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Dual-response colorimetric sensor array for the identification of amines in water based on supramolecular host–guest complexation

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ABSTRACT

Amines have been found as a challenging compound class in previous works on chemical tongues. Herein, we describe the successful application of libraries based on host–guest inclusion complexes in cyclodextrins (CDs) and cucurbiturils (CBs) for the discrimination of primary, secondary, tertiary, aliphatic and aromatic as well as linear and branched amines in water. Besides the clear need for new detection, identification and quantification techniques of organic compounds in water, the main advantage of our approach is that an array made by combining six simple basic dyes with seven commercial organic capsules allows a perfect discrimination among 14 amines (see list in Table S1 in Supplementary data) with only very subtle structural differences.

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Development of sensor systems that can be of general use for the detection and the determination of organic compounds in water is still a challenge in analytical chemistry.[1] Most approaches remain largely based on the design of selective sensors for individual organic compounds. This type of sensors requires dedicated synthesis while frequently showing a very limited solubility in water.[1] Oppositely, Suslick and co-workers have shown that common pH indicators, solvathochromic molecules and coloured metal complexes can be used for the discrimination of organic molecules in water.[2] However they, as well as others groups working on colorimetric sensor arrays,[3] also pointed out that although amines are easily discriminated from other types of compounds they are among the most difficult analytes to be discriminated from each other. Previously it has been reported that dye-cucurbituril complexes can differentiate several amines.[4] Our previous knowledge on the properties of host–guest complexes,[5] and considering that amines can form strong hydrogen bonds with dyes and organic capsules, and are emission quenchers, let us anticipate that the interactions between amines and host–guest complexes can result in specific variations of the optical spectrum that can serve to sensor these organic compounds in water. Therefore, the principle of our sensor is the formation of supramolecular[6] water-soluble host–guest complexes that possess a large range of binding constants, and exhibit differences in their optical and emission spectra and emission quantum yields when the complex is disturbed. The proposed sensor array is presented in Figure 1 (see SI for experimental details). Each of the rows of the plate receives one of the six common on the shelf tricyclic basic dyes, while seven host

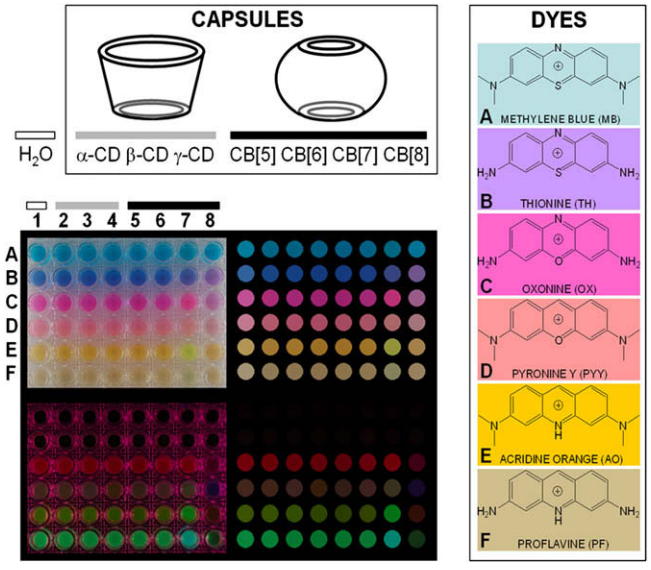

Figure 1. Pictures of a plate in absence of analyte taken under 'white' ([400–700] nm, upper left) and monochromatic UV (330 nm, lower left) lights, respectively. The original image (left) has been digitalized (right). The numbers and capital letters indicate the capsule (column, see grey codes) and dye (line, see structures for the letters) present in the well.

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capsules and water are distributed in columns. The capsule-free column provides a reference that shows the relevance of the complexation between capsules and dyes in the discrimination process. The selected pool of capsules is composed of three cyclodextrins (α-, β- γ-CDs) and four cucurbit[*n*]urils (CB[*n*] with $n = 5–8$) because they form host–guest inclusion complexes with simple organic dyes,[5] where the binding constant varies in the range 1–10.[5] Fifteen multi-well plates are identically prepared with 200 μl of water or capsule solution (1×10^{-4} M), and 70 μl of dye (3.86×10^{-4} M). It has been demonstrated[5] that the inclusion complex in γ-CD and CB[8] corresponds to dimeric or trimeric aggregate species, while for β-CD and CB[7] only the monomer is accommodated inside the organic capsule.[5] Bearing in mind that the stoichiometry of the complexes can be 1:1, 1:2, 2:2 and 1:3, the selected dye concentration allows a clear visual observation of the colour, and meets a good compromise for all the dyes.

