



## Synthesis of a new heterocyclic dye compound as an indicator in acid and base reactions

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In the present research, the use of 2-(3-hydroxyamino-2,3-dihydroimidazo[1,2-*a*]pyridine-2-ylidene)-2-(2-thienyl)acetonitrile as a new acid and base indicator in aquatic environments has been investigated. This compound has been synthesized by the reaction of 3-nitroimidazo [1,2-*a*] pyridine and 2-(2-thienyl) acetonitrile in a methanol solution by the hydrogen nucleophilic substitution. The aqueous-ethanol solution of this compound shows a change in color by adding acid and an base. For the potential function of this reagent as an indicator, the spectral properties of UV-Vis and the equilibrium of acid and base source have been examined. The results show that the reagent is an amphoteric with two stable ionization factors  $K_a$  and  $K_b$  with poor acid and base properties. Indicator dissociation constants in aqueous solutions specified by spectrophotometric method are  $pK_a = 9.73$  and  $pK_b = 11.57$ . The types of base that can be titrated with this index have been reported. This index has been compared with effective acid and base indexes with similar pH range.

**Keywords:** 3-Nitroimidazo [1,2-*a*] pyridine, nucleophilic substitution of hydrogen, indicator, spectroscopy

At present, in spite of the available techniques for analyzing various chemical samples, common analytical methods are still considerable. Titration is one of the most common analytical techniques that are still known. In the titration (volumetric), the balance point is often specified by the endpoint. In the titration, the endpoint is usually determined by indicators well showing distinct color changes at certain pH intervals. There are different types of detectors available for the titration method. Organic colors that are weak acids and bases are used as indicators for acid and base titration. imidazo 1,2-*a* pyridines are an important category of heterocyclic compounds with antiviral, antifungal, anti-parasitic, anti-cancer, anti-anxiety, anti-malarial, anti-proliferation, anti-inflammatory and anti-infectious agents as well as digestive diseases<sup>1-5</sup>.

Given this study and the continued studies on the synthesis of new organic dyes<sup>6-10</sup>, in this research work, a new heterocyclic violet dye called 2-(3-hydroxyimino-2,3-dihydroimidazo[1,2-*a*]pyridine-2-ylidene)-2-(2-thienyl)acetonitrile has been synthesized by reacting 3-nitroimidazo[1,2-*a*]pyridine and 2-(2-thienyl)acetonitrile in methanol solution with hydrogen nucleophilic substitution and its use as a

new acid and base indicator in the aqueous environment has been reported.

### Results and Discussion

In order to prepare the new compound that is expected to have dye properties according to past researched<sup>6-10</sup>, the synthesis of imidazo[1 and 2-*a*] pyridine is prepared from the 2-amino pyridine reaction with (2-bromo-1-oxo-ethoxy) ethane in the base environment, methanol solvent and reflux conditions. A mixture of 3-nitro-imidazo[1,2-*a*]pyridine is produced from nitrating the resulting compound in sulfuric acid and concentrated nitric acid. Then, in the next step, the reaction of this compound with 2-thionyl-acetonitrile, a mixture of (3-hydroxyamino-2 and 3-dihydroimidazo[1 and 2-*a*]pyridine-2-ylidene)-2-(H2-2-tinyl)acetonitrile is synthesized (Figure 1). In the <sup>1</sup>H NMR spectrum of this compound, a triplet peak with a fission constant of  $J = 6.8$  Hz with an equivalent subpeak of two hydrogen in the 6.6 ppm area of the aromatic imidazo pyridine, a multiple peak with the hydrogen atoms of aromatic ring in the  $\delta$  7.10 to 7.13 ppm area with an equivalent subpeak with two hydrogen, a dual peak with a fission constant of  $J = 2.8$  Hz with an

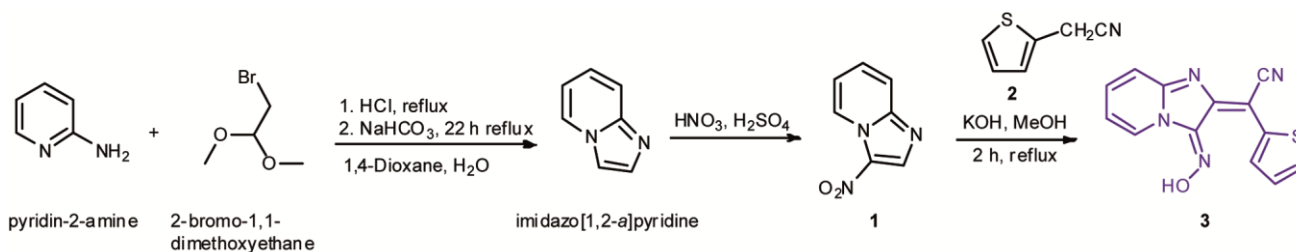


Figure 1 — Preparation of dye compound 3

equivalent subpeak with a hydrogen in the 7.3 ppm area of hydrogen atoms of thiophene aromatic ring, a multiple peak from the range of 7.5 to 7.6 ppm area with an equivalent subpeak with two hydrogen atoms corresponding to the aromatic ring and a dual peak with a fission constant of  $J = 6.8$  Hz with an equivalent subpeak with one hydrogen atom in the 9.01 ppm area corresponding to the hydrogen atoms of thiophene aromatic ring are seen.

