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Photoinduced electron transfer in \(N,N\)-bis(pyridylmethyl)naphthalenediimides: study of their potential as pH chemosensors

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**ABSTRACT**

The change in fluorescent properties of a series of \(N,N\)-bis(pyridylmethyl)naphthalenediimides (BIPy-NDIs) as function of pH were investigated. The naphthalenediimide dyes displayed OFF–ON pH sensing properties owing to photoinduced electron transfer in the pH range from 1.7 to 4.1. The fluorescence enhancement of the chemosensors studied is based on the hindering of photoinduced energy-electron transfer (PET) from pyridine ring to the naphthalene fluorophore by protonation. Moreover, using density functional theory theoretical calculations of molecular orbitals, it was verified that protonation nitrogen atom in pyridine ring inhibits the PET process. The best selective response for monitoring pH in the presence of different metal ions, was exhibited by BIPy-NDI 1\(^B\). In addition, 1\(^B\) was applied for determination of pH in real samples of commercial vinegars. The results were consistent with those obtained by glass electrode method, indicating that the new probe could be a practical pH indicator in strongly acidic conditions.

**INTRODUCTION**

Naphthalenediimides (NDIs) are a class of compounds that have become increasingly important in the last decade, with a series of applications ranging from the biomedical to material science due to their outstanding photo- and electrochemical properties (1). NDIs are excellent materials for studying electro- or photoinduced electron transfer reactions and can be incorporated into larger multi-component assemblies such as field effect transistors, biological models and supramolecular devices (2). They are excellent electron acceptors in aqueous solution and ideal for the design of synthetic derivatives that can be used as structural probes and therapeutic agents in molecular biology and chemotherapy (3–5). NDIs have been used to reduce and oxidise proteins (6–8) and DNA (9–11). Most studies in aqueous solution involve the binding to nucleic acids and many of these derivatives are used as DNA intercalators (7–11). They also show biological applications rely mainly on their pharmacological activity as local anesthetics (12, 13), tumoricidal (14, 15) and antiviral (16–18).

Photophysical characterisation of NDIs is limited to a few derivatives mainly due to their low solubility in aqueous media. However, Içli and co-workers (19) reported the photoinduced energy-electron transfer (PET) in NDIs and demonstrated that electron donor groups in the \(N\)-substituent of the NDI quench the fluorescence emission.
Otherwise, the measurement of pH is very important in biological, chemical and industrial fields. The most commonly approach used for measuring pH, relies on the electrochemical method which has various drawbacks such as electrode failures, low sensitivity and ambiguity in the causes of the impedance change (20). In recent years, the optical pH sensing technique based on the absorption or emission of certain organic compounds with structural diversity, has received increasing attention because it offers many advantages over the potentiometric method, such as rapid response time and without the requisite reference electrode (21–24). Many approaches have been developed for constructing optical pH sensors, in particular fluorescent pH sensors and switches based in PET has attracted much research effort due to their obvious advantages of higher sensitivity and selectivity (25, 26). Most of them operate in the range of pH 5–9, but there are few optical probes sensitive in the low pH interval (pH < 3) (24, 27–33). Such low pH-sensitive sensor may be useful for determining the pH in strongly acidic media as in human stomach (pH = 1.0 to 3.0) or wastewaters derived from specific processes (pH = 0.8) where the use of pH glass electrode is not appropriated (34, 35). Previously, has been reported the effect of pH over the fluorescence intensity of NDIs bearing alkyl amino and morphine groups as substituents in the imide (36). There is an important enhancement of NDI fluorescence as the pH decreases from 8.9 to 4.6, due to the suppression of PET occurring from the alkyl amino to the NDI core. Recently, fluorescent H+ chemosensors based on core-substituted NDIs (cNDIs) with N-benzyl and N-methylpiperazine have been reported (37, 38). Both compounds present an emission band at 620 nm, which grows as the amount of H+ is increased, inhibiting the PET process by protonation of the N-alkyl nitrogen atom. The N-benzyl analogue was evaluated only in chloroform with trifluoroacetic acid, because its poor solubility in water, which is an important disadvantage, whereas the N-methyl analogue was evaluated in aqueous media as pH hybrid fluorescent nanoprobe for real-time cell labelling and endocytosis tracking in a range of pH of 3.4 to 8.4 (39). In order to improve the water solubility and enhance the application of NDIs as intracellular pH (40) and functional cell imaging sensors (41), different polar and ionisable groups were introduced in the NDI core and in the imide group. These cNDIs present the advantage of having absorption and emission bands in the visible region (42). Recently has been reported the incorporation of N-methylpiperazyl cNDI in a novel hydrophilic fluorescent copolymer as pH sensor film into a high throughput microbioreactor with a linear response in the pH range of 4.6–8.0 (43).

