

## Synthesis of New Azo Dyes Containing Pyrazole and 1,3,4-Thiadiazole Derivatives and Investigation of Their Solvatochromic Properties

Nesrin ŞENER<sup>1\*</sup>, Ali Basim Shihab SHIHAB<sup>2</sup>, Merve ZURNACI<sup>3</sup>, İzzet ŞENER<sup>4</sup>

<sup>1</sup>Department of Chemistry, Faculty of Science, Kastamonu University, 37200, Kastamonu, Turkey

<sup>2</sup>Institute of Science, Kastamonu University, 37200 Kastamonu, Turkey

<sup>3</sup>Central Research Laboratory, Kastamonu University, Kastamonu, Turkey

<sup>4</sup>Food Engineering Department, Faculty of Engineering and Architecture, Kastamonu University, Kastamonu, Turkey

(Alınış / Received: 24.10.2025, Kabul / Accepted: 09.03.2026, Online Yayınlanma / Published Online: 24.04.2026)

### Keywords

Pyrazole,  
Thiadiazole,  
Azo dyes,  
Solvatochromic.

**Abstract:** In this study, where 2-amino-1,3,4-thiadiazole and 5-mercapto-2-amino-1,3,4-thiadiazole compounds were used as starting materials, five new azo dyes were synthesized using 3-amino-5-methyl pyrazolone, 3-amino-1-phenyl-5-methyl pyrazolone, and barbituric acid as coupling components. <sup>1</sup>H-NMR and ATR-FTIR spectroscopic methods determined the molecular structures of the synthesized compounds. In addition, UV-Vis and absorption spectra of the synthesized compounds were taken, and their solvatochromic properties were investigated. As a result of absorption studies, positive solvatochromism was observed in the synthesis compounds.

## Pirazol ve 1,3,4-Tiyadiazol Türevlerini İçeren Yeni Azo Boyalarının Sentezi ve Solvatokromik Özelliklerinin İncelenmesi

### Anahtar Kelimeler

Pirazol,  
Tiyadiazol,  
Azo boyarmadde,  
Solvatokromik.

**Öz:** 2-amino-1,3,4-tiyadiazol ve 5-merkapto-2-amino-1,3,4-tiyadiazol bileşiklerinin başlangıç maddesi olarak kullanıldığı bu çalışmada; 3-amino-5-metil pirazolon, 3-amino-1-fenil-5-metil pirazolon ve barbütirik asitin kenetleme bileşenleri olarak kullanıldığı beş yeni azo boyarmadde sentezlenmiştir. Sentezlenen bileşiklerin moleküler yapıları <sup>1</sup>H-NMR, ATR-FTIR spektroskopik yöntemleri ile belirlenmiştir. Ayrıca, sentezlenen bileşiklerin UV-Vis. absorpsiyon spektrumları alınmış ve solvatokromik özellikleri incelenmiştir. Absorpsiyon çalışmaları sonucunda, sentezlenen bileşiklerde pozitif solvatokromizm gözlenmiştir.

### 1. Introduction

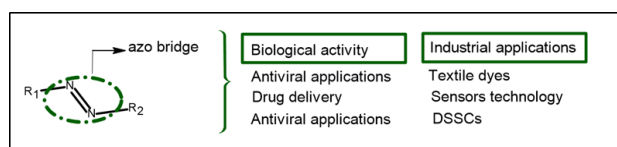
Heterocyclic compounds are essential as they are intermediates in many biological molecules [1] and generally contain five and six-membered rings [2]. The synthesis of heterocyclic compounds is generally due to their potential biological and industrial applications [3-5]. In addition, these compounds have a wide range of pharmacological properties, such as antibacterial [6], antiviral [7], and anti-inflammatory agents [8], and they also play an important role in biochemical techniques [9]. Sulfur and nitrogen-containing heterocyclic compounds have attracted researchers' attention to the development of organic synthesis [10]. For this reason, one of the popular compounds is 1,3,4-thiadiazole compounds. The sulfur and nitrogen atoms in the 1,3,4-thiadiazole ring contribute very

different properties to the molecules they form, primarily pharmacological properties [11,12]. Similarly, the biological importance of pyrazolone-linked compounds attracts the attention of many researchers [13,14]. It is known that compounds containing pyrazole and 1,3,4-thiadiazole rings in particular have potential as drugs [15,16]. Therefore, synthesizing different derivatives of biologically active molecules, such as dyes, is of great importance today. Solvation properties between the molecule and the solvent, such as solvatochromism [17-22]. Solvatochromism is used to describe the apparent change in position and sometimes intensity of the UV-Vis absorption band following a change in the polarity of the medium. It is known that solvatochromism is commonly used in many fields of chemical and biological research to study bulk and local polarity in

\*Corresponding author: nsener@kastamonu.edu.tr

macrosystems, or even the conformation and binding of proteins [23-26].

