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Photochromism of flavylium systems. An overview of a versatile multistate system

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ABSTRACT

Flavylium is the basic structure of anthocyanins, an important family of natural dyes responsible for the color in many flowers and fruits. While anthocyanins *in vitro* are involved in a pH dependent equilibrium between a flavylium cation (acidic species) and a hemiketal (as major basic species), some synthetic flavylium compounds present the *trans*-chalcone as the major basic species. In this case irradiation of the *trans*-chalcone leads to appearance of colored products, either a flavylium cation and/or a quinoidal base, via *cis*-chalcone and hemiketal. Taking profit from the complexity of the network it is possible to design photochromic systems, exhibiting a thermal back reaction, or models for optical memories, when the back reaction is prevented. The flavylium photochromism was also observed in ionic liquids, gels, micelles and reversed micelles opening up possible applications. In this work an overview of the photochromism of synthetic flavylium compounds is presented, from the first observations of the light effect to recent developments.

1. Historical background

The compounds described through this work are all derivatives of the 2-arylbenzopyrylium (flavylium), Fig. 1. This important family comprises anthocyanins, the ubiquitous colorants responsible for most of the beautiful colors in flowers and fruits. Anthocyanins are benzopyrylium derivatives characterized by the existence of a glucoside in position 3 (monoglucoside). A sugar can also be simultaneously present in position 5 (diglucosides) or, less frequently, in position 7 [1]. In anthocyanidins the hydroxy groups take the positions of the glucosides, leading to unstable structures in solution [2], while desoxyanthocyanins are anthocyanins lacking the glucoside in position 3 (but bearing a glucoside in position 5).

The history of the synthetic flavylium compounds (the photochromic compounds described through this work) and the natural flavylium compounds, have been interconnected since their respective discovery. This is not surprising taken into account that both groups are derivatives of 2-aryl-1-benzopyrylium. As far as we known, the first reference to flavylium compounds regards precisely the synthetic compounds, 4-methyl-7-hydroxyflavylium described by Bülow in 1901 [3], Scheme 1. A decade latter, the celebrated chemist Willstätter [4,5], was able to elucidate the structure of anthocyanins and synthesize three anthocyanidins, Fig. 2. The same anthocyanidins were independently prepared by Robinson [6] who latter was able to synthesize and isolate anthocyanines from the plants anthocyanins [7].

1.1. The network of chemical reactions

Scheme 2 summarizes the network of chemical reactions involving flavylium compounds in acidic to neutral pH values. The equilibrium species at sufficiently acidic pH values is the flavylium cation, **AH$^+$**. When the pH is raised the flavylium cation can be involved in two parallel reactions: i) proton transfer to form the quinoidal base, **A**, ii) hydration to give the hemiketal, **B**. The proton transfer is faster than the hydration but in many cases the other basic species (**B**, **Cc**, **Ct**) are more stable than **A** at equilibrium. This means that **A** can be formed as a kinetic product during the first instance of the pH increase, and later totally or partially disappears to give the equilibrium distribution of species. The *cis*-chalcone (**Cc**) is formed from **B** by a tautomeric process and the *trans*-chalcone (**Ct**) by isomerization of the former. It is worth noting that the colored species are **AH$^+$** and **A**, in common anthocyanins which are red and blue respectively. Photochemistry arises from the *trans* to *cis* isomerization, which depending on pH, leads to the colored species **AH$^+$** and **A**, see below.

The elucidation of the chemical reactions reported in Scheme 2 is another example how the history of natural and synthetic compounds has crossed through the years. The sequence of chemical reactions involving the network was established by

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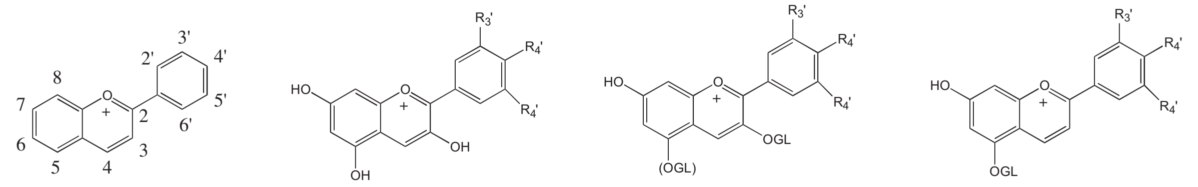


Flavylium Anthocyanidin Anthocyanin Deoxyanthocyanin

Fig. 1. Example of benzopyrylium compounds [1,2].

Dubois and Brouillard (anthocyanins) [8–10], in particular a crucial point of the kinetic process: at moderately acidic pH values **B** is formed from hydration of $\mathbf{AH}^+$ and not from **A** [11]. Initially these authors gave less importance to the formation of the *trans*-chalcone because this species is minor in common anthocyanins at room temperature. Only after the work of McClelland carried out with synthetic flavylium salts, where a *trans*-chalcone is the major species at moderately acidic pH values [12], a clear outlook of the network was available. It is worth to note that following their work on synthetic flavylium compounds, Preston and Timberlake [13] were able to identify what presently we known to be a *trans*-chalcone of malvidin-3-glucoside (but they considered to be the *cis* isomer) by heating a solution at 100 °C followed by separation by HPLC. A complete elucidation of all of the pH dependent components of the multiple equilibria of malvin (malvidin-3,5-diglucoside) in water was carried out by H. Santos and co-workers using one- and two-dimensional NMR spectroscopy [14].

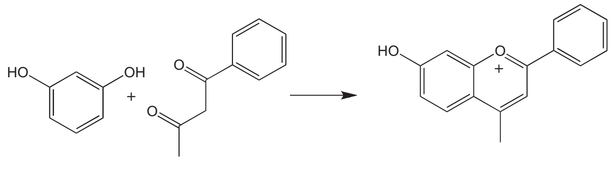
The effect of light in the network of chemical reactions was reported by Timberlak and Bridle [15]. They observed that the true equilibrium of the system is obtained only in darkness. The question is that these authors worked also with anthocyanins, where the mole fraction distribution of the *trans*-chalcone at the equilibrium (room temperature) is small [16] and the photochemical properties difficult to ascertain. Once more, clarity came from the synthetic flavylium compounds, due to the work of Jurd carried out with 7,4′-dihydroxyflavylium and 5,7,4′-trimethoxyflavylium, Fig. 3 [17].

Jurd proposed the facile isomerization of the *trans*-chalcone, to form the *cis*-analog followed by cyclization to give the flavylium. Jurd carryied out his studies before the work of Dubois and Brouillard and used the (incorrect) sequence $\mathbf{AH}^+ \Leftrightarrow \mathbf{A} \Leftrightarrow \mathbf{B} \Leftrightarrow \mathbf{Cc} \Leftrightarrow \mathbf{Ct}$ accepted at that time. While he was able to touch the essential, a full explanation of the photochemical process could not be done at the time. The complete elucidation of the photochemistry of the flavylium network was reported only in 1984, for the compound 7,4′-dihydroxyflavylium [18].

