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A new fluorescent and colorimetric sensor for copper(II) ion detection based on a 4-styryl-1,8-naphthalimide derivative

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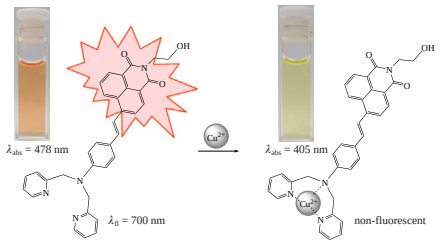
A new derivative of 4-styryl-1,8-naphthalimide containing a dipicolylamine receptor moiety demonstrated selective optical response to Cu^{2+} cations in an aqueous Tris-HCl buffer solution due to the formation of 1 : 1 ligand–metal complexes.



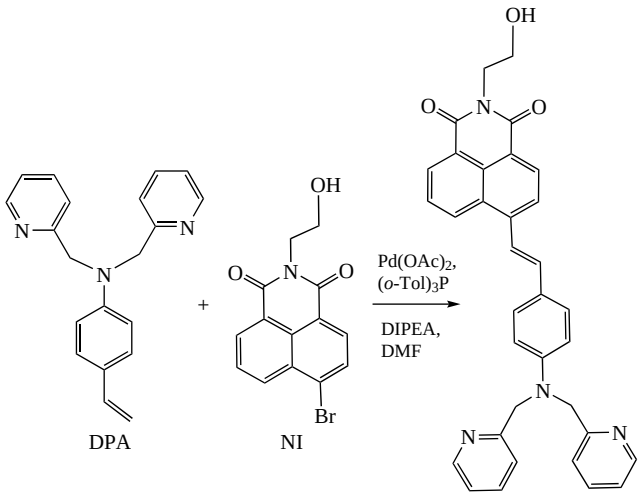
Keywords: sensor, copper cation, fluorescence, 1,8-naphthalimide, dipicolylamine, intramolecular charge transfer.

Determination of the content of metal cations in biological objects is of importance in medicine and ecology since metal ions are involved in the key biochemical processes in living organisms.[1,2] The Cu^{2+} ion, the third most abundant cation among transition metal ions in the human body, is involved in many redox reactions and plays an important role in energy metabolism and respiration processes.[2–4] The changes in copper levels in the body can be due to the Menkes and Wilson diseases, neurodegenerative diseases such as Parkinson's and Alzheimer's diseases, and various cancers.[3,4] Therefore, a highly accurate and selective determination of the content of copper cations in biological media is an important task of medicinal chemistry.

Optical electronic spectroscopy is among the most suitable physicochemical methods of analysis used for this purpose, as it allows one to perform high-precision analysis quickly and with relatively simple and compact equipment.[5] To determine the content of metal cations by optical spectroscopy, it is necessary to develop optical chemosensors, *i.e.*, molecules containing a receptor moiety responsible for the selective binding of a metal cation, as well as a signal moiety – a chromophore whose spectral characteristics change upon complexation.[6] Derivatives of 1,8-naphthalimide are among the main types of organic phosphors that have a great practical importance. Today they are actively used as a basis for the development of fluorescent markers for biology,[7,8] drugs for the diagnosis and therapy of oncological diseases,[9–12] fluorescent photochromes,[13] as well as optical chemosensors for metal cations,[14–18] anions[21–24] and neutral molecules[25–27] that can work in biological media.

In this study, a 4-styryl-*N*-hydroxyethyl-1,8-naphthalimide derivative NI-DPA (Scheme 1) containing a dipicolylamine (DPA) receptor as a donor substituent in the styryl moiety was suggested as a photoactive platform of a chemosensor for Cu^{2+} cations. It is known that 4-styryl derivatives of naphthalimide can be used as fluorescent markers and sensors for cellular studies,[28,29] since they possess the ability to penetrate cell membrane and luminesce intensely in a cell environment. For example, a selective colorimetric and fluorescent sensor for the detection of mercury cations within living cells was obtained on the basis of 4-styryl-1,8-naphthalimide and azadithia-15-crown-5-ether.[30] The dipicolylamine receptor moiety of the NI-DPA molecule is a known chelator of transition metal ions.[31–33] The combination of naphthalimide chromophore and DPA receptor was reported for the determination of manganese[34,35] and zinc ions.[36] Optical sensors for heavy and transition metal cations were also prepared by combining DPA with 4-amino and 4-amido derivatives of naphthalimide, but they are not sufficiently selective and show an optical response in acetonitrile solution.[37]

The method of combining the receptor and signal moieties in a sensor, where the receptor atoms enter into conjugation with the chromophore part of the molecule, is a typical approach for creating Intramolecular Charge Transfer (ICT) sensors.[16] The optical response of sensors of this type is based on the variation in the efficiency of charge transfer in a molecule after



Scheme 1

coordination with a metal cation, and the shift in the absorption and fluorescence maxima upon binding (manifested as a change in the color of the solution being analyzed) usually serves as the analytical signal. Since the amino group of the NI-DPA receptor moiety is part of the molecule's chromophore moiety, its electron pair should be removed from conjugation with the styryl moiety of the chromophore upon coordination with a Cu^{2+} cation. As a result, the efficiency of the ICT process in the molecule decreases, leading to a hypsochromic shift of the absorption maximum of NI-DPA after coordination with the Cu^{2+} cation.