Numerous studies suggest the synthesis of biologically active thiadiazole and pyrazole-containing compounds [27]. In addition, many studies examine the solvatochromic properties of such compounds [28,29]. However, the molecule in which these two compounds are combined has not been studied much in the literature. This study synthesized new azo dyes containing five different pyrazole and thiadiazole rings. Spectrophotometric methods such as ATR-FTIR and  $^1\text{H-NMR}$  were used to elucidate the molecular structures of these compounds. Additionally, solvatochromic behaviors of the synthesis compounds were investigated with their UV-Vis absorption spectra.



**Scheme 1.** General Structure and Functional Applications of Azo Compounds

## 2. Materials and Methods

The chemicals, substances, and solvents (spectroscopic purity) used in this study were supplied by Sigma-Aldrich (USA) and Merck Company (Germany). In addition, these products were used directly without any purification. 2-Amino-1,3,4-thiadiazole, 2-amino-5-mercapto-1,3,4-thiadiazole, 3-methyl-5-pyrazolone, 1-phenyl-3-methyl-5-pyrazolone, barbituric acid, sodium nitrite, sodium hydroxide compounds, and hydrochloric acid, acetic acid, pyridine, and DMSO solvents were purchased from Sigma-Aldrich. An electrothermal SMP30 device was used to determine the melting point of the obtained compounds.

### 2.1. Synthesis of compound I

0.5 g (0.004 mol) of 2-amino-1,3,4-thiadiazole compound was taken into a 100 mL beaker. 6 mL of acetic acid and 3 mL of HCl were added, and the mixture was placed in an ice bath and stirred. The solution of  $\text{NaNO}_2$  prepared in minimum water was added dropwise to the cooled mixture. At the end of two hours, the diazonium salt was prepared. The mixture of 0.49 g (0.004 mol) of 3-Methyl-5-pyrazolone compound dissolved in 0.1 g NaOH aqueous solution was added dropwise to the diazonium solution in an ice bath and stirred for two hours. At the end of the reaction, the mixture was precipitated with water and filtered. The dried precipitate was crystallized from DMSO-Water mixture (10:1). The experimental setup of the synthesized compounds is available in Figure 1. As a result, the light-yellow compound obtained was successfully synthesized with 68% yield. Melting

point:  $239\text{ }^\circ\text{C}$  > decomposition, **ATR-FTIR ( $\text{cm}^{-1}$ )  $\nu_{\text{max}}$ :** 3266.78 (-NH stretching vibration), 1432.93 (-NH bending vibration), 3074.32 and 3014.36 (aromatic C-H stretching vibration), 2925.25 (aliphatic C-H stretching vibration), 1661.56 (C=O stretching vibration), 1561.80 (C=N stretching vibration), 1502.02 (N=N stretching vibration), 1352.41 (N=N bending vibration), 716.44 (C-S-C stretching vibration).  **$^1\text{H-NMR}$  ( $\delta$ , ppm,  $\text{DMSO-d}_6$ ):** 2.28 (s,  $-\text{CH}_3$  in the 3H pyrazole ring), 5.38 (s,  $-\text{CH}$  in the 1H pyrazole ring), 9.29 (s,  $-\text{CH}$  in the 1H thiadiazole ring), 9.00-9.50 (b,  $-\text{NH}$  in the 1H pyrazole ring).

