



Synthesis of Hydrazone Based Ion Sensor and Photophysical Characterization

Hidrazon Temelli İyon Sensör Sentezi ve Fotofiziksel Karakterizasyonu

Seda Çınar[✉]

Ankara Hacı Bayram Veli University, Chemistry Department, Polatli Campus, Polatli, Ankara, Türkiye.

ABSTRACT

Hydrazone compounds are susceptible to nucleophilic attacks of anions such as fluoride or cyanide due to their tendency toward deprotonation of hydrogen bonded to nitrogen atom in the structure and found applications as ion sensors. In this work, from the condensation reaction of 4-hydroxybenzaldehyde and 2,4-dinitrophenylhydrazine, phenolic hydrazone compound was obtained and the following substitution reaction with 4-nitrobenzenesulfonyl chloride was studied to synthesize a new hydrazone compound with elongated conjugation. Structures of the synthesized compounds were accomplished with ¹H NMR, ¹³C NMR and UV-Vis absorption spectroscopic techniques. According to the spectroscopic data, absorption maximum of the new hydrazone compound was found to shift bathochromically with ca. 120 nm in the presence of nucleophilic fluoride, cyanide, acetate, hydroxide and dihydrogenphosphate anions.

Key Words

2,4-dinitrophenylhydrazone, bathochromic shift, ion sensor.

ÖZ

Hidrazon bileşikler yapılarındaki azota bağlı hidrojen atomunun deprotone olabilme yetkinliğinden dolayı florür ya da siyanür gibi nükleofilik anyonların atağına açıktır ve bu özellikleri ile iyon sensörü olarak kullanım alanı bulmuşlardır. Bu çalışmada, 4-hidroksibenzaldehit ve 2,4-dinitrofenilhidrazin bileşiklerinin kondenzasyon tepkimesinden fenolik hidrazon yapısı elde edilmiş ve bu yapının 4-nitrobenzenesülfonil klorür ile yer değiştirme tepkimesi çalışılarak daha konjuge yeni bir hidrazon bileşiği sentezlenmiştir. Sentezlenen bileşiklerin yapıları ¹H NMR, ¹³C NMR ve UV-Vis absorpsiyon spektroskopisi yöntemleri ile aydınlatılmıştır. Elde edilen absorpsiyon verilerine göre, yeni bileşiğin nükleofilik özellikteki florür, siyanür, asetat, hidroksit ve dihidrojenfosfat anyonları varlığında absorpsiyon maksimumunda yaklaşık 120 nm'lik kırmızıya kayma şeklinde tepki verdiği belirlenmiştir.

Anahtar Kelimeler

2,4-dinitrofenilhidrazon, kırmızıya kayma, iyon sensörü.

Article History: May 7, 2024; Accepted: Aug 26, 2024; Available Online: Dec 11, 2024.

DOI: <https://doi.org/10.15671/hjbc.1477580>

Correspondence to: S. Çınar, Ankara Hacı Bayram Veli University, Chemistry Department, Polatli Campus, Polatli, Ankara, Türkiye.

E-Mail: seda.cinar@hbv.edu.tr

INTRODUCTION

Environmental pollution is significantly increasing due to unconscious consumption of biochemical or organic pollutants in many areas of daily life resulting with the affection of the natural life as well as public and individual health. Among the pollutants, fluoride and cyanide are prominent as they are used in lower concentrations widely in cleaning chemicals or metallurgy [1,2]. However, large quantities of these anions are harmful for human health and nature. Therefore, chemical sensing and removal of fluoride or cyanide ions in biological and environmental samples is very important. Colorimetric selective detection of analytes using simple chemical sensors is an area of interest to reach environmentally-friendly, low cost and easy handling analyzing systems. Colorimetric naked eye detection of fluoride or cyanide ions indeed is important for living systems. Various chemosensors for the detection of anions have been developed based on quinones, quinolines, bodipy, coumarin, porphyrin dyes or hydrazone derivatives [3-10]. In these structures, receptor sites are responsible for binding of specific ionic substrates with the formation of substrate-molecule complexes. Formation of new complexes changes the colorimetric or fluorometric behavior at a particular wavelength which enables the detection of ionic species by spectroscopic methods. Fluoride or cyanide ions are known to have nucleophilic character in which they can abstract an acidic proton in a molecular system [11,12]. In this manner, hydrazone derivatives with –NH protons in the structure are good candidates for the detection of fluoride or cyanide ions.