2. Mathematical model for the thermal equilibrium of the flavylium network

The complex network of flavylium compounds in water is accounted for by eq. (1) to eq. (4) [9,10,19,20],

$$\mathbf{AH}^+ + \mathrm{H_2O} \rightleftharpoons \mathbf{A} + \mathrm{H_3O}^+ \quad K_a \text{ Proton transfer} \tag{1}$$



Scheme 1. Büllow synthetic flavylium compound.

$$\mathbf{AH}^+ + 2\mathrm{H_2O} \rightleftharpoons \mathbf{B} + \mathrm{H_3O}^+ \quad K_h \text{ Hydration} \tag{2}$$

$$\mathbf{B} \rightleftharpoons \mathbf{Cc} \qquad K_t \text{ Tautomerization} \tag{3}$$

$$\mathbf{Cc} \rightleftharpoons \mathbf{Ct} \qquad K_i \text{ Isomerization} \tag{4}$$

Eqs. (1)–(4) can be summarized in a single acid–base equilibrium, in which **CB** represents all species existing in basic conditions (**A**, **B**, **Cc** and **Ct**).

$$\mathbf{AH}^+\mathrm{H_2O} \rightleftharpoons \mathbf{CB} + \mathrm{H_3O}^+ \quad K'_a = \frac{[\mathrm{CB}]\left[\mathrm{H_3O}^+\right]}{\left[\mathrm{AH}^+\right]} \tag{5}$$

$$K'_a = K_a + K_h + K_hK_t + K_hK_tK_i \quad [\mathbf{CB}] = [\mathbf{Ct}] + [\mathbf{Cc}] + [\mathbf{B}] + [\mathbf{A}] \tag{6}$$

The mole fraction distribution of the different species is calculated as follows:

$$\begin{aligned}\chi_{\mathbf{AH}^+} &= \frac{\left[\mathrm{H}^+\right]}{\left[\mathrm{H}^+\right] + K'_a};\ \chi_{\mathbf{A}} = \frac{K_a}{\left[\mathrm{H}^+\right] + K'_a}\ \chi_{\mathbf{B}} = \frac{K_h}{\left[\mathrm{H}^+\right] + K'_a}\ \chi_{\mathbf{Cc}} \\ &= \frac{K_hK_t}{\left[\mathrm{H}^+\right] + K'_a}\ \chi_{\mathbf{Ct}} = \frac{K_hK_tK_i}{\left[\mathrm{H}^+\right] + K'_a}\end{aligned} \tag{7}$$

Experimentally, a routine procedure based on pH dependent UV–VIS spectroscopy, NMR spectroscopy and stopped flow measurements enabling the calculation of the equilibrium constants was established [20, 21].

A convenient way to represent the flavylium network is the use of an energy level diagram where the Gibbs free energy, ΔG°, of the different equilibria is represented at different pH values, Scheme 3 [22].

At low pH values $\mathbf{AH}^+$ is the most stable species. As pH increases the components of the conjugated base **CB** become the more stable species, the respective equilibrium concentrations depending on their relative energy levels. This diagram is also useful to account for the kinetic process, see below. As an alternative the flavylium network can be described through the mole fraction distribution of the several species by means of eq. (7), see Fig. 4.

3. The pseudo-equilibrium

The pseudo-equilibrium can be assumed when the *cis*–*trans* isomerization barrier is high enough to slow the respective isomerization, allowing consideration of the fact that $\mathbf{AH}^+$, **A**, **B** and **Cc** are equilibrated (before significant modification on the concentration of **Ct**). Such a state occurs for example when solutions of the flavylium cation, which is the stable species at low pH values, are basified. The formalism of the pseudo-equilibrium is accounted for by eqs. (1)–(3).

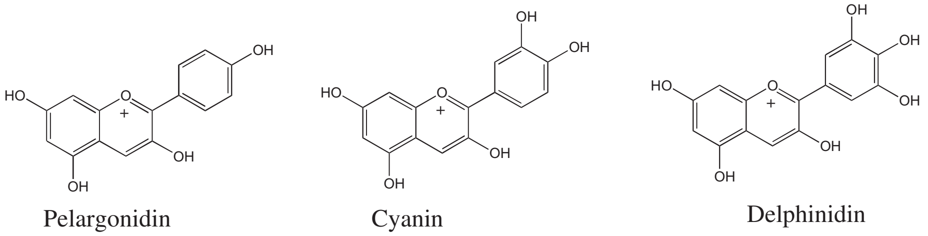


Fig. 2. Willstätter anthocyanidins [4,5].

Eqs. (1)–(3) can be substituted by a single acid–base equilibrium

$$\mathbf{AH}^{+} + \mathrm{H_2O} \rightleftharpoons \mathbf{CB}^{\wedge} + \mathrm{H_3O}^{+} \quad K_a = \frac{\left[\mathrm{CB}^{\wedge}\right]\left[\mathrm{H}^{+}\right]}{\left[\mathrm{AH}^{+}\right]} \tag{8}$$

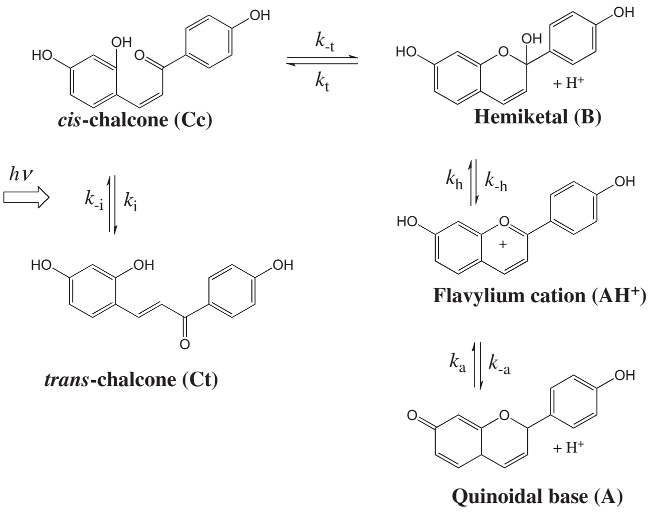
$$K_a^{\wedge} = K_a + k_h + K_h K_t \quad \left[\mathbf{CB}^{\wedge}\right] = [\mathbf{Cc}] + [\mathbf{B}] + [\mathbf{A}] \tag{9}$$

The mole fraction distribution of the different species is calculated as follows:

$$\chi^{\wedge}_{\mathbf{AH}^{+}} = \frac{\left[\mathrm{H}^{+}\right]}{\left[\mathrm{H}^{+}\right] + K_a^{\wedge}};\ \chi^{\wedge}_{\mathbf{A}} = \frac{K_a}{\left[\mathrm{H}^{+}\right] + K_a^{\wedge}};\ \chi^{\wedge}_{\mathbf{B}} = \frac{K_h}{\left[H^{+}\right] + K^{\wedge}};\ \chi^{\wedge}_{\mathbf{Cc}} = \frac{K_h K_t}{\left[\mathrm{H}^{+}\right] + K_a^{\wedge}} \tag{10}$$