### 2.2. Synthesis of compound II

0.5 g (0.0037 mol) of 2-amino-5-mercapto-1,3,4-thiadiazole compound was taken into a 100 mL beaker. 6 mL of acetic acid and 3 mL of HCl were added and the mixture was placed in an ice bath and stirred. A solution of 0.38 g of  $\text{NaNO}_2$  prepared in minimum water was added dropwise to the cooled mixture. At the end of two hours, the diazonium salt was prepared. 0.37 g (0.0037 mol) of 3-Methyl-5-pyrazolone compound was dissolved in an aqueous solution of 0.1 g of NaOH in another beaker and added dropwise to the diazonium solution in an ice bath, and stirred for two hours. At the end of the reaction, the mixture was precipitated with water and filtered. The dried precipitate was crystallized from DMSO-Water mixture (10:1). As a result, the dark yellow compound obtained was successfully synthesized with 63% yield, mp:  $109\text{ }^\circ\text{C}$  > decomposition, **ATR-FTIR ( $\text{cm}^{-1}$ )  $\nu_{\text{max}}$ :** 3150.58 (-NH stretching vibration), 1448.39 (-NH bending vibration), 3066.60 (aromatic C-H stretching vibration), 2983.44 (aliphatic C-H stretching vibration), 2662 (S-H stretching vibration), 1691.90 (C=O stretching vibration), 1620.96 (C=C stretching vibration), 1389.95 (N=N bending vibration), 700.82 (C-S-C stretching vibration).  **$^1\text{H-NMR}$  ( $\delta$ , ppm,  $\text{DMSO-d}_6$ ):** 2.28 (s, 3H  $-\text{CH}_3$ ), 6.33 (s, 1H pyrazole  $-\text{CH}$ ), 7.87 (b, 1H pyrazole  $-\text{NH}$ ), 13.09 (b, 1H, S-H).

### 2.3. Synthesis of compound III

0.5 g (0.0038 mol) of 2-amino-5-mercapto-1,3,4-thiadiazole compound was taken into a 100 mL beaker. 6 mL of acetic acid and 3 mL of HCl were added and the mixture was placed in an ice bath and mixed. 0.38 g of  $\text{NaNO}_2$  solution prepared in minimum water was added dropwise to the cooled mixture. At the end of two hours, the diazonium salt was prepared. The mixture of 0.65 g (0.0038 mol) of 1-Phenyl-3-methyl-5-pyrazolone compound dissolved in 0.1 g of NaOH aqueous solution was added to the diazonium solution dropwise in an ice bath and stirred for two hours. At the end of the reaction, the mixture was precipitated with water and filtered. The dried precipitate was crystallized from the DMSO-Water mixture (10:1). As a result, the dark orange compound obtained was successfully synthesized with 68% yield, mp:  $100\text{ }^\circ\text{C}$  > decomposition, **ATR-FTIR ( $\text{cm}^{-1}$ )  $\nu_{\text{max}}$ :** 3246.97 (-

NH stretching vibration), 1443.17 (-NH bending vibration), 3053.83 (aromatic C-H stretching vibration), 2994.59 (aliphatic C-H stretching vibration), 2665 (S-H stretching vibration), 1702.58 (C=O stretching vibration), 1494.53 (N=N stretching vibration), 1391.76 (N=N bending vibration), 698.07 (C-S-C stretching vibration). **<sup>1</sup>H-NMR (δ, ppm, DMSO-d<sub>6</sub>):** 2.27 (s, 3H -CH<sub>3</sub>), 7.49 (t, 1H phenyl proton), 7.69 (t, 1H phenyl proton), 7.91 (t, 1H phenyl proton), 13.06 (b, 1H -SH).

#### 2.4. Synthesis of compound IV

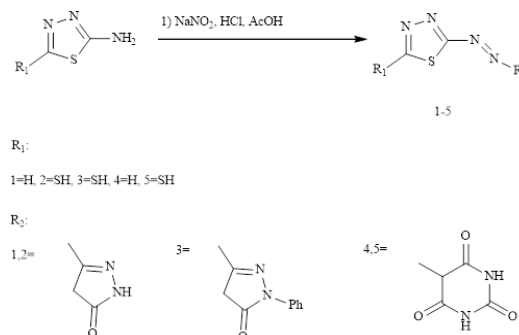
0.5 g (0.004 mol) of 2-amino-1,3,4-thiadiazole compound was taken into a 100 mL beaker. 6 mL of acetic acid and 3 mL of HCl were added and the mixture was placed in an ice bath and stirred. The solution of NaNO<sub>2</sub> prepared in minimum water was added dropwise to the cooled mixture. At the end of two hours, the diazonium salt was prepared. The mixture of 0.63 g (0.004 mol) of barbituric acid compound dissolved in 10 mL of pyridine was added dropwise to the diazonium solution in an ice bath and stirred for two hours. At the end of the reaction, the mixture was precipitated with water and filtered. The dried precipitate was crystallized from the DMSO-Water mixture (10:1). As a result, the yellow compound obtained was successfully synthesized with 71% yield, mp: 235 °C > decomposition, **ATR-FTIR (cm<sup>-1</sup>) v<sub>max</sub>:** 3199.49 (-NH stretching vibration), 1437.97 (-NH bending vibration), 3098.30 and 3065.69 (aromatic C-H stretching vibration), 2734.89 (aliphatic C-H stretching vibration), 1712.57 and 1672.33 (C=O stretching vibration), 1584.84 (C=N stretching vibration), 1503.21 (N=N stretching vibration), 1399.50 (N=N bending vibration), 689.43 (C-S-C stretching vibration). **<sup>1</sup>H-NMR (δ, ppm, DMSO-d<sub>6</sub>):** 9.27 (s, 1H aromatic in the barbituric acid ring -CH), 11.56 (s, 1H thiadiazole -CH), 11.88 (s, 2H barbituric -NH).

