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A simple quinoxaline-based highly sensitive colorimetric and ratiometric sensor, selective for nickel and effective in very high dilution

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ABSTRACT

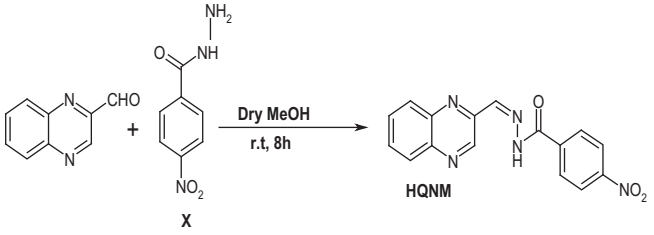
A new quinoxaline based receptor (**HQNM**) has been designed and synthesized which shows a remarkable color change from colorless to yellow on specific binding with nickel. The cation recognition property of the receptor is monitored by the UV–vis and ^{1}H NMR titrations. It is observed that the receptor shows a specific selectivity toward nickel over other interfering cations. Thus, a significant bathochromic shift in UV–vis spectrum with a sharp yellow color in 'naked-eye' makes the receptor suitable for the easy detection of nickel ion.

Cations play an important role in the field of supramolecular chemistry. In this communication, we are discussing the design and synthesis of a simple highly sensitive sensor for nickel. Nickel is used in various industrial applications for example, in Ni–Cd batteries, electroplating, rods for arc welding, pigments for paints, ceramics, surgical and dental prostheses, catalysts for hydrogenation, and as magnetic tapes of computers. Enzymes of some microorganisms and plants contain nickel as an active site, which makes the metal an essential nutrient for them. Number of methods, such as atomic absorption spectrometry (AAS), flame atomic absorption spectrometry-electro thermal atomization (AAS-ETA),[1,2] ICP-AES, and flame photometry[3] can be used for the determination of nickel. On the other hand, it is also a toxic metal and known to cause pneumonitis, asthma, and cancer of lungs and also cause disorder of respiratory and central nervous system.[4–9]

In this Letter, we report a designed Schiff's [1] base between the phenyl hydrazine compound (**X**) and quinoxaline aldehyde[10–13] and its cation binding properties were investigated by means of UV–visible, and by 'naked-eye' and ^{1}H NMR titration. The amine was synthesized between *p*-nitro benzoate ester and hydrazine hydrate in dry methanol medium under refluxing condition by the reported procedure.[14a] The target deep yellow imine receptor **HQNM** was formed in one step by the facile Schiff's base condensation reaction of quinoxaline aldehyde with the yellowish amine (**X**) in methanol medium (Scheme 1) and was produced in 80% yield after recrystallization from methanol. Its molecular structure and purity were established from different spectroscopic studies like ^{1}H NMR, LCMS, and FT-IR.

The binding behavior of receptor **(HQNM)** with different cations was studied in CH_3CN–HEPES buffer (9:1, v/v, pH 7.4) solvent. The titration was carried out in CH_3CN–HEPES buffer (9:1, v/v, pH 7.4) at 1×10^{-5} M concentration of receptor **HQNM** upon the addition of incremental amounts from 0–200 μl of nickel chloride solution (2×10^{-4} M).

The UV–visible spectrum of the receptor (**HQNM**) is characterized by two bands centered at 340 and 442 nm (Fig. 1). As shown in Figure 1, upon gradual increasing the nickel ion concentration, the band at 340 nm gradually weakens and a new band appears at 442 nm with an isosbestic point at 370 nm, indicating the



Scheme 1. Synthesis of the receptor (**HQNM**).

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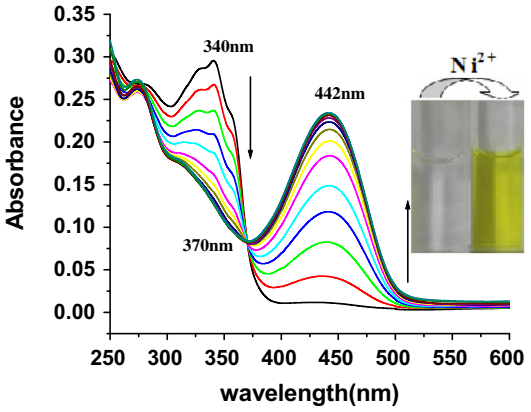


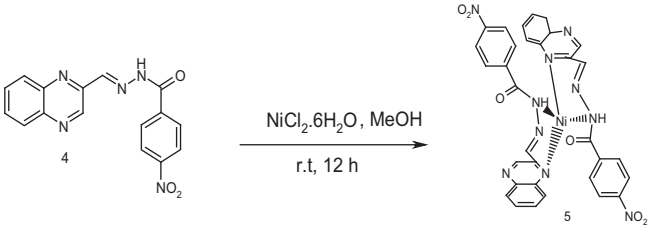
Figure 1. UV–vis absorption spectra of **HQNM** (1×10^{-5} M) in CH_3CN–HEPES buffer (9:1, v/v, pH 7.4) upon titration with nickel chloride ($NiCl_2{\cdot}6H_2O$, 0.8 equiv). The arrows show changes due to the increasing concentration of Ni^{2+}. Inset, binding isotherms were recorded at 250 and 600 nm with Ni^{2+}. The solid line is global least-squares fit to the experimental data.