The synthesis of the NI-DPA sensor (see Scheme 1) is based on the Heck reaction between 4-bromo-*N*-(2-hydroxyethyl)-1,8-naphthalimide NI and styrene derivative DPA (for synthetic details and characterization, see Online Supplementary Materials).

The optical and complexing properties of NI-DPA were studied in an aqueous solution of Tris-HCl buffer (0.01 mol dm^{-3}, pH 7.0). This buffer solution is often used to analyze the sensor characteristics of fluoroionophore systems under conditions simulating physiological environments.[36,38] The electronic absorption spectrum of NI-DPA contains a band with a maximum at 478 nm due to charge transfer from the amino group of the styryl moiety at position 4 of the naphthalimide core to the carbonyl groups of the dicarboxyimide residue [Figure 1(*a*) and Figure S2 from Online Supplementary Materials]. The fluorescence band of NI-DPA is in the long-wave region of the spectrum and has a maximum at 697 nm. The quantum yield of NI-DPA fluorescence is 0.7%. The low luminescence efficiency in protonic polar solvents is characteristic of 4-styryl derivatives of naphthalimide containing donor groups in the styryl moiety[39] and is due to the formation of a 'twisted' charge transfer state (TICT, Twisted Intramolecular Charge Transfer).[40-42] The formation of a TICT state involves two stages: charge transfer and subsequent rotation of the donor relative to the rest of the molecule. In most cases, TICT states relax in non-radiation way and their formation decreases the fluorescence quantum yield.[40]

The absorption and fluorescence spectra of a NI-DPA sensor solution upon addition of copper(II) perchlorate were recorded [see Figure 1(*a*),(*b*)]. Addition of Cu^{2+} cations to a NI-DPA solution caused a decrease in the intensity of the long-wave absorption band of the ligand and the emergence of a new band with a maximum at 405 nm in the absorption spectrum. The observed hypsochromic shift of the NI-DPA absorption band indicates the participation of the nitrogen atom of the amino group of the receptor moiety in the coordination of Cu^{2+}, which results in a decrease in the efficiency of the ICT process in the molecule. A similar spectral effect took place for an ICT-sensor with a similar structure based on 4-styrylnaphthalimide containing an azadithia-15-crown-5-ether receptor moiety instead of a dipicolylamino group, upon its coordination with the mercury(II) cation.[30]

The fluorescence of the ligand is quenched upon gradual addition of Cu^{2+} [see Figure 1(*b*)] due to the paramagnetic properties of the copper(II) ion.[43] It was found that the experimental data on the variation in the fluorescence intensity of the NI-DPA solution with an increase in Cu^{2+} concentration are in the best agreement with the calculated curve if the formation of one type of complex occurs in solution according to the following equation:

$$\text{NI-DPA} + Cu^{2+} \rightleftarrows (\text{NI-DPA}) \cdot Cu^{2+}.$$

The calculated logarithm of the stability constant of the ligand–metal 1 : 1 complex ($\log K_{(\text{NI-DPA}) \cdot Cu^{2+}}$) amounted to 4.86 ± 0.07 according to spectrofluorimetric titration data. The formation of a ligand–metal 1 : 1 complex was also confirmed by ESI mass

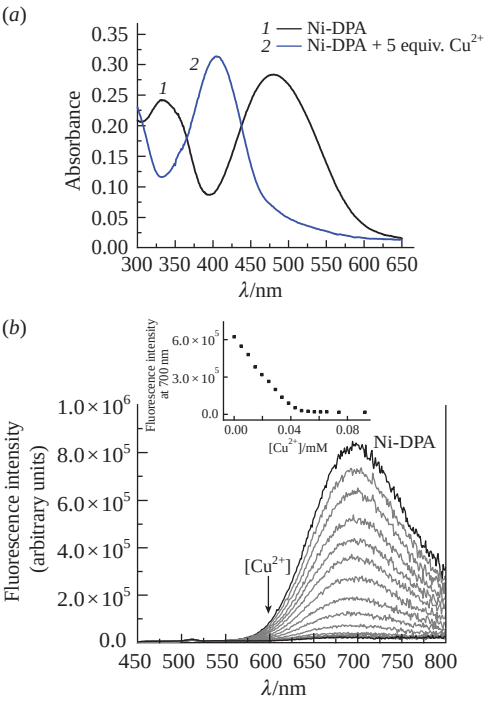


Figure 1 Variation in the (*a*) absorption and (*b*) fluorescence spectra of a solution of compound NI-DPA (2×10^{-5} mol dm^{-3}) in Tris-HCl buffer solution (0.01 mol dm^{-3}, pH 7.00) upon addition of $Cu(CO_4)_2$. The excitation wavelength is 435 nm. The inset in part *b* shows the fluorescence intensity at 700 nm *vs*. the Cu^{2+} concentration.

spectrum data (Figure S3), in which the peaks corresponding to the $[Cu(\text{NI-DPA})MeCN]^+$ species (*m/z*, found: 644.40; calculated: 644.15) and $[(\text{NI-DPA})Cu]^+$ species (*m/z*, found: 603.40; calculated: 603.15) were present.