#### 2.5. Synthesis of compound V

0.5 g (0.0038 mol) of 2-amino-5-mercapto-1,3,4-thiadiazole compound was taken into a 100 mL beaker. 6 mL of acetic acid and 3 mL of HCl were added and the mixture was placed in an ice bath and stirred. The solution of NaNO<sub>2</sub> prepared in minimum water was added dropwise to the cooled mixture. At the end of two hours, the diazonium salt was prepared. The mixture of 0.49 g (0.0038 mol) of barbituric acid compound dissolved in 10 mL of pyridine was added dropwise to the diazonium solution in an ice bath and stirred for two hours. At the end of the reaction, the mixture was precipitated with water and filtered. The dried precipitate was crystallized from DMSO-Water mixture (10:1). As a result, the light orange compound obtained was successfully synthesized with 71% yield, mp: 104 °C > decomposition, **ATR-FTIR (cm<sup>-1</sup>) v<sub>max</sub>:** 3298.92 and 3168.33 (-NH stretching vibration), 3066.94 (aromatic C-H stretching vibration), 2663 (S-

H stretching vibration), 1703.81 (C=O stretching vibration), 1590.35 (C=N stretching vibration), 1492.12 (N=N stretching vibration), 1355.17 (N=N bending vibration), 699.16 (C-S-C stretching vibration). **<sup>1</sup>H-NMR (δ, ppm, DMSO-d<sub>6</sub>):** 9.27 (s, 1H aromatic in the barbituric acid ring -CH), 11.58 (s, 2H barbituric -NH), 11.86 (b, 1H -SH).

The experimental setup of the synthesized compounds is available in **Figure 1**.



**Figure 1.** Reaction schemes of the synthesized compounds (1-5)

#### 2.6. Absorption study

The visible region absorption spectra of the obtained compounds in DMSO, DMF, acetonitrile, methanol, acetic acid, and chloroform, and the change of maximum absorption wavelengths (300 and 700nm) in these solvents were investigated (10<sup>-8</sup> - 10<sup>-6</sup> mol/L). The maximum wavelengths of the compounds in each solvent are different due to the different solubilities of the compounds in these solvents. In addition, UV-Vis. absorption of these three different solutions prepared at similar concentrations (10<sup>-8</sup> - 10<sup>-6</sup> mol/L) was also taken to observe the changes in the methanol solution of each compound with the addition of HCl (0.1 M) and KOH (0.1 M).

### 3. Results and Discussion

#### 3.1. ATR-FTIR results

Spectra of the synthesized compounds were studied in the 4000-400 cm<sup>-1</sup> range for infrared spectroscopy (ATR-FTIR, Bruker). Spectrum analysis results are shown in Table 1. Stretching vibration bands of the -NH group in the structure of the compounds were recorded in the range of 3266.78 and 3150.58 cm<sup>-1</sup>. While the bands from aromatic -CH stretching vibrations in the structures were observed in the range of 3074.32 to 3014.36 cm<sup>-1</sup>, the bands from aliphatic -CH stretching vibrations in the structures were observed in the range of 2994.59 to 2734.89 cm<sup>-1</sup>. The S-H stretching vibration bands for Compounds II, III, and V were observed at 2662, 2665, and 2663 cm<sup>-1</sup>, respectively. When the ATR-FTIR spectrum results were examined, it was thought that the sharp bands recorded between 1712.57 and 1661.56 cm<sup>-1</sup> were caused by C=O bond stretching vibrations. It is

understood that the bands observed between 1590.35 and 1661.80  $\text{cm}^{-1}$  belong to C=N stretching vibrations. While the stretching vibrations of N=N bonds were observed between 1502.02 and 1492.12  $\text{cm}^{-1}$ , the bending vibrations of the same group were observed between 1399.50 and 1352.41  $\text{cm}^{-1}$ . Stretching vibrations of the C-S-C bonds in the 1,3,4-thiadiazole ring found in all compounds were observed in the range of 716.44 and 689.43  $\text{cm}^{-1}$ .

