

## Coordinative and electrostatic forces in action: from the design of differential chromogenic anion sensors to selective carboxylate recognition†

Beatriz García-Acosta,<sup>a</sup> Xavier Albiach-Martí,<sup>a</sup> Eduardo García,<sup>b</sup> Luis Gil,<sup>b</sup> Ramón Martínez-Máñez,<sup>\*a</sup> Knut Rurack,<sup>\*c</sup> Félix Sancenón<sup>a</sup> and Juan Soto<sup>a</sup>

<sup>a</sup> GDDS, Dpto de Química, Universidad Politécnica de Valencia, Camino de Vera s/n, Valencia 46071, Spain. E-mail: rmaez@qim.upv.es; Fax: +34 96 3879349; Tel: +34 96 3877343

<sup>b</sup> Group of Hybrid Microelectronics, Dpto de Ingeniería Electrónica, Universidad Politécnica de Valencia, Camino de Vera s/n, Valencia 46071, Spain. E-mail: lgil@eln.upv.es; Fax: +34 96 3876009

<sup>c</sup> Div. I.3, Bundesanstalt für Materialforschung und –prüfung (BAM), Richard-Willstätter-Strasse 11, D-12489 Berlin, Germany. E-mail: knut.rurack@bam.de; Fax: +49 30 81045005

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A new family of differential chromogenic anion chemosensors is described based on anilino-pyridine–metal cation coordinative signalling ensembles.

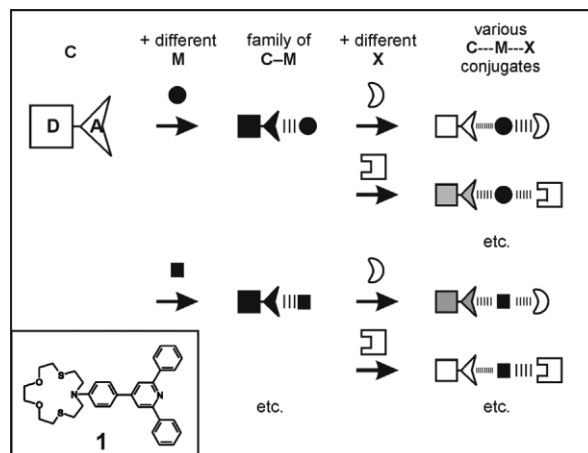
The field of chromogenic anion receptors has been growing in interest over the last years, however, the number of examples is still limited.<sup>1</sup> Here, design commonly follows the “binding site–signalling subunit” approach where the two units are covalently linked to give a colorimetric response upon selective anion binding. The development of such chemosensors requires i) target-optimization of the binding site, ii) selection of an appropriate mechanism for signal generation and iii) choice of a suitable chromophore as transducer of the coordination event. Although the strong point of this approach is selectivity, it usually harbours the disadvantage of requiring extensive and time-consuming synthetic efforts to tune structurally complicated hosts. Recently, for certain applications the use of differential receptors has been proposed as an alternative concept.<sup>2</sup> This strategy relies on a set of suitable sensors that respond rather unspecifically yet differently toward a group of related guests, generating signal patterns that can be analyzed by multicomponent algorithms. Prominent examples comprise sophisticated biosensor arrays, electronic noses or tongues.<sup>3</sup> Furthermore, in molecular biochemistry, the importance of metal ions as versatile species that control the signalling at the molecular level has very recently also gained considerable attention. For instance, metal–ligand coordinative interactions allow certain metalloenzymes to signal various species such as nitric oxide, carbon monoxide and reactive oxygen species in a very similar fashion.<sup>4</sup> However and despite all these advances, the field of differential recognition utilizing actual chromogenic sensor molecules or their complexes is still largely unexplored.<sup>5</sup>