Here in this work, we designed the synthesis of a hydrazone derivative bearing electron withdrawing nitrobenzenesulfonyl moiety **2** for the naked eye detection of fluoride and cyanide anions. At first, phenolic hydrazone **1** was synthesized and the subsequent substitution with 4-nitrobenzenesulfonyl chloride resulted with the formation of targeted **2**. Colorimetric detection of anions was verified with absorption spectroscopy technique.

MATERIALS and METHODS

Chemicals and Instrument

Chemicals and solvents were purchased from Acros Organics, Sigma Aldrich, Fisher Scientific, and were used without further purification. Technical grade hexane and ethyl acetate were obtained from Birpa (Türkiye)

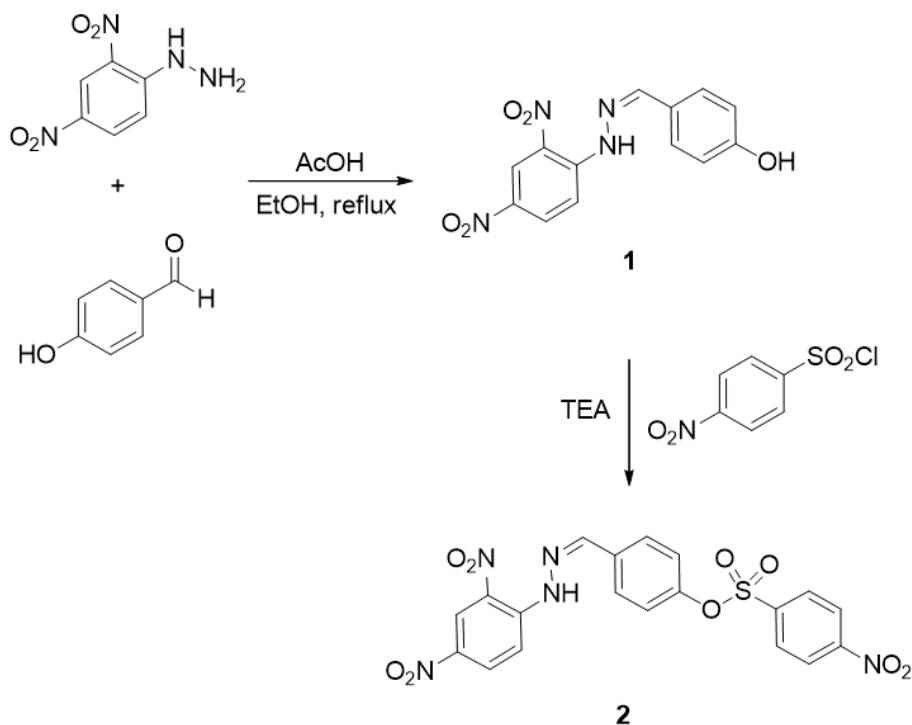
and purified by fractional distillation before use. Reactions were monitored by TLC using precoated silica plates (Kieselgel 60, F254, E.Merck), visualized with UV light. ^1H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded using SiMe_4 and H_3PO_4 as an internal reference with Bruker DPX-400 FT NMR spectrometer. Chemical shifts (δ) were given as ppm and coupling constants (J) as Hz. UV-Vis spectra were recorded on a Shimadzu UV-Mini 1240 UV-Vis Spectrophotometer.