**Table 1.** ATR-FTIR value of synthesized compounds ( $\text{cm}^{-1}$ )

Comp. Name	ATR-FTIR ( $\text{cm}^{-1}$ )							vC-S-C
	vNH	vAromatic-H	vAliphatic-H	vS-H	vC=O	vC=N	vN=N	
I	3266 1432	3074 3014	2925	-	1661	1561	1502 1352	716
II	3150 1448	3066	2983	2662	1691	-	- 1389	700
III	3246 1443	3053	2994	2665	1702	-	1494 1391	698
IV	3199 1437	3098	2734	-	1712 1672	1584	1503 1399	689
V	3298 3168	3066	-	2663	1703	1590 1495	1492 1355	699

### 3.2. $^1\text{H-NMR}$ results

Bruker Spectrometer 400-MHz instrument (Germany) was used for  $^1\text{H-NMR}$  spectrum analysis of the synthesized compounds and their solutions prepared in  $\text{DMSO-d}_6$ . As seen in the analysis results in **Table 2**, the peaks belonging to the aliphatic  $-\text{CH}_3$  protons in the molecular structures were observed between 2.27 and 2.28 ppm. The molecules' aromatic  $-\text{CH}$  protons in the thiadiazole, pyrazole, and barbituric acid ring were observed between 5.38 and 11.56 ppm. The  $-\text{NH}$  protons in the barbituric ring were recorded in the range of 11.50-11.88 ppm. Finally, the  $-\text{SH}$  protons in compounds II, III, and IV were obtained at the values of 11.71, 13.06, and 11.86 ppm, respectively.

**Table 2.**  $^1\text{H-NMR}$  ( $\delta$ , ppm,  $\text{DMSO-d}_6$ ) values for synthesized compounds

Comp. Name	$^1\text{H-NMR}$ ( $\delta$ , ppm, $\text{DMSO-d}_6$ )		
	Aliphatic -H	Aromatic -H	X-H
I	2.28	5.38	9.00-9.50
II	2.28	6.33	7.87, 13.09
III	2.27	7.49, 7.69, 7.91	13.06
IV	-	11.56	11.88
V	-	9.27	11.58, 11.86

**Table 3.** Maximum wavelengths of the synthesized compounds in different solvents

Compound Name	$\lambda(\text{nm})$					
	DMSO	DMF	Acetonitrile	Methanol	Acetic acid	Chloroform
I	364	417	301	400	350	453
II	290	304	440	448	338	388
III	308	309	451	441	377	453
IV	366, 417	411	354	401	350	438
V	308	387	359	387	358	372

I	2.28 (s, 3H; $-\text{CH}_3$ in the pyrazole ring)	5.38 (s, 1H; pyrazole $-\text{CH}$ ) 9.29 (s, 1H; thiadiazole $-\text{CH}$ )	9.00-9.50 (b, 1H; $-\text{NH}$ in the pyrazole ring)
II	2.28 (s, 3H; $-\text{CH}_3$ in the pyrazole)	6.33 (s, 1H; pyrazole $-\text{CH}$ ) 7.49 (t, 1H; $-\text{CH}$ in the phenyl ring)	7.87 (b, 1H; pyrazole $-\text{NH}$ ) 13.09 (b, 1H; $-\text{SH}$ )
III	2.27 (s, 3H; $-\text{CH}_3$ in the pyrazole)	7.69 (t, 2H; $-\text{CH}$ in the phenyl ring) 7.91 (d, 1H; $-\text{CH}$ in the phenyl ring)	13.06 (b, 1H; $-\text{SH}$ )
IV	-	9.27 (s, 1H; aromatic $-\text{CH}$ in the barbituric acid ring) 11.56 (s, 1H; aromatic $-\text{CH}$ in the thiadiazole ring)	11.88 (s, 2H; barbituric $-\text{NH}$ )
V	-	9.27 (s, 1H; aromatic $-\text{CH}$ in the barbituric acid ring)	11.58 (s, 2H; barbituric $-\text{NH}$ ) 11.86 (b, 1H $-\text{SH}$ )

