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Colorimetric Signaling of Large Aromatic Hydrocarbons via the Enhancement of Aggregation Processes

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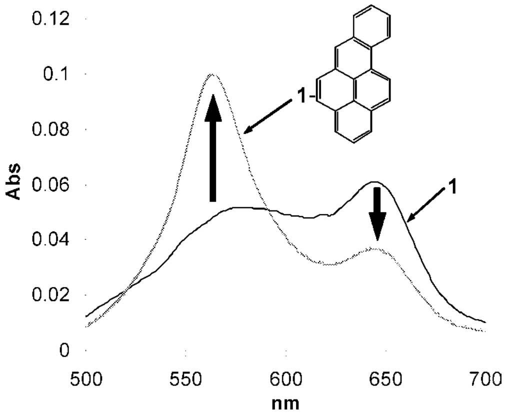
ABSTRACT



In this paper, the use of aggregation processes in squaraine derivatives as signaling protocols in the development of colorimetric probes for certain neutral guest (aromatic hydrocarbons) has been studied.

There is an increasing interest in the development of molecular chemosensors capable of connecting receptor−guest interactions with spectroscopic responses. In the search for new methodologies for chemical sensing, those involving spectroscopic protocols using chromogenic or fluorogenic molecular sensors are especially attractive. Among these, visible absorption represents an easily perceived output signal because it utilizes widely used instrumentation and it may also make possible the sensing of target species with only the naked eye. Several approaches have been followed for the design of chromogenic probes for a wide range of guests, especially for cations and anions.[1] However, there still are a number of facets in this field that need to be adequately addressed. In particular, chromogenic molecular probes capable of sensing neutral species without any functional group in water or mixed aqueous environments are extremely rare.[2]

Following a general approach, the development of systems for the chromogenic signaling of neutral species should involve suitable receptor−guest interactions coupled with reversible colorimetric events. However, the interaction of receptors with neutral guests is customarily weak and usually only observed in nonaqueous environments. Nonetheless, although this is a seldom studied field, we believed that it might be possible to generate colorimetric probes for target uncharged guests using suitable rational designs. As proof of this concept, we have chosen as a chromogenic signaling protocol the interaction of selected guests with a certain class of supramolecular structures: molecular aggregates. Molec-

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[1] For further information, see: (a) Martínez-Máñez, R.; Sancenón, F. *Chem. Rev.* **2003**, *103*, 4419. (b) Fabbrizzi, L.; Licchelli, M.; Rabaioli, G.; Taglietti, A. *Coord. Chem. Rev.* **2000**, *205*, 85. (c) Wiskur, S. L.; Aït-Haddou, H.; Lavigne, J. J.; Anslyn, E. V. *Acc. Chem. Res.* **2001**, *34*, 963. (d) Rurack, K.; Resch-Genger, U. *Chem. Soc. Rev.* **2002**, *31*, 116. (e) Valeur, B.; Leray, I. *Coord. Chem. Rev.* **2000**, *205*, 3.

[2] (a) Yang, R.; Li, K.; Liu, F.; Li, N.; Zhao, F.; Chan, W. *Anal. Chem.* **2003**, *75*, 3908. (b) Zheng, Q. Y.; Chen, C. F.; Huang, Z. T. *Tetrahedron* **1997**, *53*, 10345. (c) Mertz, E.; Zimmerman, S. C. *J. Am. Chem. Soc.* **2003**, *125*, 3424. (d) Möhr, G. J.; Demuth, C.; Spichiger-Keller, U. E. *Anal. Chem.* **1998**, *70*, 3868.

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ular aggregates are well documented systems whose optical response differs from that displayed by the monomers. It is known that this different optical answer arises from collective effects caused by the interaction between molecules within the aggregate. It was envisaged that the interaction of selected guests with certain aggregates could result in remarkable color variations. To meet additional requirements for ideal application, (i) the system should show a large change in color in relation to the aggregation process and (ii) the method should be operable in aqueous environments. All of the above led us to choose squaraine derivatives as the chromogenic systems. Squaraines are highly π-delocalized polymethine chromophores that consist of a central four-membered squaric ring 1,3-substituted by aniline moieties. They show interesting photophysical properties such as a very intense absorption band (log ϵ values are usually larger than 5) at the lower end of the visible spectrum. Additionally, squaraines in mixed aqueous media tend to suffer aggregation phenomena leading to the formation of structures whose absorption is largely shifted with respect to that of the monomer.[3] We have chosen aromatic hydrocarbons as the selected neutral guests without a functional group.[4]

Aggregation−disaggregation processes have been rarely used as protocols in guest signaling. Sessler et al. used aggregation−disaggregation of saphyrines for the chromogenic sensing of certain anions.[5] In addition, in a recent study, aggregation−disaggregation protocols were used for colorimetric cation detection in acetonitrile.[6] However, despite these results and as far as we know, aggregation−disaggregation protocols have never been used in the design of chromogenic chemosensors for neutral species.

Here, compounds **1**−**4** have been synthesized. Table 1 summarizes the absorption bands of the monomer and aggregated species and the observed effect following the addition of aromatic hydrocarbons.