Using the method of standard deviations at low concentrations and spectrofluorimetry data, we calculated the detection limit of Cu^{2+} cations for NI-DPA in water at pH 7.0, which amounted to 2.3×10^{-6} mol dm^{-3} (the calculation method is given in Online Supplementary Materials). It should be noted that the detection limit value obtained is several times smaller than the maximum permissible copper content in drinking water (~20 μmol dm^{-3}) established by the U.S. Environmental Protection Agency (EPA).[44]

Transition metal cations Ni^{2+}, Cd^{2+}, Fe^{2+}, Hg^{2+}, Ag^+ and Zn^{2+}, alkaline-earth metals Ca^{2+}, Mg^{2+}, as well as Pb^{2+} were selected to study the selectivity of complexation of NI-DPA sensor with Cu^{2+}. It was found that the presence of 5 equiv. of the above cations does not cause significant changes in the absorption spectra of the ligand, while addition of 5 equiv. of copper causes a significant hypsochromic shift of the absorption maximum of NI-DPA from 478 to 405 nm [Figure S4(*a*)].

Compound NI-DPA was also found to exhibit a selective fluorescence response to copper(II) cations [Figure S4(*b*)]. Figure 2 shows a bar graph of the $(I_0 - I)/I_0$ ratio, where I_0 is the fluorescence intensity of a solution of free NI-DPA ligand at 700 nm and I is the fluorescence intensity of the NI-DPA solution in the presence of 5 equiv. of perchlorates of various metals. It can be seen from Figure 2 that significant changes in the signal are only observed in the presence of Cu^{2+}. Moreover, the presence of 5 equiv. of competitive ions such as Ni^{2+}, Cd^{2+}, Fe^{2+}, Ag^+, Zn^{2+}, Ca^{2+}, Mg^{2+}, Hg^{2+} or Pb^{2+} in the solution does not interfere with the spectrofluorimetric determination of Cu^{2+}.

Since addition of Ni^{2+}, Cd^{2+}, Fe^{2+}, Ag^+, Zn^{2+}, Ca^{2+}, Mg^{2+}, Hg^{2+}, or Pb^{2+} ions does not cause changes in either the absorption or emission spectra of NI-DPA [Figure S4(*a*),(*b*)], it can be concluded that, most likely, these metal cations (except Cu^{2+}) are not coordinated with NI-DPA. Note that examples of chemo-

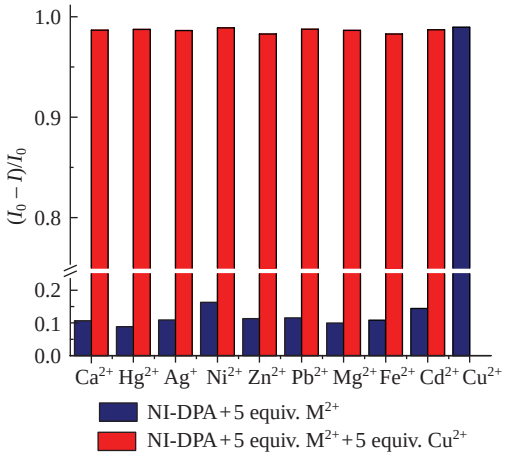


Figure 2 Variation in the fluorescence signal in the 700 nm region of the NI-DPA compound (2×10^{-5} mol dm^{-3}) in Tris-HCl, pH 7.0, in the presence of metal cations. The excitation wavelength is 435 nm.

sensors in which the dipicolylamine (DPA) receptor acts as a complexon for Zn^{2+} cations were reported in literature,[32,36,38,45] so the ^{1}H NMR spectra of the NI-DPA sensor in the presence of 5 equiv. of Zn^{2+} were additionally recorded (Figure S5). It was found that the presence of zinc ions did not cause changes in the chemical shifts of the proton signals of the NI-DPA sensor, indicating the absence of coordination with zinc ions.

To conclude, a new derivative of 1,8-naphthalimide, NI-DPA, containing a dipicolylamine moiety within the styryl substituent at position 4 of the naphthalimide core was synthesized. The resulting NI-DPA compound exhibited the properties of a selective fluorescent sensor for copper cation in Tris-HCl buffer solution, with a detection limit of 2.3×10^{-6} mol dm^{-3}. The observed blue shift of the NI-DPA absorption band in the presence of copper(II) ions is due to a decrease in the efficiency of the charge transfer process in the sensor molecule upon coordination of the receptor moiety with Cu^{2+} ions. Complexing of NI-DPA with copper(II) ions results in fluorescence quenching of the sensor due to the paramagnetic nature of Cu^{2+} ions.

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Online Supplementary Materials

Supplementary data associated with this article can be found in the online version at doi: 10.1016/j.mencom.2024.04.008.

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