### 3.3. Absorption results

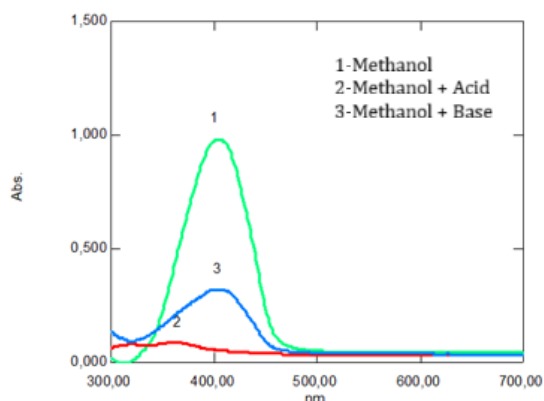
As seen in **Table 3**, UV-Vis. absorption values of the solutions of the synthesized compounds in different solvents, measured in the range of 300-700 nm, are shown. When these values are examined, it is understood that Compound 4 gives absorption at a single wavelength except for its solution in DMSO. It is seen that the compounds give different absorptions in different solutions with different dielectric constants. However, no proportional decrease or increase is observed depending on the dielectric constants.

As seen in **Table 4**, since the synthesized compounds give different absorption in different solvents, the absorption graphs of the structures with the addition of acid and base to the solution in methanol were also examined. In all synthesized compounds, it was observed that the maximum wavelengths decreased with the addition of acid (hypsochromic shift). In contrast, the maximum wavelengths increased with the addition of base (bathochromic shift). **Figure 2** provides an example of this phenomenon by showing the change in Compound IV upon addition of acid and base. This result, as stated in the literature, indicates that if a bathochromic shift is observed with increasing polarity of the medium, the dye is said to exhibit positive solvatochromism [30].

**Table 4.** Change of maximum wavelengths of synthesized compounds with acid-base addition

Compound Name	$\lambda$ (nm)		
	Methanol	Methanol + Acid	Methanol + Base
I	400	375	404
II	448	311	304, 403
III	441	309	395
IV	401	362	410
V	387	346	393

As the polarity decreased (Methanol, Acetic Acid, Chloroform), a red shift (bathochromic shift) was observed, i.e., the absorption wavelength increased. Chloroform, which has a polarity index of 1.1, was generally observed to have the longest wavelength. When Compound IV was examined in detail, it was seen that the lowest wavelength was in acetic acid (6.2), which has the highest polarity index. The longest wavelength was in chloroform (1.1), which has the lowest polarity index. A blue (hypsochromic) shift was generally observed in acidic media, and the absorption wavelengths became shorter. The most significant change in acidic media was observed in Compounds II and III (~137 nm and ~132 nm). A red shift (bathochromic shift) was generally observed in basic media. In some compounds, two absorption bands were observed in basic media (For example, Compound II: 304 and 403 nm). Compound II, with this difference, may have different resonance structures, suggesting that the absorption wavelength in all compounds except Compound III increased in basic medium.

**Figure 2.** Absorption spectrum showing the change of compound IV upon acid-base addition.

### 3.4. Substituent effects

As indicated in **Table 3**, changes in absorbance wavelength occurred with the shift of substituents in azo dyes. The substituent effect was mostly observed in acetonitrile among all solvents. The least change was observed in acetic acid. There is conjugation between the phenyl group and the pyrazolone ring attached to the azo bridge, which causes the absorbance to shift to higher wavelengths (longer UV regions). When Compounds II and III were compared,

the bathochromic shift resulting from this conjugation was clearly seen.

The electronegativity of -SH can change the electron density of the system by changing the electron density in the molecule, which can shift the wavelength of absorbance. When Compound I and II structures and Compound IV and V, to which -H and -SH were attached, were compared, weak shifts were observed.

## 4. Conclusion

Within the scope of this study, five different new 1,3,4-thiadiazole derivative dyes were synthesized. The structure determination of the obtained compounds was carried out by spectroscopic methods such as FT-IR,  $^1\text{H-NMR}$ , and it was seen that the compounds were synthesized successfully. UV-Vis. absorption spectra of the synthesis compounds were examined and the results were interpreted. It is thought that the compounds have the feature of being used as indicators due to their absorption in the visible region. In addition, it can be predicted that the obtained compounds can be used in the dyeing of textile products because they are heterocyclic azo dyes.