To take an example, **1** shows an intense absorption of the monomer at 642 nm in water−acetonitrile mixtures up to 67% water. Further increasing the amount of water results in the appearance of a new blue-shifted band at 563 nm due to the formation of H-aggregates (attributed to face-to-face π-stacking interactions between squaraine monomers). The aggregation process is accompanied by a quenching of the fluorescence, as the H aggregates are nonfluorescent.

Table 1. Spectroscopic Data of **1**−**4** and Changes Observed upon Addition of Aromatic Hydrocarbons

receptor[a]	λ_{monomer} (nm)	$\lambda_{\text{aggregated form}}$ (nm)	band enhancement upon guest addition[b]
1	640	563	563
2	680		
3	674	539, 591, 700	541, 593, 685
4	640	470	462, 515, 582

[a] Studies carried out in acetonitrile−water (v/v) solutions: 22:78 for **1**, 24:76 for **3**, and 11:89 for **4**. Squaraine concentration (mol dm^{-3}) of 4.8×10^{-7} for **1**, 1.2×10^{-6} for **2**, 1.0×10^{-6} for **3**, and 2.9×10^{-6} for **4**. [b] Data obtained in the presence of 1,2:5,6-dibenzanthracene.

The number of molecules in the aggregates can be estimated following a Benesi−Hildebrand-type analysis,[7] which results in an aggregation number of ca. 3 molecules for the band at 563 nm in **1**. In acetonitrile−water 22:78 (v/v) the squaraine derivative **1** shows similar intensity in both visible absorption bands due to the monomer (642 nm) and the aggregated species (563 nm). After addition of aromatic hydrocarbons, the band at 563 is enhanced, whereas the intensity of the monomer band decreases (aggregation is favored). This can be observed in Figure 2, which shows the changes in the absorbance of receptor **1** in acetonitrile−water 22:78 (v/v) solutions upon addition of 10 equiv of benzo[*a*]pyrene. The inset in Figure 2 shows the dual chromogenic signaling achieved via the intensity variations of both the monomer and the aggregated bands. Preliminary studies revealed that the monomer−aggregation equilibrium was not affected by the presence of typical anions and cations.[8]

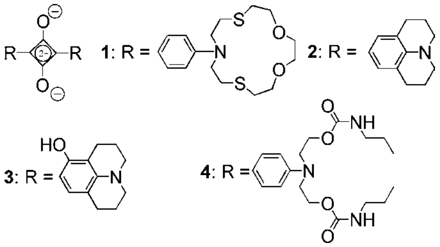

Figure 1. Representation of squaraine derivatives **1**−**4**.

Similar studies carried out with **4** in acetonitrile−water 11:89 v/v mixtures showed two absorption bands, one due to the monomer at 640 nm and the other due to H-aggregates at 470 nm with an aggregation number of 5 (following a

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(3) Different blue-shifted and red-shifted aggregated forms have been reported in the literature for squaraine derivatives in mixed aqueous media. See for instance: (a) McKerrow, A. J.; Buncel, E.; Kazmaier, P. M. *Can. J. Chem.* **1995**, *73*, 1605. (b) Liang, K.; Law, K. Y.; Whitten, D. G. *J. Phys. Chem.* **1994**, *98*, 13379. (c) Das, S.; Thanulingam, T. L.; Thomas, K. G.; Kamat, P. V.; George, M. V. *J. Phys. Chem.* **1993**, *97*, 13620.

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(5) See: (a) Iverson, B. L.; Shreder, K.; Král, V.; Sansom, P.; Lynch, V.; Sessler, J. L. *J. Am. Chem. Soc.* **1996**, *118*, 1608. (b) Sessler, J. L.; Andrievsky, A.; Král, V.; Lynch, V. *J. Am. Chem. Soc.* **1997**, *119*, 9385. (c) Král, V.; Andrievsky, A.; Sessler, J. L. *J. Chem. Soc., Chem. Commun.* **1995**, 2349. (d) Sessler, J. L.; Davis, J. M.; Král, V.; Kimbrough, T.; Lynch, V. *Org. Biomol. Chem.* **2003**, *1*, 4113.

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(7) Chen, H.; Farahat, M. S.; Law, K.-Y.; Whitten, D. G. *J. Am. Chem. Soc.* **1996**, *118*, 2584.

(8) Anion and cations such as F$^-$, Cl$^-$, Br$^-$, NO$_3^-$, phosphate, sulphate, acetate, benzoate, Fe^{3+}, Cu^{2+}, Ni^{2+}, Cd^{2+}, Pb^{2+}, Zn^{2+}, Li$^+$, Na$^+$, K$^+$, Mg^{2+}, Ca^{2+}, or Ba^{2+} at a concentration as high as 4.0×10^{-4} mol dm^{-3} showed no significant effect. The Hg^{2+} and Ag$^+$ cations affect the aggregation equilibrium in **1** due to metal coordination with the dithia-dioxa-aza crown. See: Ros-Lis, J. V.; Martínez-Máñez, R.; Rurack, K.; Sancenón, F.; Soto, J.; Spieles, M. *Inorg. Chem.* **2004**, *43*, 5183.