Synthesis of compound 1

2,4-dinitrophenylhydrazine (0.500 g, 2.52 mmol) and 4-hydroxybenzaldehyde (0.308 g, 2.52 mmol) were dissolved in ethanol and acetic acid (0.144 mL, 2.52 mmol) was added to this solution. Resulting mixture was refluxed for 3 hours (TLC monitoring). After completion of the reaction, mixture was cooled to rt, precipitates were filtered and washed with ethanol. Compound was obtained as dark red solid (95% yield). M.p: 285 °C. ^1H NMR (400 MHz, CDCl_3): δ = 6.87 (d, J = 8.6 Hz, 2H), 7.64 (d, J = 8.6 Hz, 2H), 8.05 (d, J = 9.7 Hz, 1H), 8.35 (dd, J = 9.7, 2.7 Hz, 1H), 8.60 (s, 1H), 8.86 (d, J = 2.6 Hz, 1H), 10.09 (s, 1H), 11.58 (s, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ = 116.4, 117.1, 123.6, 125.2, 129.4, 129.8, 130.2, 137.0, 144.9, 150.5, 160.5.

Synthesis of compound 2

1 (0.100 g, 0.331 mmol) and 4-nitrobenzenesulfonyl chloride (0.081 g, 0.364 mmol) were gathered in acetonitrile (ACN) and triethylamine (0.092 mL, 0.662 mmol) was added to this solution. After 5 min, solution color turned into orange from deep red and precipitates formed. Solids were filtered, washed with ACN and air dried. Compound was obtained as orange solid (93% yield). M.p: >300 °C. ^1H NMR (400 MHz, CDCl_3): δ = 11.72 (s, 1H), 8.88 (s, 1H), 8.70 (s, 1H), 8.48 (d, J = 8.9 Hz, 2H), 8.38 (d, J = 9.8 Hz, 1H), 8.19 (d, J = 8.8 Hz, 2H), 8.10 (d, J = 9.5 Hz, 1H), 7.83 (d, J = 8.7 Hz, 2H), 7.21 (d, J = 8.6 Hz, 2H); ^{13}C NMR (100 MHz, CDCl_3): δ = 117.3, 123.3, 123.4, 123.9, 125.6, 127.4, 129.6, 130.3, 130.6, 133.9, 137.8, 139.7, 144.9, 148.0, 150.2.



Scheme 1. Synthetic pathway of hydrazone **2**.

RESULTS and DISCUSSION

Synthesis of **1** was performed according to the literature method (Scheme 1) [13]. Firstly, acidic condensation reaction of 4-hydroxybenzaldehyde and 2,4-dinitrophenylhydrazine was performed and phenolic hydrazone **1** was obtained in 95% yield. Then, substitution reaction of **1** with 4-nitrobenzenesulfonyl chloride was studied and new hydrazone compound **2** was synthesized with 93% yield. Structures of both compounds were identified by NMR spectroscopy.

Structure of the novel hydrazone **2** is fully conjugated and as given in Figure 1, the proton NMR signals were shown in the aromatic region in between 7-9 ppm. In addition, characteristic hydrazone NH proton resonanced at 11.72 ppm. ^{13}C NMR also confirms the structure.

With the successfully synthesized **2** in hand, photophysical properties of the compound were investigated by means of solvent change and presence of common anions. At first, absorption characteristics were screened in protic and aprotic solvents such as acetonitrile, dimethylsulfoxide, dimethylformamide, ethanol, tetrahy-

drofuran, dichloromethane, toluene and water. Basic absorption maxima are observed *ca.* 380 nm for most of the solvents except for dimethylformamide (505 nm) (Figure 2A). This could be attributed to the basic character of DMF as it can deprotonate the NH proton in the structure. As it compared to the absorption of **1** having λ_{max} at 395 nm in acetonitrile, λ_{max} of **2** is observed at 381 nm with a hypsochromical shift of 14 nm (Figure 2B). This shift is due to the electron withdrawing nature of the nitrobenzenesulfonyl group introduced to the hydrazone structure. Since NH proton of hydrazone compounds can be deprotonated by fluoride or cyanide ions, absorption behaviour of **2** was examined in the presence of various anions. As given in Figure 3, absorption maximum at 381 nm was shifted to 500 nm upon deprotonation with F^- , CN^- , OH^- and OAc^- . It can be seen from the spectra that F^- and CN^- ions fully deprotonate the hydrazone NH proton, yet OH^- , OAc^- and H_2PO_4^- ions partially deprotonate the NH proton due to the lower nucleophilic character. These spectral changes are also reflected in the colours of hydrazone **2**-anion mixtures, the more deprotonated the dark pink it becomes (inset of Figure 3).