4. Kinetic process of the flavylium network

The chemical processes taking place in Scheme 4 can be divided into four different timescales: i) microseconds for proton transfer, ii) seconds to minutes in the case of the hydration, iii) sub-seconds for tautomerization (ring opening and closing), iv) between seconds and days for the *cis–trans* isomerization. Using the appropriate technique it is possible in most cases to separate, if not all, at least three of the four kinetic processes and measure the respective rate constants. The overall kinetic process is highly dependent on the magnitude of the *cis–trans* isomerization barrier. If the barrier is high, the *cis–trans* isomerization occurring between hundreds of minutes to days is the rate-determining step and the four processes can be separated. The proton transfer reaction is very fast and the respective kinetics is available, for example, by means of temperature jump techniques. As shown previously [8,23], the system will approach the first (pseudo) equilibrium exponentially with a rate constant equal to the sum of the forward and backward reactions, $k_{\mathrm{a}} + k_{-\mathrm{a}}[\mathrm{H}^{+}]$. On the other hand, the easiest access to the other kinetics of the system is to carry out pH jumps. For example starting from flavylium cation at very acidic pH values to moderately acidic, leads to the immediate formation of the quinoidal base, **A**, as a kinetic product (not possible to follow by stopped flow techniques). The evolution of the system can be monitored by a common spectrophotometer or by stopped flow if the respective process takes place in the millisecond–second scale of time. The disappearance of **A** occurs through the hydration reaction of **AH**$^{+}$ to give **B** [24] (and not **A** to give **B**), followed by the tautomerization of **B** leading to **Cc**. In other words, **A** disappears because **AH**$^{+}$ disappears (both species are in very fast equilibrium). The rate-determining step of this process is usually the hydration and by consequence the system will approach the second (pseudo) equilibrium exponentially with a rate constant given by $k_{\mathrm{hydration}} = ([\mathrm{H}^{+}]/[\mathrm{H}^{+}] + K_a)k_h + (1 + K_t)k_{-h}[\mathrm{H}^{+}]$. Finally the slowest isomerization leading to the final equilibrium is given by $k_{\mathrm{isomerization}} = (K_h K_t/[\mathrm{H}^{+}] + K_a^{\wedge})k_i + k_{-i}$. This procedure does not permit the complete calculation of all the rate and equilibrium constants, and therefore another independent equation is needed. More information about the kinetics of the system can be achieved if the so-called reverse pH jumps are performed. The idea is to reach the pseudo-equilibrium mentioned above, before interference of the *trans*-chalcone, and follow, by stopped flow, the reacidification of the system. As the rate of the hydration reaction depends on the proton concentration, and can be made faster by increasing [H^{+}], it is possible to observe, for a flavylium compound lacking the quinoidal base (at sufficiently high proton concentration), a bi-exponential formation of the flavylium cation the initial kinetics being due to the hydration, and the second kinetics due to the tautomerization, i.e., (formation of AH^{+} from Cc through B), Fig. 5. The ratio of the amplitudes of the two curves leads directly to the equilibrium constant K_t, eq. (3). Moreover, in the case of flavylium compounds having the quinoidal base, A, at the pseudo-equilibrium an increase of the absorbance of the flavylium cation occurs during the mixing time of the stopped flow will appear at the initial time (proton transfer occurring during the mixing time).



Scheme 2.

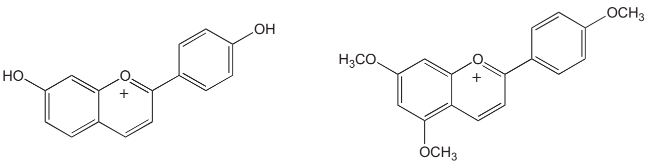
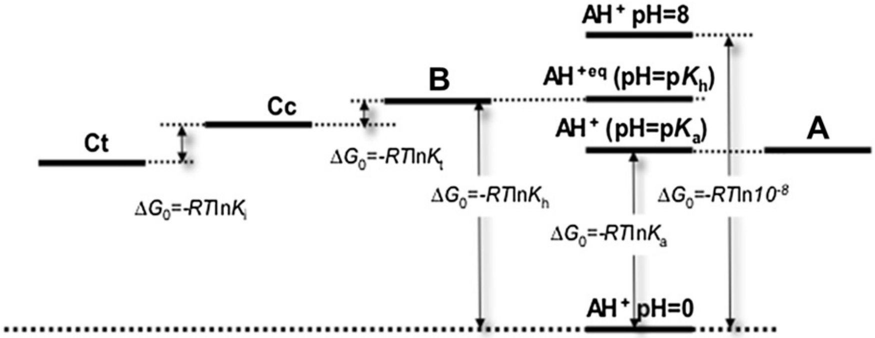


Fig. 3. 7,4′-dihydroxyflavylium and 5,7,4′-trimethoxyflavylium.



Scheme 3.

On the other hand, if the barrier is small the *cis–trans* isomerization can compete with the hydration–dehydration and the overall kinetic process is more complex. In the case of the flavylium compounds bearing a 7-hydroxy substituent, the system can be approximately described as in Scheme 4 where the hydration and the *cis–trans* isomerization are the rate controlling steps. In other words: **B** and **Cc** can be considered in fast equilibrium behaving kinetically as a single species, and the same reasoning can be made for the pair $\mathbf{AH^+}$ and **A**.

As shown elsewhere [25], application of the quasi-steady-state for **Cc** in equilibrium with **B** gives eq. (11)

$$k_{obs} = \left(\frac{\frac{[H^+]}{[H^+] + K_a} K_h K_t K_i + [H^+]}{\frac{K_t K_i}{k_{-h}} + \frac{[H^+]}{k_{-h}}} \right) \qquad (11)$$

Representation of eq. (11) as a function of pH is a bell shape curve with k_{-i} as a limit for low pHs and zero as upper limit for high pHs, Fig. 6 [10].

5. Photochemistry

It is easy to show that the quantum yield in the case of compounds lacking the *cis–trans* isomerization barrier is given by eq. (12) [45].

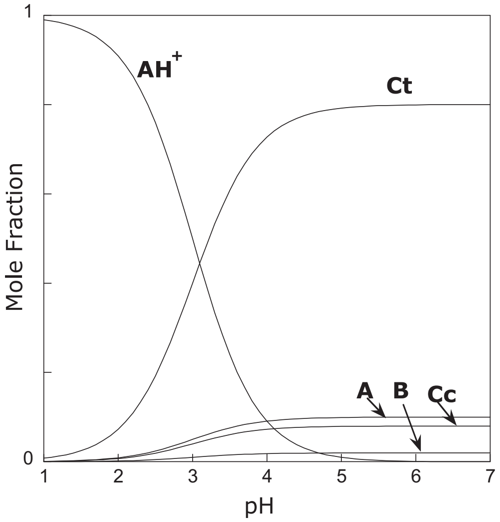


Fig. 4. Example of a mole fraction distribution of the flavylium network.

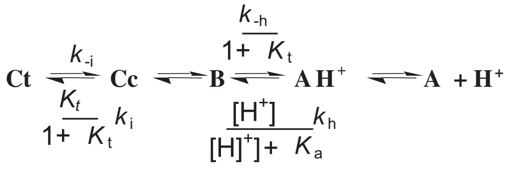
$$\Phi = \Phi_{\mathbf{Ct} \rightarrow \mathbf{Cc}} \frac{[H^+]}{[H^+] + \frac{k_i K_T}{k_{-h}}} \qquad (12)$$

where Φ represents the photochromic quantum yields measured at each pH, by the method of the initial slope. In Fig. 7 the quantum yields of the compound 7,4′-dihydroxyflavylium are represented according to eq. (12).

5.1. Maximizing the photochromic production of color. The concept of auto-lock pH

The selection of the pH to obtain the best performance (i.e., intense color) of a photochromic system based on the flavylium network is a balance between two contradictory requirements: i) the highest possible proton concentration to force the system to go forward from **Ct** to the formation of $\mathbf{AH^+/A}$ on the competition to the backward reaction that restores **Ct** in the case of systems lacking the *cis–trans* isomerization barrier, or when there is a *cis–trans* isomerization barrier to allow formation of the colored species instead of **Cc** and **B**, and ii) a sufficiently low proton concentration otherwise $\mathbf{AH^+}$ is the dominant species at the equilibrium and color exists prior to the irradiation. In the case of compounds bearing a high *cis–trans* isomerization barrier the auto-lock pH should be the one marked with the arrow in Fig. 8A: it decreases the amount of $\mathbf{AH^+}$ in the darkened state, and maximizes the colored $\mathbf{AH^+}$ species. Fig. 8A illustrates the simplest situation of an equilibrium involving $\mathbf{AH^+}$ and **Ct**, but it can be easily generalized when more species are involved.

In the case of compounds lacking the *cis–trans* isomerization barrier, as for example 7,4′-dihydroxyflavylium, a photostationary state that depends on the light intensity, quantum yields and molar absorption coefficients of the *cis* and *trans*-chalcones is achieved as reproduced in Fig. 8B. Considering the maximum production of color at the photostationary state, the pHs of the plateau are those where the major contrast between dark and irradiated solutions is observed.



Scheme 4.