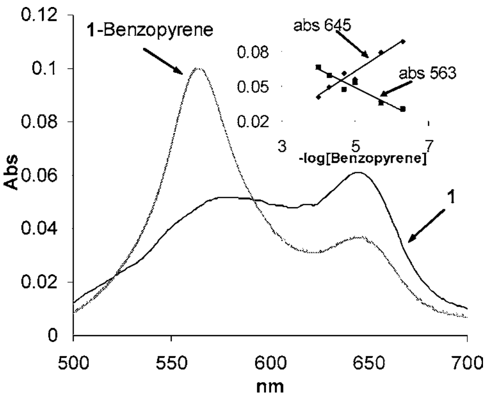

Figure 2. Absorption spectra of **1** and **1**-benzopyrene in acetonitrile−water 28:72 (v/v). [**1**] = 4.2 × 10^{-6} mol dm^{-3}. Inset: changes in the monomer and aggregated bands upon titration of **1** with benzo[*a*]pyrene under similar conditions.

Benesi−Hildebrand-type analysis). In this case, the addition of aromatic hydrocarbons results in the appearance of bands at 515 and 585 nm corresponding to aggregates with four and three molecules, respectively.

As observed for **1**, the addition of aromatic hydrocarbons to **4** produces an increase in the aggregated species and attenuation in monomer concentration. Additionally, as shown with compound **1**, a general tendency to reduce the aggregation number (from 5 to 4 and 3) can also be observed. The squaraine **2** did not reveal any aggregation processes, whereas for **3** the addition of aromatic hydrocarbons showed evidence of a similar tendency to increase the aggregation. In all cases, the guest-induced aggregation processes are coupled with remarkable color variations.

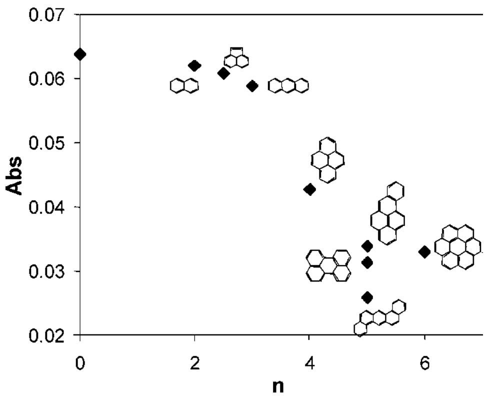

Figure 3. Absorbance of **1** at 642 nm in the presence of aromatic hydrocarbons containing a different number of aromatic rings (*n*) in acetonitrile−water 28:72 v/v solutions. [**1**] = 4.2 × 10^{-6} mol dm^{-3}; [aromatic hydrocarbons] = 4.2 × 10^{-5} mol dm^{-3}.

Further results can be observed in Figure 3, where the effect that selected aromatic hydrocarbons (naphthalene, acenaphthylene, anthracene, pyrene, benzo[*a*]pyrene, perylene, 1,2:5,6-dibenzanthracene, and coronene) have on acetonitrile−water solutions of **1** is shown. In Figure 3, the absorbance observed at the monomer band (642 nm) is plotted as a function of the number of aromatic rings. Whereas aromatic hydrocarbons of low molecular mass ($n \leq 3$) induce a very small change, aromatic hydrocarbons with a larger number of fused rings induce a noteworthy chromogenic hypochromic and hyperchromic dual-signaling variation of the 642 and 563 nm bands. This discrimination is of particular interest given that the higher the number of fused rings in polyaromatic hydrocarbons, the stronger their carcinogenic effect. For instance, compounds 1,2:5,6-dibenzanthracene and benzo[*a*]pyrene are among the most toxic nonderivatized aromatic hydrocarbons.[9]

The experimental results revealed that (i) an increase in the concentration of aromatic hydrocarbon produces an increase in the aggregation process (see Figure 2, which shows the increase in intensity of the band due to the aggregated form (at 563 nm) as the concentration of 1-benzopyrene increases) and (ii) an increase in the number of fused rings also produce an increase in the aggregation (see Figure 3). These observations appear to be indicative of hydrophobic interactions. For instance, a tendency toward an increase in aggregation as the length of N-appended hydrocarbon chains increases has also been witnessed in a family of squaraine derivatives and has also been attributed to hydrophobic-type interactions.[7]

In summary, we have shown that squaraine derivatives can display suitable physical and photophysical properties for the colorimetric sensing of neutral guests via hydrophobic interactions coupled with an enhancement of aggregation processes. In this case, we have reported the colorimetric sensing of aromatic hydrocarbons as representative neutral guests without any a functional group. A remarkable signaling of aromatic hydrocarbons with a large number of fused rings over aromatic hydrocarbons of low molecular mass ($n \leq 3$) has been found. We are currently exploring the use of other colorimetric supramolecular aggregation−disaggregation processes in aqueous solution and the use of this new design principle, alone or in combination with other proposed methods of sensing, for the development of new chromogenic signaling protocols for neutral species of interest.

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Supporting Information Available: Experimental details, Figures S1−4, and details of Benesi−Hildebrand analysis. This material is available free of charge via the Internet at http://pubs.acs.org.

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