To demonstrate the use of this host–guest library as sensor array, each of the 15 plates is employed for one given amine among 14, while the remaining one corresponds to the 'blank', for example, milli-Q water stands for the analyte (see Fig. 1). Thus, each of the 6(dyes) × 8(capsules + water) wells is filled with 30 μl of amine in aqueous solution producing instantaneous changes of colour. The colorimetric changes occurring in the array upon addition of analyte will depend in part on how the analyte influences the stability of the host–guest complex and varies of the monomer-to-dimer ratio. The colour alteration is examined by placing the plates into a black chamber illuminated under white visible ([400–700] nm) or monochromatic UV light (330 nm). For both types of illumination, a picture of the plate is taken with a CCD camera from which Red–Green–Blue (RGB) values at the central point of each well are extracted and stored. Then, various statistical analyses of all collected RGB colour components are performed. Firstly, the reproducibility of the pipetting and RGB extraction is meticulously evaluated (see Fig. S1 in SI). This allows quantifying the total experimental error on which RGB values depend. Finally different algorithms,[11] classification trees,[8] principal component analysis[6,9] (PCA) are employed in order to search for colorimetric features that make each analyte unique turning the sensor array into a fingerprint system considering these compounds at a given concentration. Note that many other algorithmic approaches such as support vector machine[8] (SVM) and neural networks[8–10] (NN) could have been employed. For the library that exemplifies the concept, four of the six dyes exhibit an intense fluorescence giving the advantage with respect to optical spectroscopy of being much more sensitive to lesser analyte concentrations. Consequently, the dual-response specificity of the sensor array allows acquiring 240 variables, $6_{UV} + 4_{WHITE}$ (dyes) × 8(water + 7capsules) × 3(RGB) per analyte and per concentration of analyte. The specific response of the array for each compound has been digitalized based on quantification of the RGB components for each dye-ligand combination at seven different concentrations 10^{-x} M, with $x = [0–6]$, *for example*, a total of 99 plates (7 × 14 + blank). As an illustration of the discriminatory power of the sensor array, Figure 2 shows a restricted selection of seven wells which permits a perfect identification of the 14 amines at 10^{-2} M. It can be observed how the sensor is able to differentiate the slightest structural change in the amine