Adachi et al. developed a pH-responsive fluorescent chemical sensor constituted by conjugated polymers containing pyridine rings as H+ receptors (44). Addition of HCl decreased and red-shifted the fluorescence intensity of poly(p-pyridiniumphenylene ethynylene) (PPyPE) due to contained pyridines protonation. On the contrary, fluorescence intensity of the polymers increased upon addition of NaOH solution. The synthesised PPyPE was found to be an effective and reusable chemical sensor for pH sensing.

Following our interest in pH chemosensors based on naphthalimide fluorophores (45), we proposed a pH chemosensor where the NDI fluorescence would be affected by the interaction of pyridine receptor with H+. As well known, NDI is electron deficient and pyridine is an electron rich group; therefore, a suppression of PET process from the pyridine to NDI in the presence of H+ would enhance the fluorescence. In this paper, we present results regarding to the study of the influence of H+ over the fluorescence intensity of BIPy-NDIs and their potential as fluorescent pH chemosensors in a low pH range.

**Experimental**

**General**

All reagents purchased were of the highest quality available and were used without further purification. All the organic solvents that were used (dimethylformamide (DMF) and acetonitrile) were spectroscopic or HPLC grade. Infrared spectra (FTIR) were measured on a Perkin Elmer FT-IR 1600 spectrophotometer. FAB mass spectra and HRMS were recorded in a MStation JMS-700 JEOL. Electronic impact mass spectra were obtained by direct insertion in an Agilent 5975C mass spectrometer, and the intensities were reported as a relative percentage to the base peak after the corresponding m/z value. Nuclear magnetic resonance 1H (at 200 MHz) and 13C (at 50 MHz) spectra were recorded on a Varian Mercury 200 MHz Spectrometer in DMSO-d6 with TMS as internal standard.

**Spectroscopic measurements**

Fluorescence spectra were measured on a RF-5301PC Shimadzu spectrofluorimeter. The measurements were done at room temperature in 1-cm quartz cuvettes. The effect of metal ions on fluorescence intensity was examined by successive additions of few microlitres (total volume <90 µL) of ion stock solution to be tested to 3 mL of BIPy-NDI, following an established procedure (46). Sample solutions for studying the pH dependence of the emission spectra were prepared adjusting at the desired pH, with solutions of 0.001 M NaOH and 0.001 M HCl. Fluorescence quantum yields were measured using anthracene in toluene as a standard with a known quantum yield of 0.30. Emission intensities were normalised against the most intense band of the corresponding free ligand.
General procedure for the synthesis of NDIs

N,N’-bis(benzyl)naphthalenediimide and N,N’-bis(pyridyl methyl)naphthalenediimide were prepared in a 100-mL round bottom flask. 5 eq (0.398 g) of the amine and 5 eq (0.376 g) triethylamine were dissolved in 20-mL DMF. To this solution, 200 mg of 1,4,5,8-naphthalenetetracarboxylic acid dianhydride (NAD) were added under constant stirring. The solution was kept at 70 °C for 2 h, hot water was added and the solid separated by filtration.