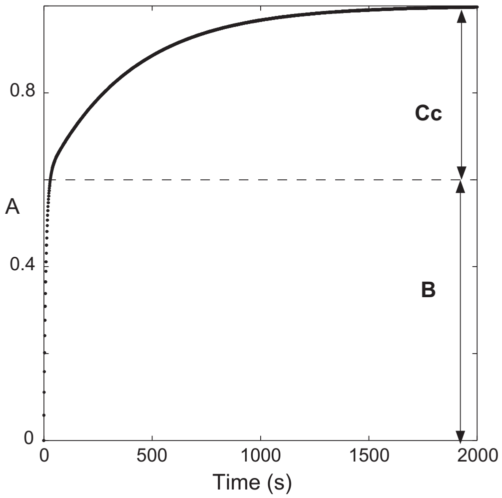


Fig. 5. Example of the stopped flow trace of a reverse pH jump monitored at a flavylium cation absorption wavelength.

6. Stopped flow measurements

As mentioned above, one powerful method to study the flavylium network is the use of the stopped flow technique. Kinetic information can be achieved by carrying out pH jumps from equilibrated solutions of the flavylium cation (at acidic pH values) to higher pH values. In the case of compounds possessing hydroxy substituents, the quinoidal base is the first product to be formed (as discussed above) and the subsequent kinetic processes are generally sufficiently slow to be followed by a common spectrophotometer. However in some cases a stopped flow apparatus should be used, because the disappearance of **A** takes place in the sub-second time scale. Stopped flow should also be used to monitor the reverse pH jumps, as mentioned above. In this case the flavylium cation (acidic pH values) is converted into the species **Cc** and **B** by changing the pH to higher values. This solution is then re-acidified (before formation of **Ct**) and the absorption monitored. Fig. 9 shows the traces obtained for different (final) pH values. For final acidic pHs the data is fitted with two exponentials: i) the first process resulting from the conversion of **B** into **AH$^+$** (pH dependent), and the second from the conversion of **Cc** into more **AH$^+$** via **B**. For low proton concentration the rate-determining step becomes the dehydration, **B** to give **AH$^+$** and a single exponential is observed. When the two exponentials are observed their ratio is proportional to the amount of **B** and **Cc** at the pseudo-equilibrium allowing the equilibrium constant K_t, eq. (3), to be obtained. Moreover the pH dependence of the hydration reaction gives information about the rate constants k_h and k_{-h}.

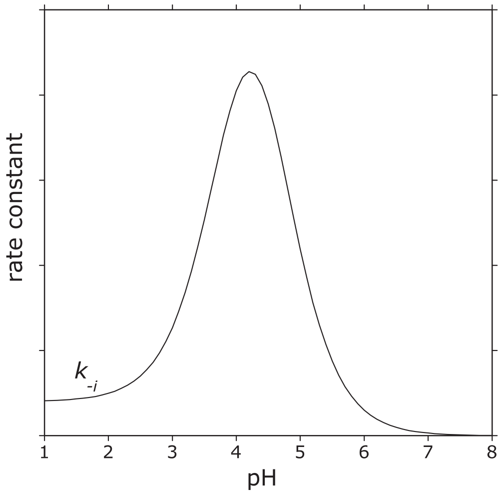


Fig. 6. Example of the pH dependence of the observed rate constant of a flavylium network lacking the *cis–trans* isomerization barrier.

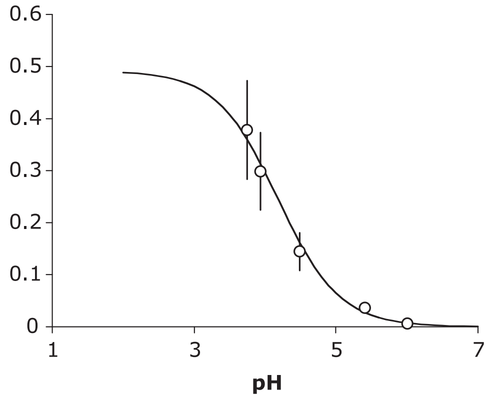


Fig. 7. Photochromic quantum yields fitted with eq. (12).

7. Flash photolysis

The use of flash photolysis to study the network of flavylium compounds was introduced by Pina and Maestri in 1997 [22]. In Fig. 10, the flash photolysis traces of the compound 7,4′-dihydroxyflavylium are presented at different pH values, following the absorption of **Ct** (360 nm) and flavylium (460 nm). Immediately after the flash, the bleaching of the **Ct** absorption is observed indicating that this species is consumed to give **Cc**, which is expected by analogy with other flavylium compounds, to possess a lower molar absorption coefficient at this wavelength. Subsequently, two processes exhibiting the same lifetime are observed: i) recovery of **Ct** absorption (bottom), and ii) formation of **AH$^+$** (top). As the pH increases, the amount of flavylium cation decreases with concomitant increase of **Ct** recovery.

The global kinetics is compatible with eq. (13)

$$k_{\text{flash}} = \frac{k_{-h}}{1+K_t}\left[\mathrm{H}^+\right] + \frac{k_i K_t}{1+K_t} \tag{13}$$

Eq. (13) is valid in the framework of the approximation of eq. (11), i.e., both hydration and *cis–trans* isomerization are much slower than the tautomerization and, in this case, a linear relation of the rate constant as a function of the proton concentration should be observed. For high concentration of protons the hydration could become faster than the tautomerization and the linear relationship is not observed.

In compounds possessing the *cis–trans* isomerization barrier no recovery of the absorption of **Ct** occurs and only the increase of the absorption due to the formation of the flavylium cation is detected.

8. Information storage and neuronal behavior

A photon is simultaneously a quantum of energy and a bit of information, Scheme 5. Energy conversion exploits the first property while the second one deals with molecular-level switching devices capable of generation, conversion, storage and detection of signals; a subject coined semiochemistry by J.-M. Lehn [27].

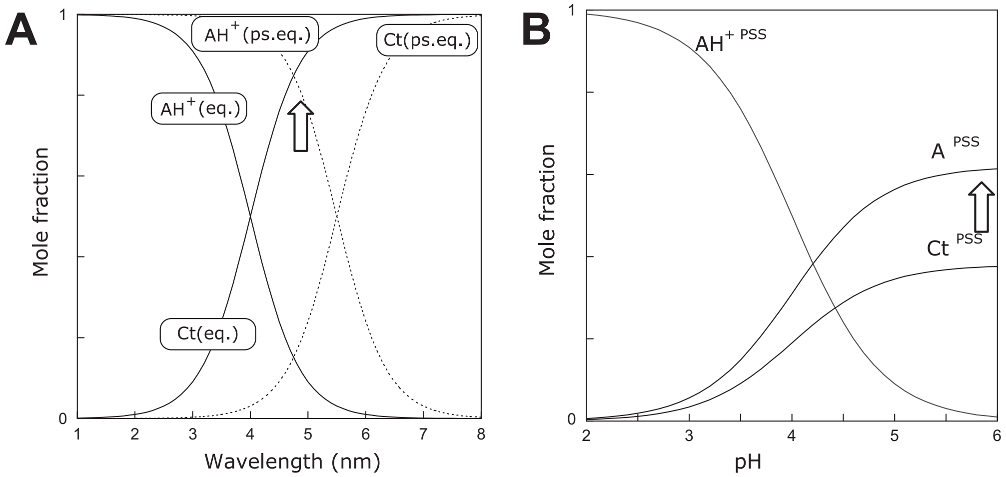


Fig. 8. Auto-lock definition for compounds bearing a *cis-trans* isomerization barrier (A) or lacking it (B): ps.eq. represents the pseudo-equilibrium and PSS the photostationary state.

8.1. Models for optical memories

By definition, a photochromic system gives rise to a photoproduct that should revert back to the initial state (dark one). Such a system can be used to simulate a temporary optical memory, but not a permanent one, which implies the irreversibility of the photoproduct to prevent the auto-erasing of the signal [28]. This is not an easy task to accomplish with a common photochromic system. However the peculiarities of the flavylium network render this *desideratum* possible, Scheme 6.

