



Synthesis and evaluation of the chromo-fluorogenic recognition ability of imidazoquinoline derivatives toward ions



Cristina Marín-Hernández ^{a, b}, Luis E. Santos-Figueroa ^{a, b}, Sameh El Sayed ^{a, b},
Teresa Pardo ^{a, b}, M. Manuela M. Raposo ^{c, **}, Rosa M.F. Batista ^c, Susana P.G. Costa ^c,
Félix Sancenón ^{a, b}, Ramón Martínez-Mañez ^{a, b, *}

^a Centro de Reconocimiento Molecular y Desarrollo Tecnológico (IDM), Unidad Mixta Universidad de Valencia-Universidad Politécnica de Valencia, Camino de Vera s/n, 46022 Valencia, Spain

^b CIBER de Bioingeniería, Biomateriales y Nanomedicina (CIBER-BBN), Spain

^c Centro de Química, Universidade do Minho, Campus de Gualtar, 4710-057 Braga, Portugal

ARTICLE INFO

Article history:

Received 13 March 2015

Received in revised form

2 June 2015

Accepted 3 June 2015

Available online 19 June 2015

Keywords:

Imidazoquinolines

Cation recognition

Anion recognition

Colour

Fluorescence

Proton transfer

ABSTRACT

Four imidazoquinolines functionalized with different carbocycles and heterocycles have been synthesized and characterized. Acetonitrile solutions of the four receptors presented absorption bands in the 330–370 nm range. The four probes were also emissive with fluorescence bands in the 390–460 nm interval. In a first step, the chromo-fluorogenic behaviour of the four probes was evaluated in the presence of selected anions. Addition of F^- induced the appearance of a new red-shifted absorption band together with a moderate quenching of the fluorescence in all four receptors. In a second step, the UV–visible and emission behaviour of the four receptors in the presence of cations was tested. Addition of Hg^{2+} , Cu^{2+} , Co^{2+} , Fe^{3+} , Fe^{2+} , Zn^{2+} , Pb^{2+} , Cd^{2+} , Cr^{3+} and Al^{3+} induced a similar optical change in all four receptors (appearance of a broad red-shifted absorption band together with a remarkable quenching of the emission band).

© 2015 Published by Elsevier Ltd.

1. Introduction

From the early years of supramolecular chemistry foundations, two concepts that have been extensively developed are the preparation of molecular receptors and, more recently, the design of chemical sensors [1]. Molecular receptors are chemical species designed to achieve a high degree of complementarity with a selected guest. When synthetic receptors are coupled with certain signalling units, that could change one or more physical properties (e.g. colour, fluorescence, redox potential) upon receptor–guest interaction, a molecular sensor is obtained [2]. In this field especially appealing is the use of optical outputs such as changes in colour and/or fluorescence that allow the use low-cost and widely

available instrumentation [3]. Moreover, in the case of chromogenic chemosensors, a straightforward semiquantitative and *in situ* “naked-eye” (direct visual observation) detection is possible [4] and chromo-fluorogenic chemosensors displaying a displacement of the absorption or emission bands are interesting for the development of ratiometric procedures [5].

Three main paradigms have been used in the development of chromo-fluorogenic chemosensors namely (i) the binding site–signalling subunit approach, (ii) the displacement approach and (iii) the chemodosimeter approach [6]. In the first paradigm, the binding site, designed in such a way that possesses a high degree of complementarity with selected guests, is covalently linked with a signalling subunit that is able to change colour or absorption/emission upon guest coordination with the binding site [7]. The displacement approach also uses a binding site and a signalling subunit which are not covalently linked yet forming a coordination complex. In the presence of the target guest the signalling subunit is displaced and an optical signal is generated [8]. Finally, the chemodosimeter approach makes use of specific chemical reactions induced by the guest on the designed probe that are coupled to

* Corresponding author. Centro de Reconocimiento Molecular y Desarrollo Tecnológico (IDM), Unidad Mixta Universidad de Valencia-Universidad Politécnica de Valencia, Camino de Vera s/n, 46022 Valencia, Spain.

** Corresponding author.

E-mail addresses: mfox@quimica.uminho.pt (M.M.M. Raposo), rmaez@qim.upv.es (R. Martínez-Mañez).

colour modulations [9]. Based on these three paradigms cited above a number of chromo-fluorogenic sensors for anions, cations and neutral molecules have been described recently [10]. Perhaps, the most widely used approach to design probes is the binding site-signalling subunit paradigm [11]. However, the covalent linking of binding sites with signalling subunits require in most cases great synthetic efforts in order to achieve certain selectivity with the guest and to impart the desired functionality, regarding colour and/or emission changes upon coordination. In order to minimize the synthetic requirements, recently, the preparation of simple chemical species that integrated binding subunits into the structure of certain dyes or fluorophores has deserved great attention [12]. Moreover, the possibility of using the same probe to sense both anions and cations is an area of importance within the chemical sensing field [13].

From another point of view, imidazole derivatives have been demonstrated to be good neutral binding groups for coordinating anions [14]. Besides, the coordination ability of the imidazole group depends on the acidity of the NH proton that can be modulated by the presence in the structure of easily delocalizable heteroaromatic rings, such as thiophene, pyrrole and furan [12a,15]. Moreover, the presence in imidazole derivatives of two nitrogen atoms, one of them with a free electron pair, favours the coordination of metal cations with this five-membered heterocycle [16]. Also, some quinoline derivatives have been reported to be suitable systems for the colorimetric sensing of certain anions and for the recognition of metal cations [17]. Moreover quinolines have been increasingly studied by their bioactive properties and have been used as anti-malarial [18], antiviral [19], anticonvulsant [20] and anticancer agents [21].