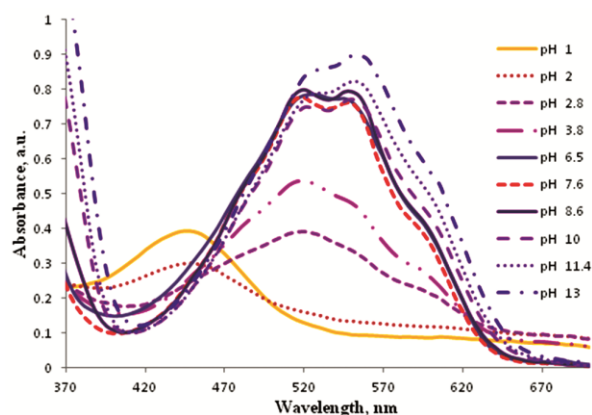
Given the structure of this compound that can be considered as a weak acidic or organic base, it can be utilized as a reagent for acid-base titrations.

To investigate the impact of  $pH$  on the visible absorption of the indicator, an aqueous-ethanol solution was prepared from dye 3. Figure 2 shows this impact on the indicators absorption in the visible spectrum. As observed in Figure 2, the visible spectrum of the reagent significantly varies with decreasing and increasing the solution's  $pH$ . Due to the amphoteric nature of dye 3, the equilibriums indicated in Figure 3 can be considered. From Figure 3, it can be deduced that the cationic form of yellow color is at  $\lambda_{\text{abs}} = 450$  nm at a low  $pH$  ( $pH$  2 and lower) and the anionic form of blue color is at  $\lambda_{\text{abs}} = 550$  nm at a high  $pH$  ( $pH$  11.2 and Higher); and the neutral form of purple color is at  $\lambda_{\text{abs}} = 520$  nm.

Generally, the reason for this phenomenon is attributed to the changes occurred in the composition of the compound. The absorption of the compound 3 increases after elimination of hydrogen from the hydroxyl group, which is due to the creation of a stronger electron donor group in the base environment; thus, in comparison with neutral molecules, it needs less energy for excitation and absorption at higher wavelengths.

On the other hand, protonation of nitrogen in the 5-membered rings in the acidic environment results in the decreased number of resonance structures, and consequently, water displacement.

Dissociation constant of dye 3 was measured by spectrophotometric method that was described in detail in the experimental part.

Figure 2 — The effect of  $pH$  on the absorption of the indicator's UV-Vis spectrum

Since the yellow color change ( $pH$  2) to purple ( $pH$  2.8) is considered to be much easier than that from purple to blue ( $pH$  13), the appropriate color change range for the compound 3 is  $pH$  2.0-2.8. Considering these ranges, it can be deduced that dye 3 is more useful for titration of strong acids with weak bases.

To prove the efficacy of this compound, this indicator should be compared with other reagents used in this approximate  $pH$  range.

Table I summarizes the results of the present study. Obviously, in most cases, indicator 3 is stronger than malachite green and methyl green. The freshly prepared solution of compound 3 have remained stable for 3 months and no signs of color change have been observed in its indicator's properties during this period.

### Experimental Section

The melting point was recorded by the IA9100 electrothermal melting point apparatus. The  $^1\text{H}$  NMR spectrum was captured by the DRX-400 FT spectrometer at the frequency of 400 MHz using a DMSO solvent. Chemical displacements of  $^1\text{H}$  NMR were measured by tetramethylsilane (TMS) as the internal standard. The absorption spectrum was recorded on the Varian Cary 50-bio UV-Vis

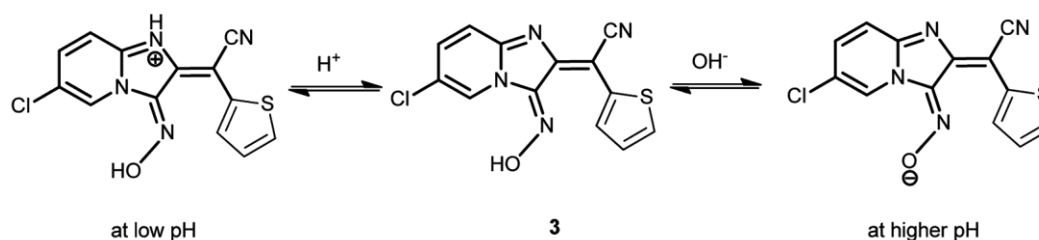


Figure 3 — Dye equilibriums at different pH values

Table I — Comparison of the efficiency of the detector **3** with other well-known reagents in the same due variation range.