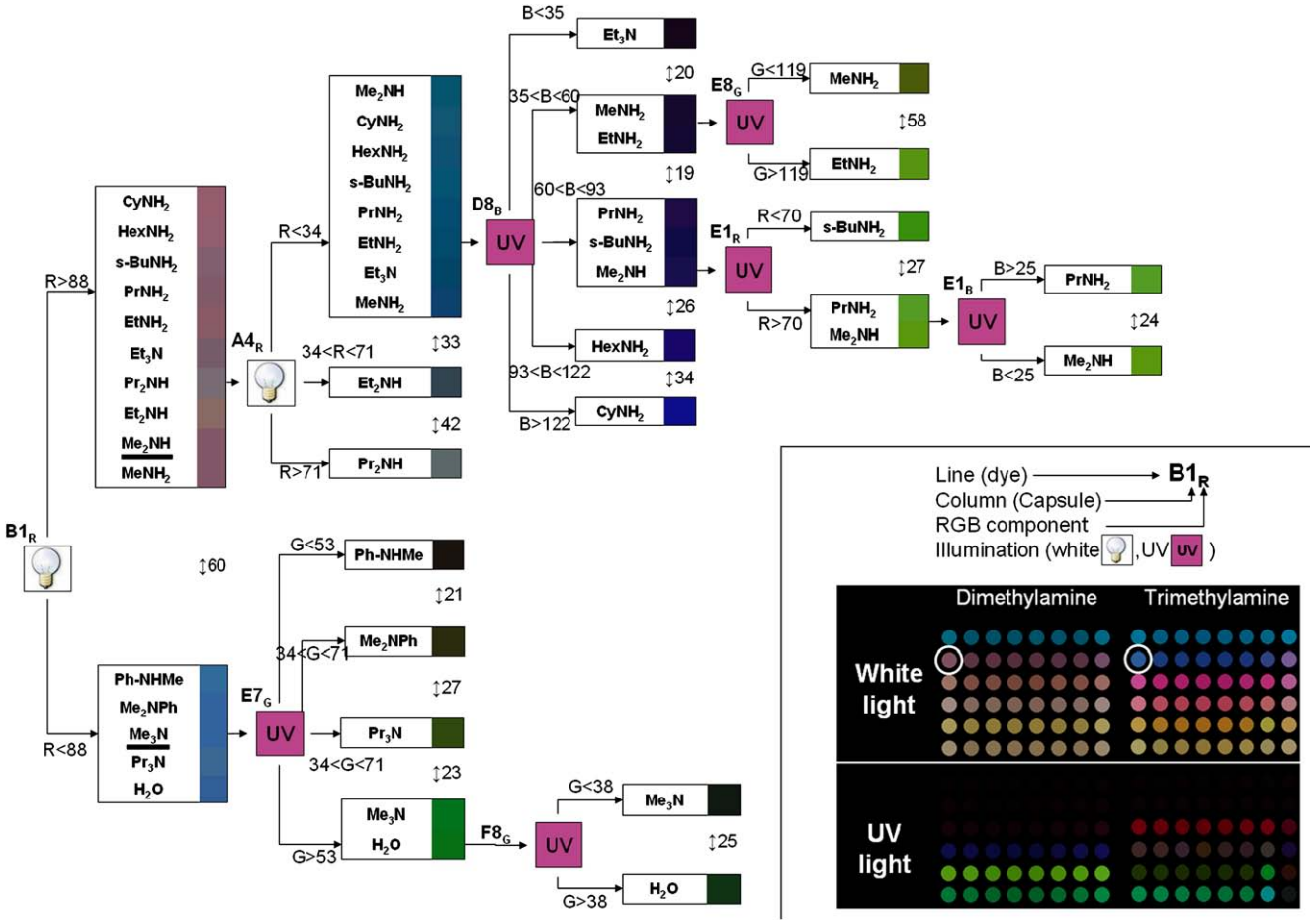

Figure 2. Selected classification tree among the numerous possible ones indicating the sequence of colour tests that allows to discriminate 14 amines upon illumination with white (polychromatic) and UV (330 nm) lights. In each node, the first capital letter and following number correspond to the well position as defined in 1. Squared icons refer to white or fluorescent illumination, while 'R', 'G' or 'B' is the selected colour component used for splitting the tree.

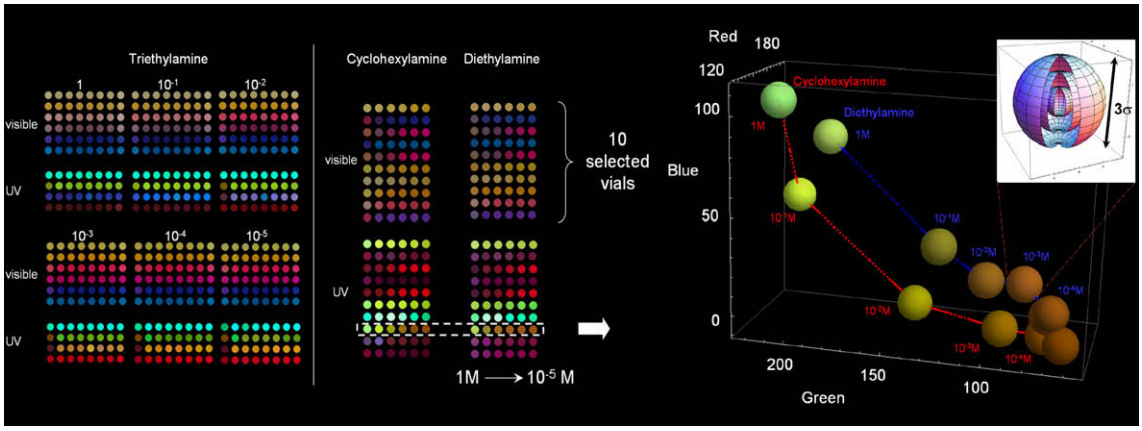

Figure 3. (Left) Influence of the concentration on the sensor array images upon visible and UV (only four dyes are fluorescent) light exposure for triethylamine. The tested analyte concentration (M) is indicated above the image. (Right) Influence of the concentration on the discrimination between cyclohexylamine and diethylamine. Each column corresponds to a concentration decreasing gradually by 1/10. The most right image shows the points corresponding to each concentration for each amine in the RGB space, where each point is coloured with its respective RGB values.