Based on our experience with colorimetric chemosensors,<sup>6</sup> we developed a new design concept for chromogenic anion sensing that utilizes metal–ligand coordinative interaction of weak metal complexes<sup>7</sup> of charge-transfer (CT) chromophores. The idea is outlined in Scheme 1. The free chromophore **C** shows a certain CT absorption band. Upon coordination of a metal ion **M** to the acceptor (Scheme 1, **C–M**), the strength of the latter substantially increases and the band is displaced to longer wavelengths. In the final step of the sensing protocol, the anion (**X**) is electrostatically attracted by the cation, forming an ion pair–complex conjugate (**C–M–X**) which induces a weakening of the **C–M** bond. The latter effect is fed back into the chromophore, showing again a reduced CT character with the corresponding appearance of a band again at shorter wavelengths. Considering the forces at play, the response of a certain **C–M** pair toward a certain anion **X** is given by the intrinsic chemical natures of **M** and **X** such as *e.g.* charge density, valency or hard- and softness. These subtle differences should in turn be

reflected in the respective spectral fingerprint of each **C–M–X** complex. We envisioned that combination of a suitable **C** with different metal ions **M** should yield a family of differential chemosensor ensembles for the pattern recognition of anions.

With this concept in mind, we chose the CT-active anilino-pyridine dye **1** as the chromophore component of the ensemble (Scheme 1, inset). In **1**, the 2,6-diphenylpyridine acceptor (A) unit promised to show the required metal ion binding features.<sup>8</sup> Since under the conditions employed, simple dimethylanilino donors (D) are also known to weakly coordinate certain transition metal ions, the donor side of **1** was equipped with a dithia dioxo crown-type “shielding” group. This chemical modification, which was inspired by previous studies on thia anilino-crowned D–A dyes,<sup>6</sup> led to the preferential coordination of aminophilic cations to the pyridine unit. In the present studies, we thus focused on the Fe<sup>3+</sup>, Cu<sup>2+</sup>, Zn<sup>2+</sup> and Pb<sup>2+</sup> complexes of **1** in MeCN.<sup>9</sup>

The different spectroscopic characteristics of the **1–M** ensembles can be rationalized as follows. By analogy with the photophysics of a closely related anilino-pyrimidine dye,<sup>10</sup> **1** also shows CT features connected with largely planar conformations and favourable extinction coefficients for sensitive chromogenic indication. The maximum of the absorption band of **1** is found at 338 nm in acetonitrile ( $\epsilon \approx 23\,000\text{ M}^{-1}\text{ cm}^{-1}$ ). In the presence of Fe<sup>3+</sup>, Cu<sup>2+</sup>, Zn<sup>2+</sup> and Pb<sup>2+</sup>, the centre of the band appears at  $432 \pm 4\text{ nm}$ , while maintaining the high extinction coefficients. This increase in CT character, due to the higher electron deficiency of the pyridine acceptor moiety in **1–M**, is responsible for the colour change of the solution from colourless (absorption in the UV) to yellow. Monitoring the intensity changes at 340 and 440 nm upon addition

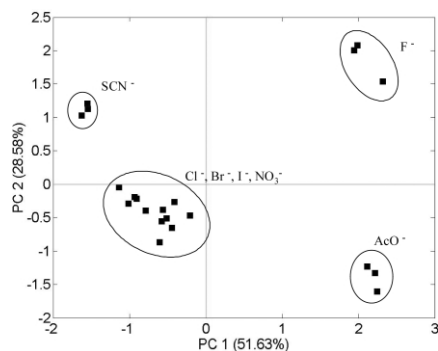


**Scheme 1** Signalling protocol for chromogenic anion recognition using D–A chromophore–metal ion coordinative compounds. Schematic representation of bond strengths and response of the dye is shown, the CT character increasing from white *via* grey to black.

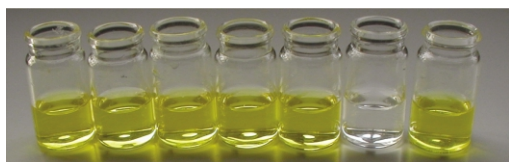
† Electronic Supplementary Information (ESI) available: details on synthesis, **1–M** interaction, complex stability constants and fluorescence decay measurements. See <http://www.rsc.org/suppdata/cc/b3/b314997h/>