The key step to produce a model for a permanent optical memory is the introduction of a second input, addition of protons immediately after the light input, i.e., write followed by lock [29]. The existence of a thermal *cis*–*trans* isomerization barrier is a necessary requirement, to avoid the back reaction of **Cc** to **Ct** between the two inputs. The addition of protons transforms, in the time of sub-seconds, the *cis*-chalcone into the flavylium cation, which is the signal output. **AH**$^+$ is thermodynamically stable at low pH values and can be read without erase. In order to re-use the memory it is necessary to neutralize the acid previously introduced to form **Cc** (**B**), and the system will tend to form the thermodynamically stable species at higher pH values the **Ct** form (erase step). Light or heat can accelerate the erasing step. It is questionable if this kind of system will have a practical application, because it works in solution and protons have to be added and neutralized (mass addition). However the brain is not a solid device and in cells the protons play a role of a stimulus in many processes of life. Moreover, the flavylium system can be incorporated in polymers and gels, and possible applications on this theme can be envisaged.

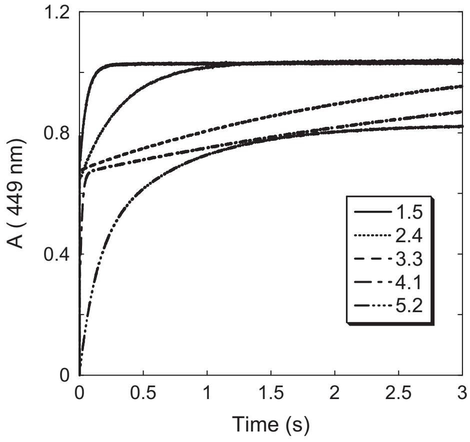


Fig. 9. Stopped flow traces of the compound 4′-methoxyflavylium 2.4×10^{-5} M, in the presence of SDS micelles 0.1 M after a pH jump from pseudo-equilibrated solutions at pH = 8.0. Final pHs in the inset [26].

A more complex model system was achieved with the compound 4′-hydroxyflavylium, Scheme 6 (up-right) [30]. Considering the cycle commences at pH = 4, the write-lock-read is made as in the previous example. The unlock (back to pH = 4) and erase steps are, in this compound, very slow, but profit can be taken by changing the pH to 12. In this case the **AH**$^+$ species is immediately transformed into **A** and through the attack of OH$^-$ into **Cc**$^{2-}$. The last one is slowly transformed into **Ct**$^{2-}$, due to the high barrier for the isomerization also in basic solutions in this compound. The process can be accelerated by light. In other words, after the write step form **Ct** (pH = 4) that forms **Cc**, if the pH is increased to 12 instead of decreased to 1, a shallow memory is obtained. On the other hand, **Cc**$^{2-}$ can be used to write if this step is carried out after the memory is enabled i.e., prepare the **Cc**$^{2-}$ species from **Cc** and apply the light immediately. The final reset is obtained by transforming **Ct**$^{2-}$ into **Ct** at pH = 4.

Much greater complexity can be achieved if one flavylium is chemically transformed into another flavylium as in Scheme 7 [31]. The compound 4-acetamidoflavylium can perform write–read–erase cycles in acidic and basic medium. However, in very acidic conditions, 4-acetamidoflavylium is transformed in to the 4-aminoflavylium, which in turn gives rise to another series of cycles involving the usual species as well as the protonated chacone at the amino substituent. On the basis of these cycles a step further to illustrate the concept of memory algorithm was provided, Scheme 8 [31]. It is possible to start form **Ct**$^-$, and according to the pH input, make the system follow the circular cycle, or the square cycle, or return back. After operation of the circular cycle a heat input followed by another pH input leads again to alternatives that depend on the pH, and successively as shown in the diagram. Practical applications of such a system are once more questionable, but the fact that it is possible to conceive a molecular system responding to a complex algorithm shows the potential of the network.

8.2. Mimicking a simple function of a neuron

Neurons are very complex structures, but some functions they achieve are simple, as for example accumulation of inputs and after

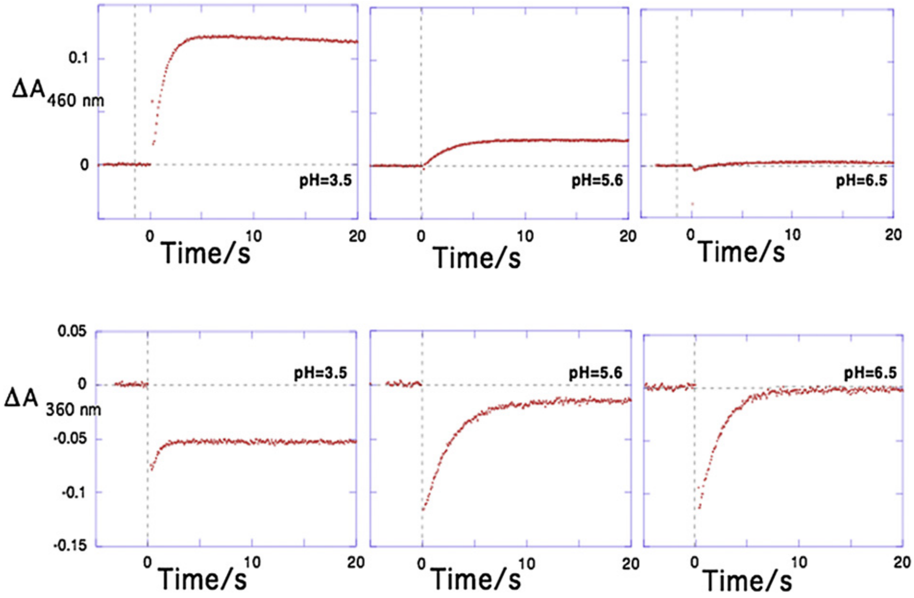


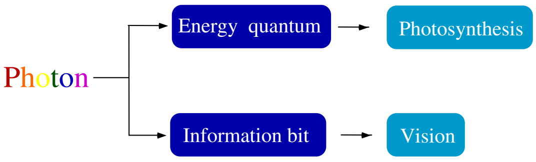
Fig. 10. Traces obtained by flash photolysis monitored at 460 nm (Flavylium cation/quinoidal base) and 360 nm Ct.

a certain threshold give rise to an output signal. The simplest analogous behavior in terms of logic gates is to consider that the sum of two inputs is a different result than each one individually, which mathematically is expressed by an XOR logic gate, see Scheme 9 [32].

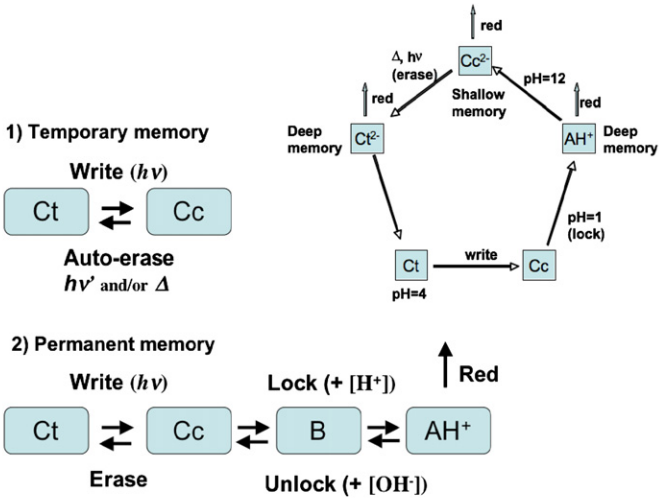
The system is prepared by mixing two photoactive compounds: a *trans*-chalcone and hexacyanocobaltate(III). The light is absorbed by both components, but the *trans*-chalcone picks up the major part of the light during the first stages of the reaction, leading to **AH**$^+$ and the signal appearance. However, the pH of the solutions increases as long as **AH**$^+$ is formed (**AH**$^+$ consumes protons), and the flavylium cation tends to hydrate more and more with consequent disappearance of the signal. Because the pH variation using exclusively the flavylium network is not enough to change the pH to the desired values, the compound hexacyanocobaltate was used to perform this function. Release of the cyanide ligand under light irradiation increases the pH by several units, but this only occurs after consumption of significant quantities of **Ct** (the competing compound for the irradiation light). The final result is the disappearance of the colored flavylium cation, only after a certain irradiation time.

