Tüzün, C. Kaya, I. B. Obot, J. Taiwan Inst. Chem. Eng. 2016, 58, 528.
- [32] S. Kaya, L. Guo, C. Kaya, B. Tüzün, I. B. Obot, R. Touir, N. Islam, J. Taiwan Inst. Chem. Eng. 2016, 65, 522.
- [33] S. Kaya, C. Kaya, L. Guo, F. Kandemirli, B. Tüzün, İ. Uğurlu, L. H. Madkour, M. Saraçoğlu, J. Mol. Liq. 2016, 219, 497.
- [34] I. B. Obot, S. Kaya, C. Kaya, B. Tüzün, Phys. E 2016, 80, 82.
- [35] S. Kaya, P. Banerjee, S. K. Saha, B. Tüzün, C. Kaya, RSC Adv. 2016, 6, 74550.
- [36] I. B. Obot, S. Kaya, C. Kaya, B. Tüzün, Res. Chem. Intermed. 2016, 42, 4963.
- [37] L. Guo, Z. Safi, S. Kaya, W. Shi, B. Tüzün, N. Altunay, C. Kaya, Front Chem 2018, 6(155), 1.
- [38] C. Hepokur, A. Günsel, M. N. Yarasir, A. T. Bilgiçli, B. Tüzün, G. Tüzün, I. Yaylim, *RSC Adv.* 2017, *89*, 56296.
- [39] L. E. Brus, J Chem Phys 1983, 79(11), 5566.
- [40] R. G. Parr, W. Yang, Density functional theory of atoms and molecules, Oxford University Press, Oxford 1989.
- [41] B. Jeżowska-Trzebiatowska, H. Kozłowski, L. Latos-Grażyński, T. Kowalik, Chem. Phys. Lett. 1975, 30(3), 355.
- [42] B. J. Fuhr, D. L. Rabenstein, J. Am. Chem. Soc. 1973, 95(21), 6944.

- [43] K. Hanaoka, K. Kikuchi, H. Kojima, Y. Urano, T. Nagano, J. Am. Chem. Soc. 2004, 126, 12470.
- [44] X. Peng, F. Song, E. Lu, Y. Wang, W. Zhou, J. Fan, Y. Gao, J. Am. Chem. Soc. 2005, 127, 4170.
- [45] L. Long, Y. Wu, L. W. A. Gong, R. Hu, C. Zhang, Anal. Chim. Acta 2016, 908, 1.
- [46] J. Hong, E. Zhou, S. Gong, G. Feng, Dyes Pigm. 2019, 160, 787.
- [47] S. M. Z. Al-Kindy, J. N. Miller, Luminescence 2011, 26, 148.
- [48] Y. S. Yang, C. M. Ma, Y. P. Zhang, Q. H. Xue, J. X. Ru, X. Y. Liu, H. C. Guo, Anal. Methods 2018, 10, 1833.
- [49] C. Balakrishnan, M. Theetharappan, S. Natarajan, S. Thalamuthu, M. A. Neelakantan, *RSC Adv.* 2015, 5, 105453.
- [50] P. Ashokkumar, V. T. Ramakrishnan, P. Ramamurthy, *J Phys Chem a* 2011, 115, 14292.
- [51] J. Y. Choi, D. Kim, J. Yoon, Dyes Pigm. 2013, 96, 176.
- [52] Z. Xu, K. H. Baek, H. N. Kim, J. Cui, X. Qian, D. R. Spring, I. Shin, J. Yoon, J. Am. Chem. Soc. 2010, 132, 601.
- [53] B. A. Wong, S. Friedle, S. J. Lippard, J. Am. Chem. Soc. 2009, 131, 7142.
- [54] Zinc in Drinking-water, Background document for development of WHO Guidelines for Drinking-water Quality. WHO/-SDE/WSH/03.04/17, WHO, 2003
- [55] K. Alaoui, R. Touir, M. Galai, H. Serrar, M. Ouakki, S. Kaya, B. Tüzün, S. Boukhris, M. E. Touhami, Y. El Kacimi, J. Bioand Tribo-Corrosion 2018, 4(3), 37. 1–18
- [56] B. Tüzün, C. Kaya, J. Bio-and Tribo-Corrosion 2018, 4(4), 69. 1–11
- [57] B. Tüzün, K. Sayin, Spectrochim. Acta, Part a 2019, 208, 48.
- [58] E. Güzel, A. Günsel, B. Tüzün, G. Y. Atmaca, A. T. Bilgiçli, A. Erdoğmuş, M. N. Yarasir, *Polyhedron* 2019, 158, 316.
- [59] A. Günsel, E. Kırbaç, B. Tüzün, A. Erdoğmuş, A. T. Bilgiçli, M. N. Yaraşır, J. Mol. Struct. 2019, 1180, 127.
- [60] A. Günsel, A. T. Bilgiçli, B. Tüzün, H. Pişkin, G. Y. Atmaca, A. Erdoğmuş, M. N. Yarasir, J. Photochem. Photobiol., a 2019, 373, 77.
- [61] M. Alam, D. U. Lee, Comput. Biol. Chem. 2016, 64, 185.
- [62] A. Günsel, A.T. Bilgicli, H. Pişkin, B. Tuzun, M.N. Yaraşır, B. Gunduz, Synthesis of non-peripherally tetra-substituted copper (II) phthalocyanines: Characterization, optical, surface properties, fabrication and photo-electrical properties of photosensitive diode, Dalton Transactions (2019) DOI:https://doi. org/10.1039/c9dt02868d

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

How to cite this article: Genç Bilgiçli H,

Bilgiçli AT, Günsel A, et al. Turn-on fluorescent probe for Zn^{2+} ions based on thiazolidine derivative. *Appl Organometal Chem*. 2020;e5624. https://doi.org/10.1002/aoc.5624

Applied Organometallic_WILEY^{21 of 21} Chemistry