Besides the anion scanning, naturally occurring biothiols such as cysteine (Cys) and glutathione (GSH) were also studied for their sensing with hydrazone **2**. It is well known that Cys or GSH are capable of S_NAr reaction in which the cleavage of nitrobenzenesulfonyl groups from sensor molecules yielding a change in sensors absorption or emission wavelengths [14,15]. Since hydrazone **2** bears 4-nitrobenzenesulfonyl group in its structure, it was thought that **2** can sense Cys or GSH via nucleophilic substitution reactions. In this manner, incremental addition of Cys or GSH solutions in water into hydrazone **2** in ACN has been employed. As given in Figure 4, no net absorption maxima shift was observed but absorption intensities of sensor **2** have been increased upon addition of Cys or GSH indicating its complexation with Cys or GSH. Complexation between sensor **2** and Cys or GSH in which the association constant (K_s) can be calculated with Formula 1 and Formula 2 given below, where A_t and A_0 are absorbance values when $\alpha = 1$ (no Cys or GSH) and $\alpha = 0$ (fully bonded with Cys or GSH), respectively [16]. K_s values for Cys or GSH binding have been calculated as $1.31 \times 10^3 \text{ M}^{-1}$ and $1.04 \times 10^4 \text{ M}^{-1}$, respectively. Larger K_s value of cysteine is also reflected in Figure 4 where a larger elevation of absorption intensity of sensor **2** upon 1 eq cysteine addition is observed in comparison with 1 eq glutathione addition.

$$\frac{a}{1-a} = \frac{1}{K_s [Cys \text{ or } GSH]} \quad (1)$$

$$a = \frac{A_t - A}{A_t - A_0} \quad (2)$$

CONCLUSION

In conclusion, we have successfully synthesized a novel hydrazone compound **2** from the phenolic hydrazone **1**. Introduction of the electron withdrawing nitrobenzenesulfonyl moiety led the absorption maximum of **1** shifted hypsochromically with 14 nm. Hydrazone **2** showed good affinity to F^- and CN^- ions along with OH^- , OAc^- and $H_2PO_4^-$ ions upon deprotonation of NH proton. As a result of deprotonation absorption maximum bathochromically shifted from 381 nm to 500 nm. This shift is reflected in the colour of the **2**-anion mixtures. These results are noteworthy that hydrazone **2** could be used as colorimetric sensor for fluoride and cyanide anions. Additionally, cysteine and glutathione were found to bind hydrazone **2** indicating that these biothiols can be detected as a result of increase in absorption intensity in which cysteine binds more effectively than glutathione according to the calculated association constant values.