N,N’-bis(benzyl)naphthalenediimide (1A). Brown solid. 333 mg, >99% yield. mp 236–238 °C. IR (KBr): 3424, 3065, 2970, 1706, 1665, 1181, 1075 cm⁻¹. ¹H NMR (DMSO-d₆, 200 MHz): δ 8.76 (s, 4H), 7.29 (m, 10H Ar), 5.38 (s, 4H). ¹³C NMR (DMSO-d₆, 50 MHz): δ 162.8, 136.5, 131.2, 129.2, 128.6, 127.9, 126.7, 44.0. MS m/z: 446.2 (M⁺, 100), 340.1 (35), 312.1 (25), 91.1 (40). HrMS (cI⁺): calculated for C₂₈H₁₉N₂O₄ [M + H]⁺, m/z = 447.1341, found for [M + H]⁺, m/z 447.1320.

N,N’-bis(4-pyridylmethyl)naphthalenediimide (1B). Gold solid. 212 mg, 64% yield. mp 316–318 °C. IR (KBr): 3038, 2953, 1699, 1650, 1240, 1090 cm⁻¹. ¹H NMR (D₂O-DCl, 200 MHz): δ 8.75 (d, J = 5.8 Hz, 4H), 8.66 (s, 4H), 8.09 (d, J = 5.8 Hz, 4H), 5.62 (s, 4H). ¹³C NMR (D₂O-DCl, 50 MHz): δ 166.5, 160.2, 144.0, 134.3, 133.7, 129.0, 128.8, 128.7, 46.1. MS (EI) m/z: 448.2 (M⁺, 100), 313.1 (50), 288.1 (20). HRMS (FAB⁺): calculated for C₂₆H₁₇N₄O₄ [M + H]⁺, m/z = 449.1250, found for [M + H]⁺, m/z 449.1211.

N,N’-bis(3-pyridylmethyl)naphthalenediimide (1C). Pink solid. 311 mg, 93.1% yield. mp 310–312 °C. IR (KBr): 3039, 2958, 1696, 1650, 1243, 1099 cm⁻¹. ¹H NMR (DMSO-d₆, 400 MHz): δ 8.95 (s, 2H), 8.72 (d, J = 6.6 Hz, 4H), 8.36 (s, 4H), 8.05 (t, J = 7.2 Hz, 2H), 5.44 (s, 4H). ¹³C NMR (D₂O-DCl, 50 MHz): δ 166.0, 150.4, 144.4, 143.2, 138.9, 134.1, 133.4, 130.4, 129.6, 128.3, 43.3. MS (EI) m/z: 448.2 (M⁺, 100), 313.1 (50), 288.1 (20), 152.1 (20). HRMS (FAB⁺): calculated for C₂₆H₁₇N₄O₄ [M + H]⁺, m/z = 449.1250, found for [M + H]⁺, m/z 449.1211.

N,N’-bis(2-pyridylmethyl)naphthalenediimide (1D). Pink solid. 315 mg, 94.3% yield. mp 318–320 °C. IR (KBr): 3082, 2996, 1704, 1664, 1245, 1001 cm⁻¹. ¹H NMR (DMSO-d₆, 400 MHz): δ 8.72 (s, 4H), 8.41 (dd, J = 5.0, 1.8, 0.9 Hz, 2H), 7.76 (t, J = 7.8, 1.8 Hz, 2H), 7.47 (d, J = 7.8 Hz, 2H), 7.25 (dd, J = 7.4, 5.0, 0.8 Hz, 2H), 5.42 (s, 4H). MS (EI) m/z: 448.2 (M⁺, 100), 403.2 (60), 269.1 (10), 241.1 (10), 152.1 (20). HRMS (FAB⁺): calculated for C₂₆H₁₇N₄O₄ [M + H]⁺, m/z = 449.1250, found for [M + H]⁺, m/z 449.1211.