9. On the mechanism of the photochromism of flavylium compounds

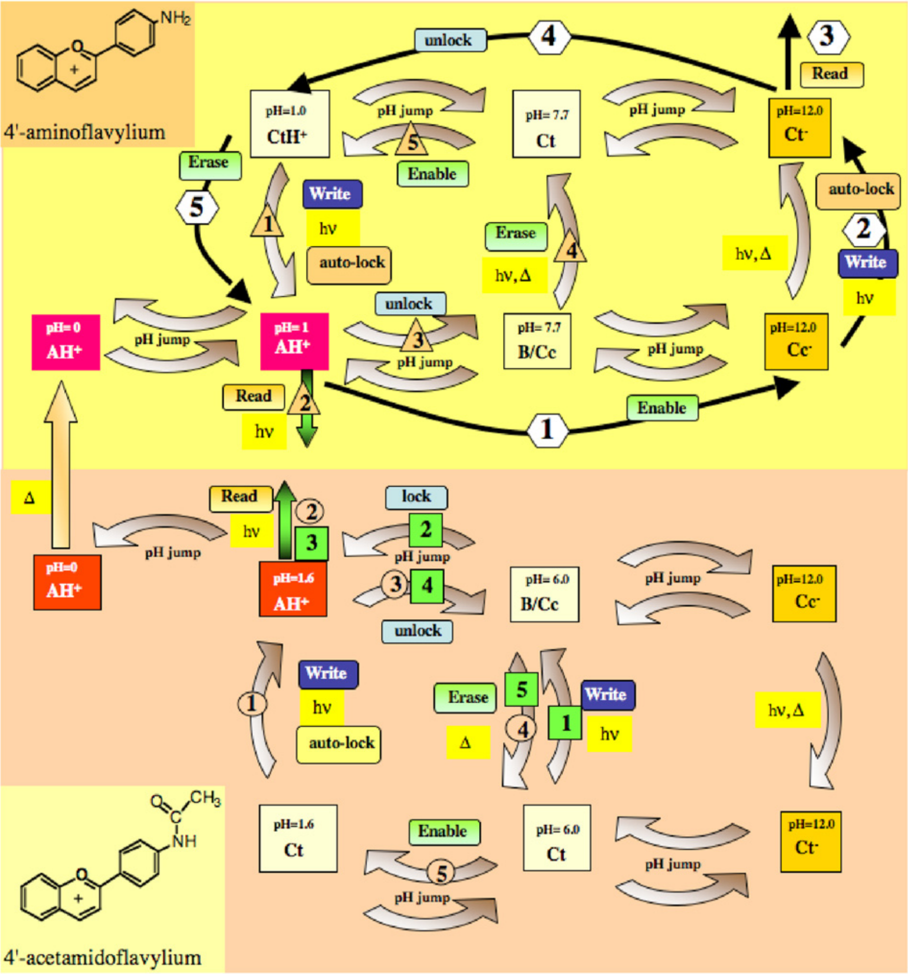
The triggering of the photochromic effect in chalcone systems is the light excitation of these compounds into the S$_1$ state [33]. Once in this electronic state, an excited state *trans*–*cis* isomerization takes place, leading to the formation of *cis*-chalcone in the ground state, which afterward eventually leads to the flavylium cation or base, giving the strong color contrast of these systems. The photoisomerization reaction is, therefore, the most important step for the photochromic effect, and it can be influenced, e.g., by the substituent groups in the chalcone structure, the solvent/medium used and temperature. The chalcone compounds present complex photophysics [34], the photoisomerization reaction being only one of the several processes taking place in the excited state. In fact, some parallels can be drawn between chalcones and other *trans*–*cis* photoisomerization model compounds (such as stilbene) but also with internal charge transfer (ICT) model compounds (such as dimethylaminobenzonitrile, DMABN [35], or substituted stilbenes) [36]. Scheme 10 summarizes the photophysical processes found in *trans*-chalcones reported in literature [34]. Upon light excitation, a locally excited (LE) state of **Ct** is formed, already with some ICT character. From the LE state, several competing processes take place afterward. Intersystem crossing, which has a minor effect on the overall photophysical processes of **Ct**, formation of



Scheme 5.



Scheme 6.



Scheme 7. [31].

a non-fluorescent biradicaloid state *P** with a low dipole moment, twisted in the C=C bond (in close parallels with stilbenes), which eventually leads to the formation of **Cc**, and several so-called TICT (twisted internal charge transfer) processes, either by twisting the bond between the carbonyl and the phenyl group (a non-fluorescent TICT) or by twisting of the amine groups bonded to the phenyl rings (a fluorescent TICT state).

The presence of amine substituents can, therefore, trigger the presence of TICT states that reduce the photochromic efficiency of the system. This is indeed a drawback, since amine derivatives exhibit stronger color contrasts when compared with non-amine derivatives and are more attractive for applications. However such an effect might be tamed by choosing other solvents rather than water. Indeed, TICT states have high dipole moments and are stabilized by the solvent polarity. Moreover, solute-solvent hydrogen bonds have a major role on the **Ct** photophysics. Experimental evidence points out for a strong hydrogen bond between the carbonyl group and protic solvents (such as alcohols or water) in the excited state. These TICT states may also be called HICT states (hydrogen bonded internal charge transfer state) in this regard. If a low polar solvent, with smaller hydrogen bond donor capacity, is chosen, the formation of TICT states can be suppressed to some extent. Therefore LE and *P** are enhanced, leading to an increase of both fluorescent and photoisomerization quantum yield. This phenomenon allows the use of aqueous systems with colloidal domains such as micelles in order to obtain photochromic systems. Although amine groups introduce or enhance TICT states that quench the photoisomerization reaction of **Ct**, micelles and other colloidal domains can greatly enhance the photochromic performance in aqueous environments of these molecules, avoiding the use of organic solvents. Ionic liquids display also similar capabilities, and are a good alternative to aqueous systems.