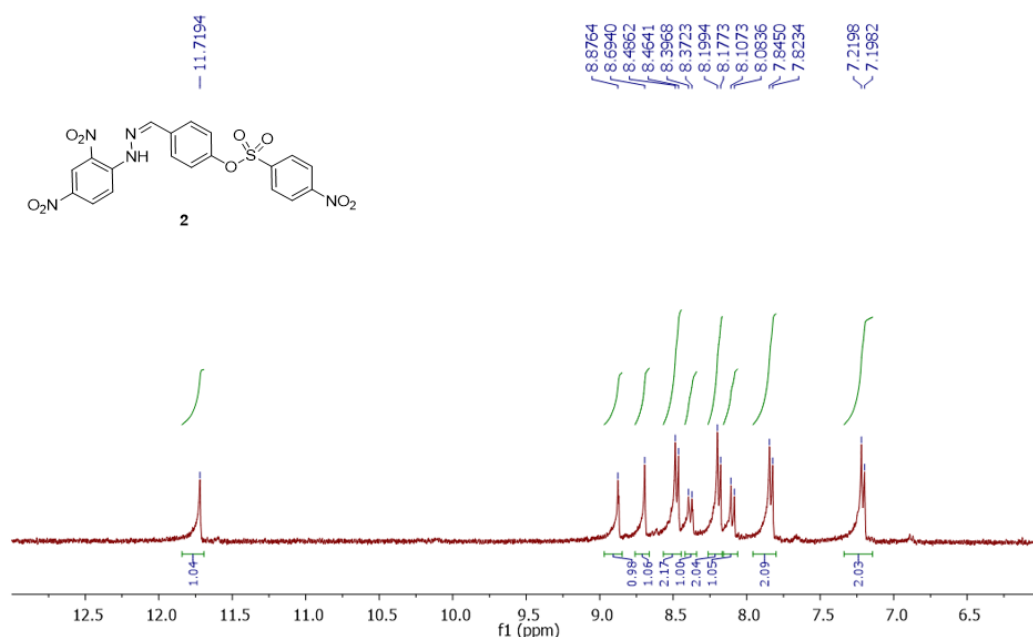


Figure 1. 1H NMR of hydrazone **2** (in d^6 -DMSO)

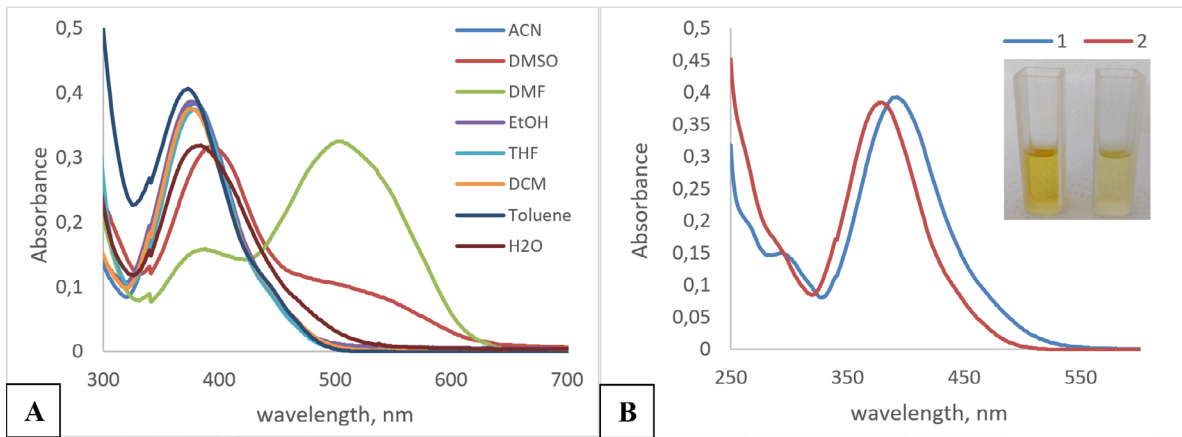


Figure 2. Absorption spectra of **2** (1×10^{-5} M) in various solvents (A) and absorption spectra comparison of **1** and **2** (1×10^{-5} M) in ACN (B).