## Acknowledgments

The authors are grateful to the Scientific Research Projects Council of Kastamonu University (KÜ-BAP01/2021-37).

## Declaration of Ethical Code

*In this study, we undertake that all the rules required to be followed within the scope of the "Higher Education Institutions Scientific Research and Publication Ethics Directive" are complied with, and that none of the actions stated under the heading "Actions Against Scientific Research and Publication Ethics" are not carried out.*

## References

- [1] Steenkamp, L., & Brady, D. (2003). Screening of commercial enzymes for the enantioselective hydrolysis of R, S-naproxen ester. *Enzyme and microbial technology*, 32(3-4), 472-477.
- [2] Shinde, S. D., & Yadav, G. D. (2015). Insight into microwave assisted immobilized *Candida antarctica* lipase B catalyzed kinetic resolution of RS-(±)-ketorolac. *Process Biochemistry*, 50(2), 230-236.
- [3] French, L. (2005). Dysmenorrhea. *American family physician*, 71(2), 285-291.
- [4] Harrington, P. J., & Lodewijk, E. (1997). Twenty years of naproxen technology. *Organic Process Research & Development*, 1(1), 72-76.
- [5] Rossi, S. (2006). *Australian medicines handbook* (pp. 143-145).
- [6] Gür, M., Yerlikaya, S., Şener, N., Özkınalı, S., Baloglu, M. C., Gökçe, H., ... & Şener, İ. (2020).