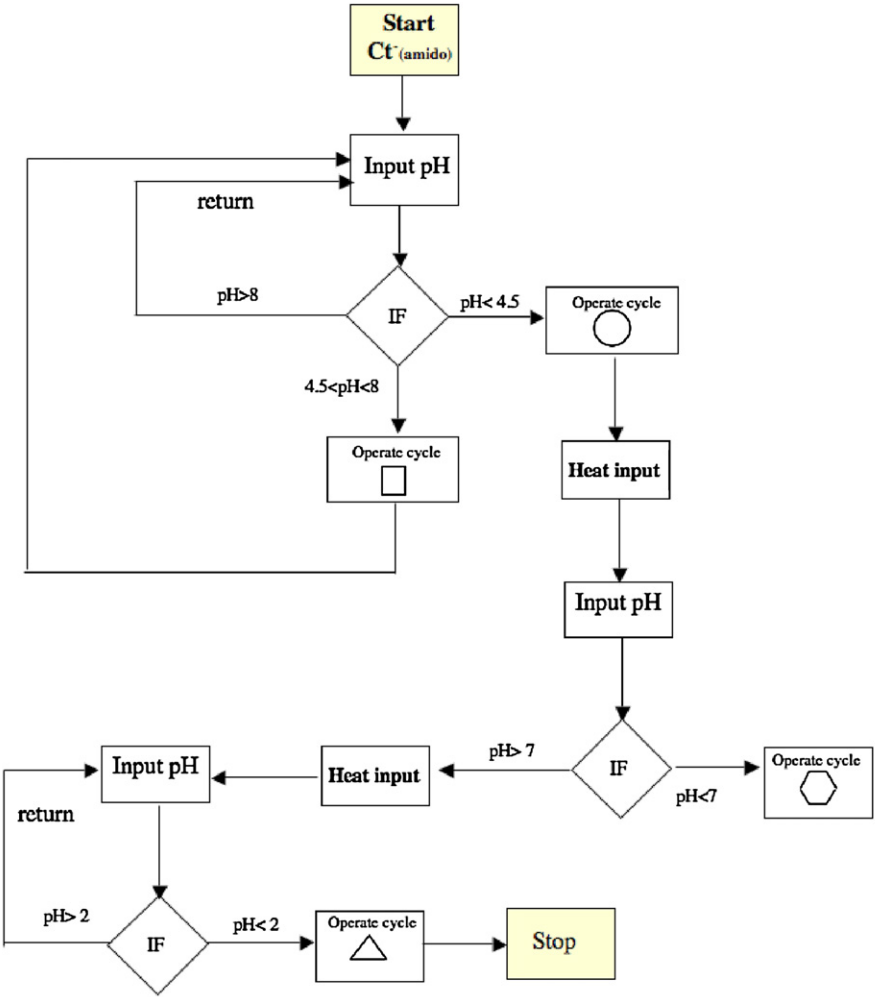
Flavylium cations also display TICT states [37]. Their photophysics is less complicated than chalcones, and some parallels may be drawn with other compounds such as xanthene dyes. In this case, the TICT is a non-emissive state, involving the twist of the phenyl ring and/or of an amine group present in the flavylium cation. In apolar solvents these compounds can exhibit very large fluorescence quantum yields, leading to the proposal of these molecules for laser dyes.

10. Other pyrylium derivatives behaving in the same framework

10.1. 2-Styryl-1-benzopyrylium compounds

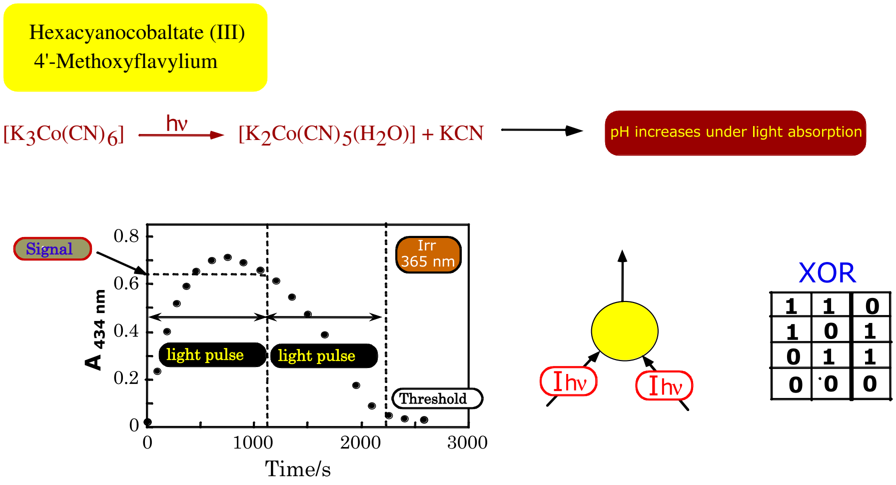
The synthesis of 2-styril-1-benzopyrylium compounds was reported in the ancient literature [38], and they were claimed as food colorants [39]. Recently new derivatives were synthesized and their photochemical properties explored [33,40] (Fig. 11).

Styrylbenzopyrylium derivatives exhibit deeper hues and their absorption spectra are substantially red shifted when



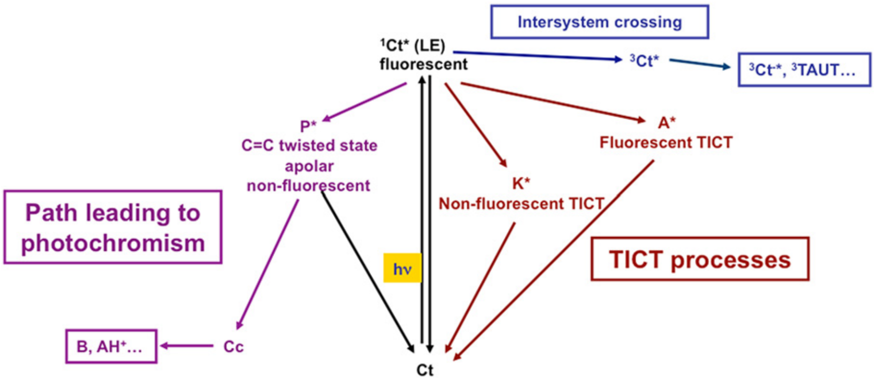
Scheme 8. [31].

compared with 2-arylbenzopyrylium analogs. They follow the same pH and light dependent network of chemical reactions previously described for 2-arylbenzopyrylium compounds. These compounds, however, lack significant photochromism in aqueous solutions. When compared with related flavylium compounds, the corresponding chalcone exhibits larger intersystem crossing and less *trans-cis* photoisomerization in water. Isomerization in the triplet state is not observed, probably due to a competing acid/base reaction, giving rise to the formation of non-reactive $\mathbf{Ct}^-$ and chalcone tautomers in the triplet state (see Scheme 10). Again, the



1	1	0
1	0	1
0	1	1
0	0	0

Scheme 9.



Scheme 10.

introduction of micelles in the aqueous system leads to a substantial increase of *trans*–*cis* photoisomerization and corresponding appearance of photochromic effect. In this compound probably the excited-state barrier for the formation of *P** is too high in aqueous systems, but in more apolar environments of CTAB micelles such barriers are reduced. The polarity effect should, indeed, be quite strong in order to overcome the more viscous environments of micelles, since TICT states are, for this molecule, relatively suppressed. Hence, a photochromic effect appears, taking profit of the unique spectroscopic characteristics of these compounds.

11. Photochromism of flavylium systems toward organized medium

11.1. Flavylium network in micelles

As mentioned above, the flavylium network is affected in the presence of micelles. The compound 4′-hydroxyflavylium was studied in the presence of a positive charged micelle cetyl trimethylammonium bromide (CTAB), neutral Triton X-100 and negatively charged sodium dodecyl sulfate (SDS), Table 1 [41].

The stability of the equilibrium AH^+/A (p*K*a) eq. (1) in the pH window, compared with water, favors the flavylium cation in SDS and the quinoidal base in the other micelles; in the case of CTAB the effect is more pronounced due to the electrostatic repulsion of the cation and the surface of the micelle. An identical trend is observed for the pseudo-equilibrium $pK_a\,\hat{}$ eq. (11), as well as for the final equilibrium pK_a eq. (5)

Micelles affect also the kinetic processes of the network, Table 2. In all cases the quantum yield increases, because the *trans*-chalcone should be solubilized by the more hydrophobic environment of the micelle, see discussion above.

The compound 7,4′-dihydroxyflavylium, similar to the previous one but bearing an additional hydroxy group in position 7, was studied in CTAB micelles [42] and AOT reversed micelles (thermodynamically stable colloidal systems with water droplets dispersed in a oil, stabilized by the surfactant AOT) [43]. Comparing results in CTAB micelles and AOT reversed micelles with the related aqueous system, a strong increase of the **Ct** isomerization quantum yield is found: while in water this value is equal to 0.5 (see Section 5.1), in CTAB micelles it increases to 0.79 and in AOT reversed micelles it approaches unity (see Table 3). Taking into account that the isomerization takes place from the singlet excited state, one possible explanation for the very efficient *trans*–*cis* isomerization in AOT reversed micelles is the decrease of the non-radiative internal conversion through the hydrogen bonds with water and/or a less efficient intersystem crossing. On one hand the **Ct** is located in the hydrophobic region of the reversed micelle interface where the water activity is very low [44], and on the other hand, no triplet absorption could be detected by laser flash photolysis in contrast with the behavior in water.