formation of a new complex between the receptor (**HQNM**) and the nickel cation (Fig. 1) which is also responsible for the generation of yellow color after the addition of nickel chloride into the solution of the receptor. Figure 1 actually indicates the change of absorbance with the concentration of nickel. Furthermore the sensing ability of **HQNM** with nickel at different pH was investigated. At lower pH range, the sensor **HQNM** has no response to nickel in absorption spectroscopy due to protonation and at pH 7.4 the sensibility of the receptor **HQNM toward** nickel is maximum and at higher pH the absorbance diminishes (Supplementary data) which may be due to the fact that the receptor **HQNM** is unstable at higher pH. This indicates that the probe may be suitable for bio-applications at the physiological pH. The free probe is highly stable under the assay conditions. Since **HQNM** has an acidic hydrogen moiety, it would act as a weak acid in acetonitrile solution. The p*K*a of **HQNM** was determined by pH-dependent UV–vis spectral changes. Supplementary Fig. S2 shows plots of absorbance at 340 nm as a function of pH. This sigmoidal plot allowed us to determine the p*K*a value of **HQNM** to be 5.14.

From the UV–visible titration data it is revealed that minimum 1.47 μM of nickel can be detected by using 10 μM of receptor **HQNM** using the equation DL = K × Sb_1/S, where $K = 3$, Sb_1 is the standard deviation of the blank solution and S is the slope of the calibration curve[14b](Supplementary data).

After addition of 0.8 equiv of nickel chloride, it reaches a saturation level. Titrations were also carried out with various cations like Na^+, K^+, Cr^{2+}, Mn^{2+}, Cd^{2+}, Fe^{2+}, Fe^{3+}, Co^{2+}, Cu^{2+}, Zn^{2+} etc as their tetra butyl ammonium salts. Interestingly there is no obvious change observed in the UV spectrum except with cobalt ion, which shows slight interference (Supplementary data). There is appearance of a small new peak at 448 nm which indicates that the receptor (**HQNM**) has a slight response to cobalt ion due to the same size of ionic radius of the two cations. The cavity of **HQNM** binds selectively to nickel over cobalt possibly because of the size of the nickel cation which better fits in the core of the cavity as created by the quinoxaline moiety and the hydrazone part (Scheme 2) forming a stable six-membered ring.

Figure 2 actually shows the selectivity for nickel over the other cations as shown by the sky blue bar. The slight interference of cobalt is shown by the yellow bar but it cannot be detected by naked eye which is shown in the inset. From the experimental data, it can be concluded that the receptor **HQNM** possesses high selectivity and sensitivity toward nickel in acetonitrile-HEPES buffer (9:1, v/v, pH 7.4) medium. The other cations except cobalt had no practical



Scheme 2. Probable host-guest binding mode in solution phase.

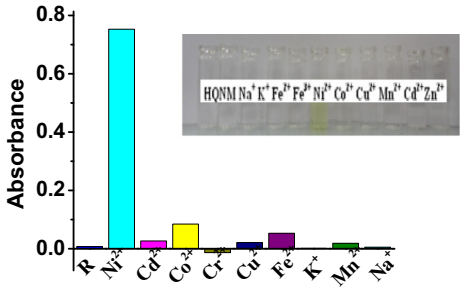


Figure 2. $(A - A_0)/A_0$ ratios of receptor **HQNM** (1×10^{-5} M) after the addition of 0.8 equiv of each of the various cations (2×10^{-4} M) in acetonitrile. Inset: color changes of receptor **HQNM** (1×10^{-5} M) upon the addition of 0.8 equiv of each of the different guest cations (2×10^{-4} M).

significant influence. The color changes are most probably due to the formation of hydrogen bonds or deprotonation of the –NH group of receptor **HQNM** on the addition of nickel ion which is shown in Scheme 2. To further explore the binding mechanism, Job's plot of the UV–vis titrations of Ni^{2+} ion with a total volume of 2 ml was revealed. A maximum absorption was observed when the molar fraction reached 0.67, which is indicative of a 2:1 stoichiometric complexation between **HQNM** and Ni^{2+} ion for the newly formed species. The ESI mass spectrum of a mixture of **HQNM** and $NiCl_2.6H_2O$ also revealed the formation of a 2:1 ligand–metal complex through the metal coordination interaction, with a major signal at $m/z = 700.0$.[possibly for $(2\,M+Ni)^+$ ions]. From the IR data the phenomenon is also well explained by the decreasing broadness of the –NH peak at 3372 cm^{-1} due to the insertion of nickel metal in **HQNM** (Supplementary data).