such as one single carbon difference. For example, Me_2NH, Et_2NH and Pr_2NH are indubitably discriminated as the well 'A4', that is, MB@γ-CD, gives strong colour variations (■, ■, ■) under white light, (*4*, *85*, *109*), (*50*, *68*, *80*), (*92*, *103*, *105*) being the respective RGB colour components for these compounds. The low number of wells necessary for a secure discrimination indicates that the array could be easily reduced to lesser wells which is interesting from a practical point of view while increasing the 'strength' of the sensor when measured through PCA analysis,[6] (see Fig. S2 in SI). On the other hand, redundant or correlated colour variation is an advantage as it increases the confidence of the discrimination through Bayesian confirmation. Moreover, this allows obtaining various discrimination manners such as responses which varied with the number of carbons, and linear versus branched structure of the alkyl chain in each type of amines, primary, secondary and tertiary.

The response to each analyte varies in a certain range as a function of its concentration. As mentioned before, each concentration for each analyte has its own specific image. Figure 3 shows the case of $CyNH_2$ and Et_2NH to illustrate the variations observed as a function of the concentration. The analysis of the digital images obtained as a function of the concentration indicates that overlapping in the images of different analytes may occur when the concentration reaches a lower threshold. This is due to the fact that all the images, independently of the analyte, tend to converge to the images in the absence of analyte, that is, blank, when the dilution is sufficiently high. Under our operation conditions, we have been able to distinguish the presence of analytes for concentrations above 10^{-5} M.

The specific response of each compound arises from how the analyte influences the complex in each well through hydrogen bonding, solution pH and compound polarity. Considering CDs which prefer to bind to neutral or anionic guests, the interactions that play a major role will be hydrophobicity and hydrogen bonding, while for CBs which exhibit a pronounced preference to interact with cationic guests, Coulombic charges, dipole moments and hydrogen bonding will be the main factors affecting the host–guest complex. Also, there could be analyte–dye interaction that could lead to energy or electron transfer quenching of fluorescence in addition to variations in the population distribution among various complexes and free dyes. The principal strength of the proposed sensor is that numerous interactions contribute in various degrees to the disturbance of the host–guest complex and are reflected in a variation in the response. Among them, changes in the solution pH upon addition the analyte, which are unavoidable in the absence of buffer, have been pointed out in precedents closely related to our work as a major factor for their sensor array.[7] Moreover, it was observed that when no pH variation occurs a significant part of the ability of reported chemical tongues and sensor arrays is lost.[7] Even if it can be assumed that no detectable pH changes should occur when comparing among similar amines of the same number of carbons or when varying the alkyl chain branching, additional experiments were conducted in which water has been substituted by a buffer solution. It was observed for three different buffers (pH value at 4, 7 or 10) that our sensor was still able to discriminate among the different amines, see Fig. S3 in SI.

In conclusion, the above results show an original and innovative colorimetric sensor array for amines in water based on a library built by combining a series of guest dyes with organic capsules. The combination of the images obtained from visible and UV light unequivocally identifies each analyte, the benefit of the dual-response being the increase of variables potentially useful for analyte discrimination. The response of this sensor array arises from the changes of colour depending on how the analyte interacts with the host–guest complex due to the combination of a large number of parameters, including hydrophilicity–hydrophobicity, Coulombic effects, dipolar interactions, hydrogen bridges, while pH changes have been shown to have minor effect, etc. The concept can be easily expanded to even more powerful libraries by increasing the number of water-soluble organic capsules (calixarenes, cyclophanes, crown ethers) and dyes to detect a large list of organic compounds of different families.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2009.02.189.

References and notes

1. Anslyn, E. V. *J. Org. Chem.* **2007**, *72*, 687–699; Wright, A. T.; Anslyn, E. V. *Chem. Soc. Rev.* **2006**, *35*, 14–28; Suslick, K. S.; Rakow, N. A.; Sen, A. *Tetrahedron* **2004**, *60*, 11133–12626; Albert, K. J.; Lewis, N. S.; Schauer, C. L.; Sotzing, G. A.; Stitzel,