- Antiproliferative-antimicrobial properties and structural analysis of newly synthesized Schiff bases derived from some 1, 3, 4-thiadiazole compounds. *Journal of Molecular Structure*, 1219, 128570.
- [7] Hagar, M., Ahmed, H. A., Aljohani, G., & Alhaddad, O. A. (2020). Investigation of some antiviral N-heterocycles as COVID 19 drug: molecular docking and DFT calculations. *International Journal of Molecular Sciences*, 21(11), 3922.
- [8] Cordell, G. A. (2008). *The alkaloids: chemistry and biology* (Vol. 65). Academic Press.
- [9] Karthikeyan, S., Grishina, M., Kandasamy, S., Mangaiyarkarasi, R., Ramamoorthi, A., Chinnathambi, S., ... & John Kennedy, L. (2023). A review on medicinally important heterocyclic compounds and importance of biophysical approach of underlying the insight mechanism in biological environment. *Journal of Biomolecular Structure and Dynamics*, 41(23), 14599-14619.
- [10] Şener, İ., Şahin, Ç., Demir, S., Şener, N., & Gür, M. (2020). A combined experimental and computational study of electrochemical and photophysical properties of new benzophenone derivatives functionalized with N-substituted-phenyl-1, 3, 4-thiadiazole-2-amine. *Journal of Molecular Structure*, 1203, 127475.
- [11] Mohite, P., Bhoge, N., Dengale, S. G., & Darekar, N. R. (2024). Synthesis, Properties, and Biological Applications of 1, 2, 4-Thiadiazoles.
- [12] Mittal, R. K., Mishra, R., Sharma, V., & Mishra, I. (2024). 1, 3, 4-thiadiazole: A versatile scaffold for drug discovery. *Letters in Organic Chemistry*, 21(5), 400-413.
- [13] Özknalı, S., Gür, M., Şener, N., Alkın, S., & Çavuş, M. S. (2018). Synthesis of new azo schiff bases of pyrazole derivatives and their spectroscopic and theoretical investigations. *Journal of Molecular Structure*, 1174, 74-83.
- [14] Şener, N., Bayrakdar, A., Kart, H. H., & Şener, İ. (2017). A combined experimental and DFT investigation of disazo dye having pyrazole skeleton. *Journal of Molecular Structure*, 1129, 222-230.
- [15] Dawood, K. M., Eldebss, T. M., El-Zahabi, H. S., Yousef, M. H., & Metz, P. (2013). Synthesis of some new pyrazole-based 1, 3-thiazoles and 1, 3, 4-thiadiazoles as anticancer agents. *European journal of medicinal chemistry*, 70, 740-749.
- [16] Abdelhamid, A. O., Shawali, A. S., Gomha, S. M., & El-Enany, W. A. M. A. (2015). Synthesis and antimicrobial evaluation of some novel thiazole, 1, 3, 4-thiadiazole and pyrido [2, 3-d][1, 2, 4]-triazolo [4, 3-a] pyrimidine derivatives incorporating pyrazole moiety. *Heterocycles*, 91(11), 2126-2142.
- [17] Rauf, M. A., & Hisaindee, S. (2013). Studies on solvatochromic behavior of dyes using spectral techniques. *Journal of Molecular Structure*, 1042, 45-56.
- [18] Şener, İ., Karçı, F., Ertan, N., & Kılıç, E. (2006). Synthesis and investigations of the absorption spectra of hetarylazo disperse dyes derived from 2, 4-quinolinediol. *Dyes and pigments*, 70(2), 143-148.
- [19] Geng, J., Dai, Y., Qian, H. F., Wang, N., & Huang, W. (2015). 2-Amino-4-chloro-5-formylthiophene-3-carbonitrile derived azo dyes. *Dyes and Pigments*, 117, 133-140.
- [20] Warde, U., & Sekar, N. (2017). NLOphoric mono-azo dyes with negative solvatochromism and in-built ESIPT unit from ethyl 1, 3-dihydroxy-2-naphthoate: Estimation of excited state dipole moment and pH study. *Dyes and Pigments*, 137, 384-394.
- [21] Seferoğlu, Z., Ertan, N., Hökelek, T., & Şahin, E. (2008). The synthesis, spectroscopic properties and crystal structure of novel, bis-hetarylazo disperse dyes. *Dyes and Pigments*, 77(3), 614-625.
- [22] Özdemir, Ü. Ö., Aktan, E., Ilbiz, F., Gündüzalp, A. B., Özbek, N., Sarı, M., ... & Saydam, S. (2014). Characterization, antibacterial, anticarbonic anhydrase II isoenzyme, anticancer, electrochemical and computational studies of sulfonic acid hydrazide derivative and its Cu (II) complex. *Inorganica Chimica Acta*, 423, 194-203.
- [23] Marini, A., Muñoz-Losa, A., Biancardi, A., & Mennucci, B. (2010). What is solvatochromism?. *The Journal of Physical Chemistry B*, 114(51), 17128-17135.
- [24] Błasiak, B., Londergan, C. H., Webb, L. J., & Cho, M. (2017). Vibrational probes: From small molecule solvatochromism theory and experiments to applications in complex systems. *Accounts of chemical research*, 50(4), 968-976.
- [25] Hemalatha, K., Madhumitha, G., Vasavi, C. S., & Munusami, P. (2015). 2, 3-Dihydroquinazolin-4 (1H)-ones: Visible light mediated synthesis, solvatochromism and biological activity. *Journal of Photochemistry and Photobiology B: Biology*, 143, 139-147.
- [26] Kakanejadifard, A., Azarbani, F., Saki, Z., Kakanejadifard, S., & Zabardasti, A. (2014). Synthesis, characterization, solvatochromism and biological properties of 2, 2'-((1E, 1' E)-((1, 2, 5-oxadiazole-3, 4-diyl) bis (azanylylidene)) bis (methan-yllylidene)) bis (4-(phenyldiazenyl) phenol). *Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy*, 132, 700-705.
- [27] Şener, N., & Aldwib, A. E. O. (2024). New Antibacterial 1, 3, 4-Thiadiazole Derivatives With

Pyridine Moiety. *Chemistry & Biodiversity*, 21(6), e202400522.

- [28] Sharma, M., Sandhu, N., & Saraswat, V. (2024). Microwave assisted facile one pot synthesis of novel pyrazole derivative for multi-analyte detection ( $\text{Fe}^{3+}$  and  $\text{Zn}^{2+}$ ) and its solvatochromic studies. *Journal of Molecular Structure*, 1318, 139183.
- [29] Zhu, H., Zhang, J., Zhang, H., Bai, J., Peng, J., & Jia, J. (2024). Triphenylamine-based 1, 3, 4-thiadiazole derivative: solvatochromism, aggregation-induced emission and reversible turn-on mechanofluorochromism. *Journal of Luminescence*, 267, 120390.
- [30] Rezende, M. C., Dominguez, M., Aracena, A., & Millán, D. (2011). Solvatochromism and electrophilicity. *Chemical Physics Letters*, 514(4-6), 267-273.