These hydrogen bonds or de-protonations affect the electronic properties of the chromophore which results in a change of color from colorless to yellow along with a new charge-transfer interaction between the nickel bound –NH moieties and the electron deficient nitro group.[15,16] Furthermore, the strong hydrogen-bonding interaction between receptor **HQNM** and nickel could enhance π

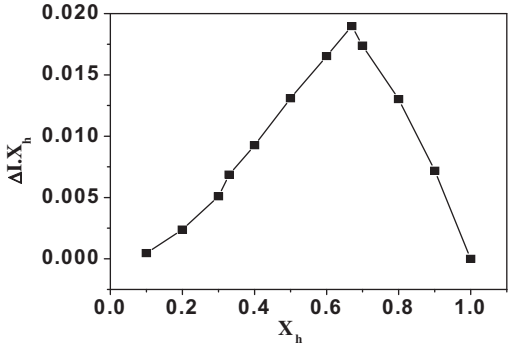


Figure 3. Job's plot diagram of receptor **HQNM** for Ni^{2+} (where Xh is the mole fraction of host and Δ*I* indicates the change of the absorbance).

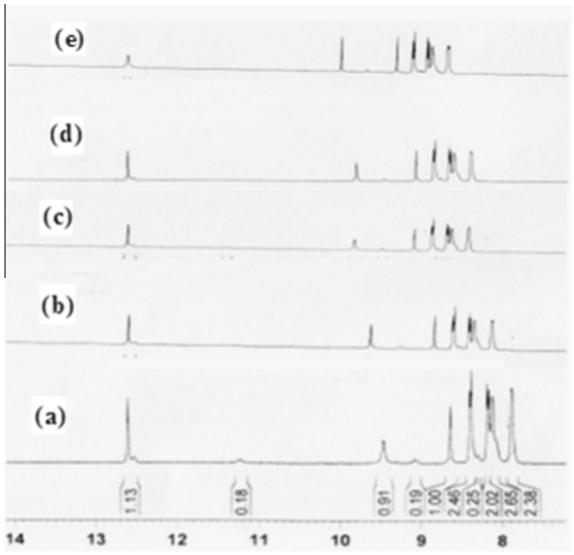


Figure 4. Partial ^{1}H NMR spectra (400 MHz) of **HQNM** in DMSO-d_6 at 25 °C and corresponding changes after the gradual addition of different equivalents of nickel chloride from .(a) **HQNM** (b) **HQNM**+0.2 equiv Ni^{2+} (c) **HQNM**+0.5 equiv Ni^{2+} (d) **HQNM**+0.8 equiv Ni^{2+} (e) **HQNM**+1.0 equiv Ni^{2+}.

delocalization, which was expected to reduce the energy of the π–π^* transition and therefore accounts for the appearance of a new absorption band near 442 nm resulting in the formation of a yellow color.[17] A well-defined isosbestic point at 370 nm emerged during the spectral titrations, which indicated the formation of the stable complex with a certain stoichiometric ratio between the receptor and the cation resulting in a new ICT (internal charge transfer) band that appeared at 442 nm. The 2:1 stoichiometry for the host–guest complexation was elaborated by the profile of the intensities of the decreasing band centered at 340 nm and increasing band at 442 nm which was also confirmed by Job's plot analysis (Fig. 3). The binding constant of **HQNM** with nickel is found to be 2.5×10^5 M^{-1} (Supplementary data). [18]

At the same time, due to complexation process, the –NH (H_b) proton of hydrazide undergoes an upfield shift from δ 12.6210 ppm to δ 12.6147 ppm because the cationic species induces an upfield chemical shift through diamagnetic shielding. Again noticeable up-field chemical shifts are also shown in the case of protons of quinoxaline –3CH of receptor **HQNM** from δ 9.4809 ppm to δ 9.4749 ppm because of the complexation with nickel cation after addition of 0.8 equiv of nickel (Fig. 4)

From NMR study, we have investigated the molecular interaction between the receptor **HQNM** and a nickel ion. The peak at slightly downfield (δ 12.6210 ppm) probably belongs to –NH of hydrazone which decreased after addition of 0.5 equiv of nickel ion indicating that there is a new complex formation (2:1) between the –NH group of hydrazone moiety and nickel ion (Scheme 2).

The selectivity of the receptor may be due to enhanced acidity of the amide NH_b of hydrazone. The selectivity here is greatly influenced based on charge-charge interactions, and the involvement of both N–H. . ..Ni bonds. The unique binding motif can find a greater utility in the development of new cation receptors/sensors with enhanced binding affinity and substrate specificity, which is actively being investigated.

In conclusion, herein we report a new receptor which selectively recognizes nickel cation over other interfering cations in CH_3CN–HEPES buffer (9:1, v/v, pH 7.4) solution. Its bold color changes only after addition of nickel ion makes it an excellent sensor for detecting nickel cation by 'naked-eye'.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.tetlet.2013.07.051.

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