Results and discussion

The synthesis of NDIs 1A-1D was readily achieved by the methodology outline in Figure 1. The synthetic procedure involves the opening and cyclisation reaction of NAD with benzylamine (A), 4-(aminomethyl) pyridine (B), 3-(aminomethyl) pyridine (C), and 2-(aminomethyl) pyridine (D) at 70 °C using DMF as solvent.

The fluorescence spectra of 1(A–D) derivatives were performed in order to evaluate how the position of pyridine group influences on the fluorescence characteristics of the synthesised materials (Figure 2). As can be observed compounds 1B-1D presented typical structured bands and the same excitation and emission maximum wavelengths (λₑₓ = 376 nm, λₑₘ = 395 nm) at 1 × 10⁻⁵ M solutions with Stokes shifts of 7, 22, and 18 nm, respectively. Compound 1B has the pyridine nitrogen in the para position showed an increase in fluorescence intensity. It was found that

![Figure 1. Synthesis of NDIs from NAD and primary amines.](image-url)

![Figure 2. Fluorescence spectra of NDIs 1A-1D at 1 × 10⁻⁵ M in H₂O.](image-url)
the fluorescence intensity depends on the electronic factor, since there was an increase in fluorescence intensity by an order versus the relative position of the pyridine nitrogen (para or ortho). Compound 1A showed non-typical spectral properties compared to other NDIs, with a decrease in fluorescence intensity and a shift of the excitation and emission bands to longer wavelengths (\(\lambda_{\text{exc}} = 393\) nm, \(\lambda_{\text{em}} = 483\) nm), which may be attributed to the formation of an intermolecular excimer. It was reported that in certain solvents the NDIs present emission bands of this type \(47\). The shift of the excitation and emission bands as well as a decrease in fluorescence intensity in the compound 1A is characteristic of an intermolecular excimer of NDI.

The fluorescence efficiency of the BIPy–NDIs was estimated by measuring the fluorescent quantum yield \(\Phi_F\) using Equation (1).

\[
\Phi = \frac{\Phi_R \times \text{Int} A_R n^2 / \text{Int}_R A^2_R}{1 + \text{Int} A_R n^2 / \text{Int}_R A^2_R}
\]  

Where \(\Phi\) is the quantum yield, \(\text{Int}\) is the area under the emission peak, \(A\) is absorbance at the excitation wavelength, and \(n\) is the refractive index of the sample. The subscript \(R\) denotes the respective values of the reference substance. The quantum yields are presented in Table 1 for NDIs measured in acetonitrile and in aqueous solution (pH = 1.7).

**Influence of protons on the fluorescence intensity of the NDIs**

The influence of pH over the electronic absorption and fluorescent response of BIPy-NDIs have been investigated. The experiments were done in a low pH range due to these compounds are soluble in acid media because of the protonation of pyridine nitrogen atoms. The pH dependence of absorbance and fluorescence has been analysed using the experimental data and the absorbance and fluorescence has been analysed using the equation to calculate the \(pK_a\) values and absorbance profiles indicate the protonation in the pyridine ring, the \(pK_{ai}\) values were determined due to the double protonation of the molecules in the pyridine ring, the \(pK_{ai}\) values are located at very low pH (0.55, 0.65, and 0.85) and the \(pK_{ai}\) values associated to the monoprotonated molecules are 2.90, 3.15, and 2.06, respectively. The absorbance profiles obtained by electronic absorption do not allow to calculate the \(pK_{ai}\) values, but only \(pK_{ai}\) values were determine and correlate well with those obtained by emission of fluorescence. Noteworthy, both absorbance and emission pH profiles followed a similar tendency (see Figure S8).