of the cations gave isosbestic points, strongly suggesting the formation of well-defined 1 : 1 complexes. Moderate  $\log K$  values with metal ions were observed (see ESI†). Preliminary studies in the presence of certain anions revealed that the long-wavelength absorption (at 440 nm) decreases as a function of **1-M-X** formation. To ensure that a decoloration of the **1-M** solution occurring upon anion addition is not due to simple dissociation of the complex, further fluorescence studies were carried out. Whereas **1** is highly emissive with a fluorescence lifetime  $\tau_f$  of 2.86 ns, **1-Pb** for instance is strongly quenched with  $\tau_f = 31$  ps. Formation of a ternary conjugate can thus be assumed when the lifetime in the presence of **X** differs significantly from  $\tau_f$  of **1**. This was indeed observed as manifested in  $\tau_f$  of 2.66 ns for **1-Pb-AcO** and similar results were also found in other **1-M-X** systems studied. In control experiments, protonated **1** ( $\tau_f < 3$  ps) was deprotonated with  $F^-$  to yield again a decay time of 2.86 ns, with the uncertainties of measurement amounting to  $\pm 3$  ps. The same lifetime of 2.86 ns was found for **1** in the presence of a non-interacting electrolyte (tetrabutylammonium perchlorate) at similar concentrations.

To test the ability of the system in terms of differential recognition of small monovalent anions, acetonitrile solutions of **1-M** chemosensors were prepared (1 : 1 metal-to-ligand ratios;  $M = Fe^{3+}, Cu^{2+}, Zn^{2+}$  and  $Pb^{2+}$ ) and mixed with aliquots of solutions containing one or more equivalents of the anions  $F^-$ ,  $Cl^-$ ,  $Br^-$ ,  $I^-$ ,  $NO_3^-$ , acetate ( $AcO^-$ ) or  $SCN^-$ . No well-defined selective colour changes were found by simple visual inspection (except in one case, see below). However, qualitative analysis of the response of the **1-M** chemosensing ensembles for different anions with PCA (Principal Component Analysis) algorithms yielded the results summarized in Fig. 1. As can be deduced from the figure, recognition patterns can be identified for  $AcO^-$ ,  $F^-$  and  $SCN^-$  whereas the proximity between scores for  $Cl^-$ ,  $Br^-$ ,  $I^-$  and  $NO_3^-$  indicates a too high similarity in colour variation with the present family of **1-M** chemosensors. It is remarkable to note that a truly selective bleaching was found for **1-Pb** and  $AcO^-$  with this kind of sensor design (Fig. 2). Selective chromogenic recognition of carboxylates is rare and to the best of our knowledge, only one acetate-selective molecular chromogenic chemosensor has been



**Fig. 1** Principal component analysis (PCA) score plot for the anions  $F^-$ ,  $Cl^-$ ,  $Br^-$ ,  $I^-$ ,  $NO_3^-$ ,  $AcO^-$  and  $SCN^-$  using **1-M** ( $M = Fe^{3+}, Cu^{2+}, Zn^{2+}$  and  $Pb^{2+}$ ) chemosensing ensembles. Data shown from three different trials using 1 : 1 or 1 : 2 **1-M** to anion ratios. PC axes are calculated to lie along lines of diminishing levels of variance in the data set.



**Fig. 2** Photograph showing the color observed in **1-Pb** acetonitrile solutions upon addition of equimolar amounts of certain monovalent anions (from left to right); no anion,  $F^-$ ,  $Cl^-$ ,  $Br^-$ ,  $NO_3^-$ ,  $AcO^-$ ,  $SCN^-$ .

described until today.<sup>11</sup> Additionally, we found that other carboxylates typically present in water<sup>12</sup> such as formate, oxalate and propionate also gave a similar response to that of acetate. To explore the suitability of simple and weakly bound metal ion-chromophore complexes for chromogenic anion analysis in real samples, the colorimetric determination of acetic acid in commercially available vinegar was carried out, yielding a satisfactory agreement with an approved method.<sup>13</sup>

In conclusion, a family of metal ion-chromophore chemosensors has been prepared and successfully employed for the differential recognition of several small monovalent anions. One of the differential receptors proved to act also as a specific chemosensor. The molecular framework used in our present approach is simple, easily tuneable and can dispense with advanced host-guest chemistry. It is assumed that the interplay of rather weak coordinative and electrostatic forces in combination with un-specific ligands and metal ions harbours an enormous potential and can open new perspectives for the future design of assays for chromogenic anion detection. We are currently developing similar systems working in a more suitable wavelength range capable to address some yet irresolvable species.

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## Notes and references

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