Taking into account the above mentioned facts and our interest in the development of optical probes [22], we report herein the synthesis, characterization and binding studies toward anions and cations of a family of probes containing imidazoquinoline moieties as both binding and signalling subunit. The probes contained electron donor rings of different strength (i.e. *N*-methylpyrrole, furan, thiophene and benzene) in the structures in order to modulate their response as chemosensors. The interaction of the four probes with anions and cations was studied by means of UV–visible, fluorescence and ^1H NMR measurements.

2. Results and discussion

2.1. Synthesis and characterization

The new compounds **3a–d** with biphenyl, arylthiophene, arylpyrrole and arylfuran π -conjugated bridges were synthesized in good to excellent yields, 52–87%. The synthesis of the formyl precursor **1c** was recently reported by us through a Suzuki coupling followed by a Vilsmeier reaction [12a]. Imidazoquinolines **3a–d** were obtained through a one step reaction involving $\text{Na}_2\text{S}_2\text{O}_4$ reduction of 5-amino-6-nitroquinoline **2** in the presence of commercially available biphenyl, arylthiophene, and arylfuran aldehydes **1a–b**, **1d**, and aldehyde **1c** in DMSO at 80 °C (Scheme 1) [23]. The crude products were purified by column chromatography on silica with chloroform or through recrystallization from dichloromethane to give the pure compounds, which were completely characterized through the use of common spectroscopic and analytical methods (see Scheme 1).

The most characteristic signals in the ^1H NMR spectrum of this family of imidazoquinoline derivatives were those corresponding to N–H proton in the imidazole moiety, which were found as singlets in the 12.13–13.55 ppm range. A certain correlation could be observed between the donor properties of the π -conjugated bridges attached to position 2 of the imidazole nucleus and the

chemical shift of the nitrogen proton of the imidazole ring in **3a–3d** (Table 1). In this context, compound **3c** bearing a more electron rich heterocyclic π -bridge exhibited the lowest chemical shift for the nitrogen proton of the imidazole ring.

2.2. Spectroscopic characterization

The spectroscopic characterization of acetonitrile solutions of the four probes was carried out. The four probes showed intense absorption bands ($\log \epsilon \approx 4.2$) in the 260–370 nm region (see Table 2). The position of the red shifted absorption bands were clearly dependent on the electron donor strength of the (hetero) aromatic group which was used as π -bridge between the imidazoquinoline and the terminal phenyl ring. When the π -bridge was a benzene ring (the least electron donor) as in **3a**, the absorption band was centred at 338 nm. On changing the π -bridge to methylpyrrole (**3c**) the absorption maximum suffered a small bathochromic shift to 341 nm whereas if the π -bridge was a furan (**3d**) or a thiophene (**3b**), the red shift was larger, to 352 and 361 nm respectively. Moreover, upon excitation at the corresponding maximum wavelength, the four probes showed broad unstructured emission bands in the 390–458 nm range (see Table 2). Also, quantum yields of the four probes were measured (using quinine sulphate 0.5 mol dm $^{-3}$ in H_2SO_4). The values obtained ranged from 0.12 to 0.36 and were shown in Table 2.

In order to assess the nature of the main absorption band of each of the four probes the HOMO and LUMO differences in energy for **3a–d** by quantum chemical calculations at the semiempirical level employing the PM3 model and with RMS gradient of 0.001 were determined. For the four probes, the HOMO and LUMO orbitals were distributed throughout the molecule. As a representative example, Fig. 1 shows the HOMO and LUMO orbitals for probe **3a**. As can be seen in the figure the HOMO and LUMO orbitals of **3a** are symmetric and delocalised over the entire π -system clearly resembling those of cyanine dyes.

2.3. Spectroscopic behaviour of **3a–d** in presence of anions

The chromogenic behaviour of the four probes in the presence of selected anions was tested. For this purpose, acetonitrile solutions of **3a–d** (1.0×10^{-4} mol dm $^{-3}$) were prepared and the changes in the UV–visible profiles tested upon addition of 10 equivalents of anions with different sizes, shapes and charges (i.e. F^- , Cl^- , Br^- , I^- , OCN^- , BzO^- , ClO_4^- , AcO^- , HSO_4^- , H_2PO_4^- and CN^-) at 25 °C. The four probes showed a very similar chromogenic response in the presence of anions. In particular only the addition of F^- induced a remarkable colour modulation from colourless to pale yellow that was visible to the naked eye. Other anions tested were unable to induce any such remarkable colour change.

Once assessed the response of probes **3a–d** toward anions, UV–visible changes in the presence of F^- were studied more in detail. The response observed for the four receptors was quite similar and as an example Fig. 2 shows the UV–visible titration profiles of probe **3a** with F^- . Acetonitrile solutions of probe **3a** displayed two intense absorption bands at 297 and 338 nm that, upon addition of increasing quantities of F^- anion, suffered a decrease in intensity concomitant with small bathochromic shifts. Besides, a new broad absorption centred at 377 nm was developed. UV–visible titration experiences carried out with probes **3b**, **3c** and **3d** showed the same behaviour as that observed for **3a**. Namely, only the addition of F^- induced a remarkable reduction of the two main absorption bands of the probes with a clear simultaneous growth of a red shifted absorption band.

The fact that colour modulations in the four probes were induced only by the addition of the more basic anion, i.e. F^- ,

Download English Version:

<https://daneshyari.com/en/article/175696>

Download Persian Version:

<https://daneshyari.com/article/175696>

[Daneshyari.com](https://daneshyari.com)