As was described above, the absorbance of NDI chromophore was dependent of pH, although the calculated \(pK_a\) values and absorbance profiles indicate the protonation in the pyridine unit (see Figure S9). Similar results with 1,8-napthalimide derivatives containing pending ionisable amino groups have been reported \(49, 50\). These reports conclude that some ground-state interaction takes place between the fluorophore and their respective terminal amines. Based on the later, it is able to propose the possible interaction of pyridine units with the NDI core in the ground-state and as the pyridine units protonates the spectral properties of NDIs are affected.

As shown in Figure 3 the fluorescence of these molecules is highly sensitive to pH changes. It can be observed that the fluorescence was quenched with increasing pH, and the fluorescence increases, as the pyridine is protonated.

**Table 1.** Fluorescence quantum yields (\(\Phi_F\)) of BIPy-NDIs in \(\text{CH}_3\text{CN}\) and \(\text{H}_2\text{O}\) (pH = 1.7).

<table>
<thead>
<tr>
<th>Compound</th>
<th>CH(_3)CN</th>
<th>H(_2)O</th>
</tr>
</thead>
<tbody>
<tr>
<td>1A</td>
<td>365</td>
<td>390</td>
</tr>
<tr>
<td>1B</td>
<td>377</td>
<td>384</td>
</tr>
<tr>
<td>1C</td>
<td>376</td>
<td>402</td>
</tr>
<tr>
<td>1D</td>
<td>377</td>
<td>403</td>
</tr>
</tbody>
</table>

**Table 2.** \(pK_a\) values calculated for BIPy-NDIs 1(B-D).

<table>
<thead>
<tr>
<th>Compound</th>
<th>UV-vis</th>
<th>Fluorescence</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(pK_{ai})</td>
<td>(pK_{ai})</td>
</tr>
<tr>
<td>1B</td>
<td>3.25 ± 0.07</td>
<td>0.55 ± 0.02</td>
</tr>
<tr>
<td>1C</td>
<td>3.26 ± 0.13</td>
<td>0.65 ± 0.03</td>
</tr>
<tr>
<td>1D</td>
<td>2.33 ± 0.09</td>
<td>0.85 ± 0.04</td>
</tr>
</tbody>
</table>
or the monoprotonated species and are independent of the $pK_a$ value due to the double protonation occurs at a pH lower than these intervals.

The reversibility of the emission pH dependence was investigated by a continuous titration of 1B from acid to base and base to acid, respectively (see Figure S10). The emission intensity in acid media (pH = 1.70) gradually decreased as the 1.0 M NaOH solution aliquots were added. On the contrary, in the titration of a 1B basic solution (pH = 4.37) with a 2.0-M HCl solution the emission intensity increased as the aliquots were added. With these results the reversibility of the fluorescent response to pH was demonstrated.

**Sensor response mechanism**

BIPy-NDIs are subjected to PET processes from the pyridine nitrogen to naphthalene. As the pH becomes lower, it increases the protonation of the pyridine nitrogen inhibiting the PET process (Figure 4).

In order to shed light on the process PET in BIPy-NDIs, optimisation of the molecular geometry of the BIPy-NDI 1B was generated first with the PM6 semiempirical method and then using the density functional theory (DFT) and the nonlocal correlation B3LYP with a 6–31 + G(d,p) basis set in the gas-phase (52). Figure 5 shows the fluorophore...
usually, the electron deficient protonated pyridine causes a PET process acting as an acceptor from an excited state of a fluorophore, and an ON–OFF fluorescent response is observed \((53)\). Nevertheless, in BIPy-NDIs the fluorophore is even more electron deficient than pyridinium unit and the pyridine electron pair acts as a PET donor and NDI as an acceptor.

**Interference of metal ions on the fluorescence intensity of BIPy-NDIs**

As pyridine moieties act as receptor sites for protons in BIPy-NDIs and the ability of pyridines to coordinate with metal ions is well known, it resulted of particular interest to investigate their interference on the fluorescent properties in order to establish the potential of BIPy-NDIs as pH chemosensors. The spectral properties of BIPy-NDIs in the presence of metal ions were investigated in a pH \(= 1.70\) aqueous solution for all the measurements since at this pH occurs a high fluorescence intensity and good receptors solubility.