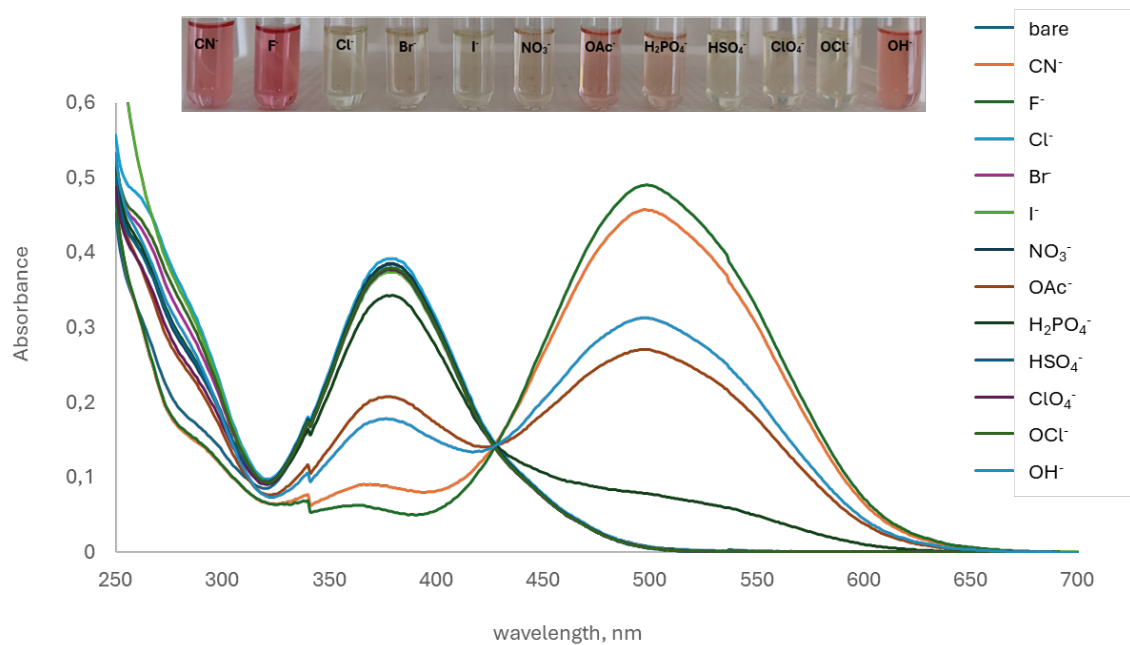


Figure 3. Absorption spectra of **2** in ACN (1×10^{-5} M) in the presence of various anions (1eq).

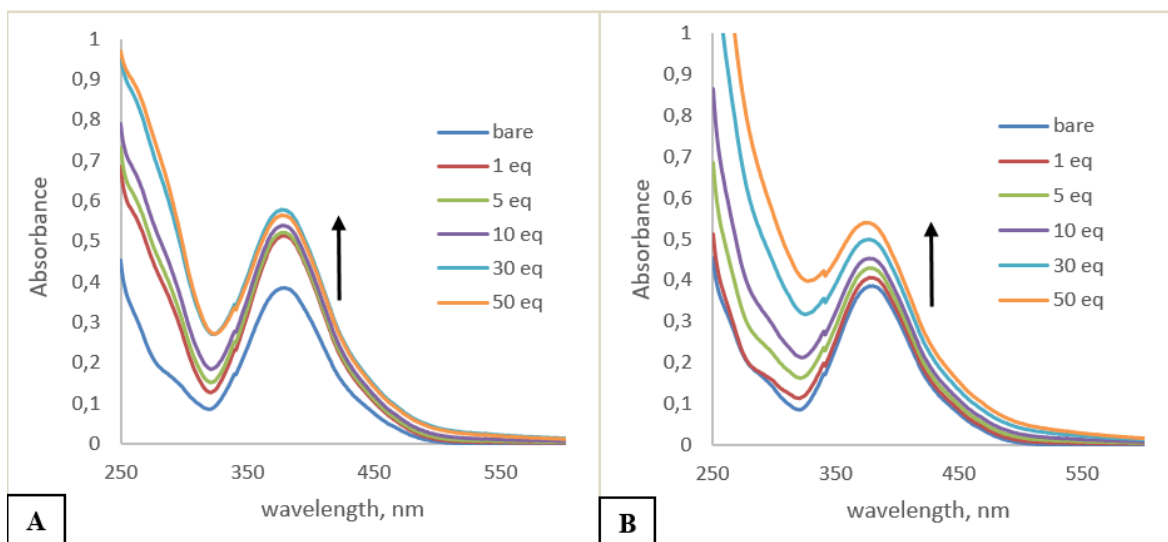


Figure 4. Absorption spectra of 2 in ACN (1×10^{-5} M) in the presence of Cys (A) and GSH (B) (1-50eq).