S. E.; Vaid, T. P.; Walt, D. R. *Chem. Rev.* **2000**, *100*, 2595–2626; Ciosek, P.; Wroblewski, W. *Analyst* **2007**, *132*, 963–978.
2. Potyrailo, R. A. *Angew. Chem., Int. Ed.* **2006**, *45*, 702–723; Gale, P. A. *Acc. Chem. Res.* **2006**, *39*, 465–475; Kuswandi, B.; Nuriman; Verboom, W.; Reinhoudt, D. N. *Sensors* **2006**, *6*, 978–1017.
3. Zhang, C.; Suslick, K. S. *J. Am. Chem. Soc.* **2005**, *127*, 11548–11549.
4. Rakow, N. A.; Sen, A.; Janzen, M. C.; Ponder, J. B.; Suslick, K. S. *Angew. Chem., Int. Ed.* **2005**, *44*, 4528–4532; Leontiev, A.; Rudkevitch, D. *J. Am. Chem. Soc.* **2005**, *127*, 14126–14127.
5. Lagona, J.; Wagner, B.; Isaacs, L. *J. Org. Chem.* **2006**, *71*, 1181–1190.
6. Lagona, J.; Mukhopadhyay, P.; Chakrabarti, S.; Isaacs, L. *Angew. Chem., Int. Ed.* **2005**, *44*, 4844–4870; Lee, J. W.; Samal, S.; Selvapalam, N.; Kim, H. J.; Kim, K. *Acc. Chem. Res.* **2003**, *36*, 621–630; Mock, W. L. In Supramol. Chem. Ii—Host Design and Molecular Recognition, Springer: Berlin, Vol. 175, 1995, pp 1–24.; Rudkevich, D. A. *Bull. Chem. Soc. Jpn.* **2002**, *75*, 393–413; Fathallah, M.; Fotiadu, F.; Jaime, C. *J. Org. Chem.* **1994**, *59*, 1288–1293; Montes-Navajas, P.; Teruel, L.; Corma, A.; Garcia, H. *Chem. Eur. J.* **2008**, *14*, 1762–1768; Koner, A. L.; Mau, W. M. *Supramol. Chem.* **2007**, *19*, 55–66; Nau, W. M.; Mohanty, J. *Int. J. Photoenergy* **2005**, *7*, 133–141.
7. Palacios, M. A.; Nishiyabu, R.; Marquez, M.; Anzenbacher, P. *J. Am. Chem. Soc.* **2007**, *129*, 7538–7544; Meier, M. A. R.; Schubert, U. S. *Chem. Commun.* **2005**, *36*, 4610–4612; Fernandez, Y. D.; Gramatges, A. P.; Amendola, V.; Foti, F.; Mangano, C.; Pallavicini, P.; Patroni, S. *Chem. Commun.* **2004**, 1650–1651; Palacios, M. A.; Wang, Z.; Montes, V. A.; Zyryanov, G. V.; Anzenbacher, P. *J. Am. Chem. Soc.* **2008**, *130*, 10307–10314; Gardner, J. W.; Bartlett, P. N. *Electronic Noses: Principles and Applications*; Oxford University Press: New York, 1999.
8. Mohanty, J.; Pal, H.; Ray, A. K.; Kumar, S.; Nau, W. M. *ChemPhysChem* **2007**, *8*, 54–56; Montes-Navajas, P.; Corma, A.; Garcia, H. *ChemPhysChem* **2008**, *9*, 713–720.
9. Baumes, L. A.; Serra, J. M.; Serna, P.; Corma, A. *J. Comb. Chem.* **2006**, *8*, 583–596; Serra, J. M.; Baumes, L. A.; Moliner, M.; Serna, P.; Corma, A. *Comb. Chem. High Throughput Screen* **2007**, *10*, 13–24.
10. Corma, A.; Moliner, M.; Serra, J. M.; Serna, P.; Díaz-Cabañas, M. J.; Baumes, L. A. *Chem. Mater.* **2006**, *18*, 3287–3296.
11. Baumes, L. A.; Farruseng, D.; Lengliz, M.; Mirodatos, C. *QSAR Comb. Sci.* **2004**, *29*, 767–778; Klanner, C.; Farrusseng, D.; Baumes, L. A.; Lengliz, M.; Mirodatos, C.; Schüth, F. *Angew. Chem., Int. Ed.* **2004**, *43*, 5347–5349; Baumes, L. A.; Moliner, M.; Corma, A. *QSAR Comb. Sci.* **2007**, *26*, 255–272; Serna, P.; Baumes, L. A.; Moliner, M.; Corma, A. *J. Catal.* **2008**, *258*, 25–34.