To investigate the metal-induced fluorescence change in the fluorescence spectra of BIPy-NDIs, solutions with three equivalents of different metal ions have been measured. The dependence of the metal ions on the fluorescence enhancement (FE) is showed in Figure 7. The FE \(= I/I_0\) was determined from the maximum fluorescence intensity \(I\) (after addition of metal ions) and the BIPy-NDI fluorescence intensity \(I_0\) (before metal ions addition). The higher enhancement of the fluorescence intensity (\(\sim 40\%\) with \(\text{Zn}^{2+}\)) and the largest decrease (\(\sim 25\%\) with \(\text{Ca}^{2+}\)) in presence of the metal ions have been observed with BIPy-NDI \(1D\) (Figure 7). The less affected compounds in their fluorescence properties were BIPy-NDI \(1B\) and \(1C\) with a maximum increase in 10% and 9% with \(\text{Zn}^{2+}\), respectively.

Considering there is no significant differences in presence of metal ions and a wider range of linear response to pH, BIPy-NDI \(1B\) demonstrate more potential as pH chemosensor.

**Sample analysis**

To evaluate the practical application of BIPy-NDIs \(1B-1D\) as pH chemosensors, the pH of two trademark commercial available vinegars (sample 1 and 2) was determined under the same conditions. First, a calibration of curve in
acetate buffer was elaborated for each BIPy-NDI (Figure 8), and then was determine the pH values of BIPy-NDIs solutions prepared using the commercial vinegar as solvent. The results obtained with fluorescent method and the glass electrode measure are compared in Table 3. Is noteworthy that BIPy-NDI 1B presented the best results with a R.S.D.% of 1.58 for sample 1 and 4.00 for sample 2, while with BIPy-NDIs 1C and 1D R.S.D.% were higher. These results are according with the competitive experiment for 1B due to its fluorescence intensity is not affected by the presence of other cationic species.

**Conclusions**

In this paper, we have presented evidence of PET process in BIPy-NDIs in aqueous media. On the basis of the present investigation it can assumed that the BIPy-NDI 1B is suitable for developing a pH chemosensor based on the quenching of PET processes at low concentration and pH range between 1.7 and 4.1. The BIPy-NDIs testing with commercial samples show that the pH chemosensor based on BIPy-NDI 1B offers the advantages of adequate sensitivity, accuracy and rapid detection of pH. The results are according with the data of conventional glass electrode method. The sensor proposed shows excellent stability, high reproducibility, and a short response time. The method may be useful for constructing pH-sensitive fluorescence chemosensor.

**Supplemental material**

Supplemental data for this article can be accessed online here: http://dx.doi.org/10.1080/10610278.2016.1162905

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**Disclosure statement**

No potential conflict of interest was reported by the authors.

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**Table 3.** pH determination of commercial vinegar using BIPy-NDIs as pH chemosensor.

<table>
<thead>
<tr>
<th>Compound</th>
<th>Sample 1</th>
<th>Glass electrode</th>
<th>R.S.D. %</th>
<th>Sample 2</th>
<th>Glass electrode</th>
<th>R.S.D. %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1B</td>
<td>2.55</td>
<td>2.51</td>
<td>1.58</td>
<td>2.55</td>
<td>2.45</td>
<td>4.00</td>
</tr>
<tr>
<td>1C</td>
<td>2.62</td>
<td>2.51</td>
<td>4.28</td>
<td>2.58</td>
<td>2.45</td>
<td>5.16</td>
</tr>
<tr>
<td>1D</td>
<td>2.96</td>
<td>2.51</td>
<td>16.10</td>
<td>2.85</td>
<td>2.45</td>
<td>15.09</td>
</tr>
</tbody>
</table>

**References**