References

- H.P. Chen, C.H. Chang, J.K. Liu, S.F. Chuang, J.Y. Yang, Effect of fluoride containing bleaching agents on enamel surface properties, *Journal of Dentistry*, 36 (2008) 718 – 725.
- N. Pandey, S. Dutta, P. Biswas, Cyanide Mitigation at Steel Metallurgical Process's Effluent, *Water, Air, Soil Pollut.*, 234 (2023) 682 – 713.
- B.R. Jali, A. K. Barick, P. Mohapatra, S. K. Sahoo, A comprehensive review on quinones based fluoride selective colorimetric and fluorescence chemosensors, *J. Fluorine Chem.*, 244 (2021) 109744 – 109759.
- H. Tong, L. Wang, X. Jing, F. Wang, "Turn-On" Conjugated Polymer Fluorescent Chemosensor for Fluoride Ion, *Macromolecules*, 36 (2003) 2584 – 2586.
- S. Madhu, M. Ravikanth, Boron-Dipyrromethene Based Reversible and Reusable Selective Chemosensor for Fluoride Detection, *Inorganic Chem.*, 53 (2014) 1646 – 1653.
- S. Chakraborty, The Advent of Bodipy-based Chemosensors for Sensing Fluoride Ions: A Literature Review, *J Fluoresc.* (2024) <https://doi.org/10.1007/s10895-024-03619-7>.
- R. D. Alharthy, S. Tariq, S. Naseem, M. Islam, N. Ahmed, A. R. Pasha, Z. Shafiq, Coumarin-based thiosemicarbazones as colorimetric and fluorescent "Turn on" chemosensors for fluoride ions and their applications in logic circuits, *J. Mol. Struct.*, 1294 (2023) 136381 – 136388.
- E. Yalçın, M. Alkış, N. Seferoğlu, Z. Seferoğlu, A novel coumarin-pyrazole-triazine based fluorescence chemosensor for fluoride detection via deprotonation process: Experimental and theoretical studies, *J. Mol. Struct.*, 1155 (2018) 573 – 581.
- V. V. Kumar, D. Ramadevi, V. M. Ankathi, Development of porphyrin-based chemosensor for highly selective sensing of fluoride ion in aqueous media, *Microchem. J.*, 157 (2020) 105028 – 105035.
- S. Gond, P. Yadav, V. P. Singh, Design and development of a highly efficient hydrazone based sensing material for selective detection of F ions, *Materials Lett.*, 351 (2023) 135003 – 135006.
- W. Saiyasombat, U. Eiamprasert, T. Chantarojsiri, K. Chainok, S. Kiattisevi, Bis-BODIPY-based fluoride and cyanide sensor mediated by unconventional deprotonation of C-H proton, *Dyes Pigments*, 206 (2022) 110643 – 110650.
- T. Samanta, N. Das, R. Shunmugam, Intramolecular Charge Transfer-Based Rapid Colorimetric In-Field Fluoride Ion Sensors, *ACS Sustainable Chem. Eng.*, 9 (2021) 10176 – 10183.
- S. Anand, A. Muthusamy, S. Dineshkumar, Synthesis, characterization, electrical and thermal properties of hydrazone polymers derived from 2,4-dinitro phenyl hydrazine, *J. Mol. Struct.*, 1248 (2022) 131502 – 131510.
- Y. Du, H. Wang, S. Zhao, J. Fan, S. Huang, Y. Hao, Design of an ICT-based fluorescent probe with excellent sensitivity for visualizing GSH levels in live cells, *Chemical Papers*, 76 (2022) 4571 – 4579.
- M. Wei, P. Yin, Y. Shen, L. Zhang, J. Deng, S. Xue, H. Li, B. Guo, Y. Zhang, S. Yao, A new turn-on fluorescent probe for selective detection of glutathione and cysteine in living cells, *Chem. Commun.*, 49 (2013) 4640 – 4642.
- Z. Yang, X. Wang, Y. Wu, X. Li, M. Chen, Two emission turn-on optical chemosensors for cysteine detection using up-conversion nanocrystals as excitation host: Synthesis, characterization and performance, *Sens. Actuators B Chem.*, 255 (2018) 1587–1594.