Indicator	pH range	Titrated base	Solvent	Endpoint status
Quinaldine Red	1.4–3.2	aniline	Water-EtOH	Poor
		aniline	MeOH	Excellent
		NaHCO <sub>3</sub>	Water-EtOH	Good
		NaHCO <sub>3</sub>	MeOH	Good
Orange IV	1.4–2.8	aniline	Water-EtOH	Excellent
		aniline	MeOH	Excellent
		NaHCO <sub>3</sub>	Water-EtOH	Excellent
		NaHCO <sub>3</sub>	MeOH	Excellent
Malachite Green	0.2–1.8	aniline	Water-EtOH	Poor
		aniline	MeOH	Good
		NaHCO <sub>3</sub>	Water-EtOH	Poor
		NaHCO <sub>3</sub>	MeOH	Good
Methyl Green	0.2–1.8	aniline	Water-EtOH	Poor
		aniline	MeOH	Good
		NaHCO <sub>3</sub>	Water-EtOH	Good
		NaHCO <sub>3</sub>	MeOH	Good
<b>3</b>	2.0–2.8	aniline	Water-EtOH	Good
		aniline	MeOH	Excellent
		NaHCO <sub>3</sub>	Water-EtOH	Good
		NaHCO <sub>3</sub>	MeOH	Excellent

spectrum. The visible wavelength was recorded in the range of 300 to 700 nm. Beckman pH meter was utilized to measure pH in aqueous systems. All measurements were carried out at room temperature. Compound No. 1 was prepared based on the published methods<sup>11</sup>. Other indicators were commercially available.

### Synthesis of 2-(3-Hydroxyimino-2,3-dihydroimidazo[1,2-*a*]pyridine-2-ylidene)-2-(2-thienyl)acetonitrile (**3**).

In a 100 mL balloon, compounds of 3-nitroimidazo[1,2-*a*]pyridine (0.815 g, 5 mmol) and 2-(2-thienyl)acetonitrile (0.861 g, 7 mmol) were added to a solution of potassium hydroxide (10 g, 180 mmol) in methanol solvent (50 mL) with stirring and then the mixture was refluxed for three hours. At the next stage, the contents of the balloon were poured into the water and following neutralization with dilute

HCl solution, the sediments collected by the Buchner funnel and were washed with water, ethanol and acetone, respectively, and dried in the open air to finally achieve the compound **3** in pure form. The melting point of this compound is 185–187°C and the reaction efficiency is 90%.

### Spectral Specification of Compound No. 3.

<sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 6.37 (1H, td, *J*<sub>1</sub>=7.2 Hz, *J*<sub>2</sub>=1.2 Hz), 7.04–7.09 (2H, m), 7.35 (1H, td, *J*<sub>1</sub>=5.2 Hz, *J*<sub>2</sub>=1.6 Hz), 7.42 (1H, dd, *J*<sub>1</sub>=4.8 Hz, *J*<sub>2</sub>=0.8 Hz), 7.55 (1H, d, *J*=5.2 Hz), 8.91 (1H, d, *J*=7.2 Hz), 9.75 (1H, br s).

### Determination of Dissociation Constant Spectrophotometry

Dissociation constant of dye **3** was described by spectrophotometry and standard methods were determined by Patterson<sup>12</sup>.

The equation used to determine *pK<sub>a</sub>* is as follows:

$$(1) \quad pK_a = pH + \log_{10} [(A - A_{In}) / (A_{HIn} - A)]$$

A: Absorption from a solution containing a specific concentration in the acid-base mixture

A<sub>In</sub>: Absorption from base at the same concentration

A<sub>HIn</sub>: Absorption from acid at the same concentration

In this method, a set of pH and absorption values are substituted in equation (1) and *pK<sub>a</sub>* is calculated for each set. The reported *pK<sub>a</sub>* is equal to the mean *pK<sub>a</sub>* calculated.

Alcohol-aqueous solutions of **3** were prepared at the concentration of 10<sup>-5</sup> mol L<sup>-1</sup> using phyrion buffer capsules at various pHs and the absorption from the solution was measured in a spectrophotometer of 300–700 nm. Since this substance is amphoteric, two analytical wavelengths of 450 nm (pH 2) and 520 nm (pH 2.8) are used to measure *pK<sub>a</sub>*. The reason for choosing the abovementioned wavelengths is the bright dye variation of the species at these wavelengths. The absorbance of the obtained solution was then

measured at  $pH$  2 and 2.8 in order to determine  $A_{H2In} +$  and  $A_{HIn}$  and the  $pK_a$  stage was calculated. The dissociation of the reagent in the aqueous solution is 2.43.

### Conclusions

Based on the results, it can be concluded that the dye **3** can be used as an acid and base indicator. To this end, the impact of  $pH$  on UV-Vis absorptions of the indicator was examined and the results revealed that the compound **3** has three forms and dyes at different  $pH$ . Index's dissociation constant in aqueous solution was specified by spectrophotometric method. The best range of dye variation of compound **3** is between  $pH$  2 (yellow) and  $pH$  2.8 (purple). This indicator was compared with other indicators used in this approximate range, and the results indicated that in most cases, the dye **3** is more effective than malachite green and methyl green.

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