The photochromic product in AOT reverse micelles is mainly **A**, which enhances significantly the color contrast of the system enabling the extension of the photochromic effect to pH values as high as 8. At pH = 7, **Ct** are the most stable species and irradiation leads to the formation of **A** with a net quantum yield of about 0.9. The reactivity of the hemiketal species in apolar solvents is the explanation given for such effect in AOT reverse micelles. While in water, **B** is stable at pH higher than 3, in more apolar media dehydration can proceed without acid catalysis, i.e., a spontaneous unimolecular process appears increasing significantly the rate of $\mathbf{AH^+/A}$ formation even in basic conditions. Also the partition of the solutes in different places of the reversed micelle helps the photochromic enhancement: in equilibrium conditions, the oil helps to stabilize **Ct**, while under irradiation $\mathbf{AH^+}$ is stabilized by the formation of ion-pairs with AOT (a negatively charged surfactant) and **A** is solubilized in the water pool (see Fig. 12).

The interplay between enhanced **Ct** photoisomerization, stabilization of each species in different micellar environments and different reactivities of intermediate species gives unique features to the flavylium compounds photochromism in this media. This phenomenon was furthered explored in more complex media such as gels and ionic liquids.

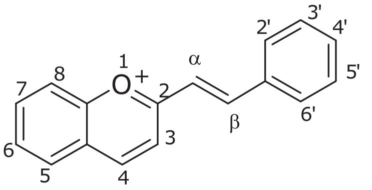


Fig. 11. Structure of 2-Styril-1-benzopyrylium.

Table 1
Equilibria constants in micellar systems.[a]

	CTAB	Triton X	Water	SDS
pK_a	3.1	3.7	5.5	6.7
$pK_a\hat{}$	2.2	2.8	4.4	6.4
pK_a'	1.3	2.0	1.9[b]	3.9

[a] Aqueous solutions 25 °C, unless otherwise noted.

[b] At 25 °C.

Table 2
Kinetic effect of micelles at the auto-lock pH.[a]

	pH	Φ[b]	$K_{\text{write}}/\text{s}^{-1}$[c]	$10^5\ K_{\text{erase}}/\text{s}^{-1}$[d]
CTAB	1.9	0.08	0.09	12.0
Triton X	2.4	0.1	0.06	8.3
SDS	5.5	0.09	2.3[e]	18.0
Water	3.2	0.04	0.7	7.8

[a] Aqueous solutions 25 °C.
[b] Quantum yield of **Ct** → **Cc** photoisomerization.
[c] Rate constant of the "writing" reaction Cc (B) → AH^+.
[d] Rate constant of the "erasing" reaction $\mathbf{AH^+}$ → **Ct**, at 60 °C.
[e] In the flash photolysis detection limit; according to reference [41].

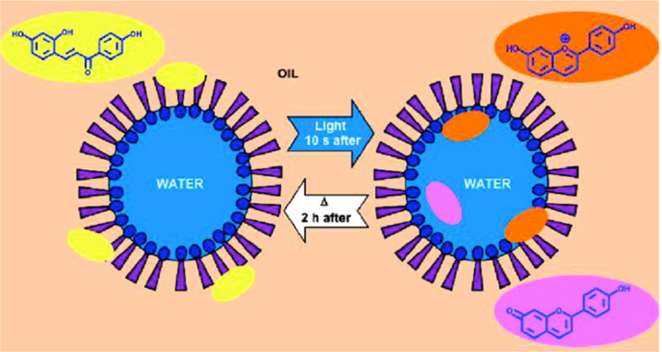


Fig. 12. Schematic description of the photochromism on AOT reversed micelles [43].

11.2. -Flavylium network in gels

Photochromic gels can provide added functionality, as they can be used in a variety of applications that exploit sol–gel transitions with their potential for fabrication of materials in a diversity of useful forms, including films and bulk monoliths. Recently Pina and Hatton described a photochromic system constituted by the incorporation of 7,4′-dihydroxyflavylium and 7-(*N*,*N*-diethylamino)-4′-hydroxyflavylium in matrixes of Pluronic® F-127, a nonionic triblock copolymer, PEO–PPO–PEO, poly(ethylene oxide) (PEO), poly(propylene oxide) (PPO), with a nominal molecular weight of 12 500 and a PEO/PPO ratio of 2:1 by weight. Gels formulated with this polymer afford excellent transparency in the visible region, which makes it a useful matrix for incorporation of photochromic compounds. As shown in Fig. 13, when the temperature of an aqueous solution of Pluronic F-127 is increased, the copolymer molecules aggregate into spherical micelles with a dehydrated PPO core and an outer shell of hydrated, swollen PEO chains. At sufficiently high concentrations and temperatures, Pluronic F-127 micellar solutions form gels which consist of two domains, an outer aqueous environment hospitable to hydrophilic molecules, and more hydrophobic PPO-rich core regions dispersed throughout the gel matrix that are suitable for incorporation of hydrophobic compounds. The temperatures at which micelles and gels form depends on the Pluronic concentration and the concentration of added salts such as buffers [45].

In Fig. 13 (right) the effect of the light on 7-(*N*,*N*-diethylamino)-4′-hydroxyflavylium incorporated in matrixes of Pluronic® F-127, is shown. At moderately acidic pH values the yellow chalcone is the equilibrium species. Its excitation leads to the formation of the red flavylium cation.

11.3. -Flavylium network in ionic liquids

Ionic liquids can constitute another useful matrix to incorporate flavylium compounds [46–48]. In some cases the ionic liquid is not miscible with other solvents and biphasic systems can be obtained. This is the case of the ionic liquid 1-*n*-butyl-3-methyl-imidazolium hexafluorophosphate ([bmim][PF_6]) and water, Fig. 14.

Fig. 14 presents a sequence of photos showing how 7-(*N*,*N*-diethylamino)-4′-hydroxyflavylium is partitioned in the biphasic system constituted by water and the ionic liquid [bmim][PF_6] [46]. Aqueous solutions of 7-(*N*,*N*-diethylamino)-4′-hydroxyflavylium at pH = 1.0 contain exclusively the flavylium cation, $\mathbf{AH^+}$, that diffuses slowly to the ionic liquid phase, remaining at the upper aqueous phase, Fig. 14a. When the system is vigorously shaken and the two phases allowed to separate, the flavylium cation completely dissolves into the ionic liquid phase, Fig. 14b. The upper aqueous phase can be made basic by addition of NaOH (or by substitution of the acidic phase by a basic solution), followed by vigorous shaking of the mixture. When the two phases separate it is possible to see a blue color in the ionic liquid phase due to the base, **A**, Fig. 14c. The blue color ($\mathbf{A^-}$) is not stable and leads to chalcones or ionized chalcones with a rate and protonation stage that are pH dependent. An interesting feature of the system is that at moderately basic pH values of the aqueous solution, it is possible to have the yellow chalcone completely dissolved in the ionic liquid phase (not shown in Fig. 14). On the other hand, high hydroxy concentrations favor the formation of orange $\mathbf{Ct^{2-}}$ that is transferred to the aqueous phase, Fig. 14d. Acidification of this last solution followed by immediate shaking of the two phases, leads to dissolution of $\mathbf{Ct/CtH^+}$ into the ionic liquid, Fig. 14e. The thermal stability of this species in the ionic liquid depends on the amount of proton added. High proton concentrations lead to spontaneous formation of AH^+, while lower proton concentrations allow to obtain the **Ct** species as the thermodynamic product. In conclusion, neutral and mono-charged species will reside preferentially in the ionic liquid, whilst doubly charged species prefer water.

The most interesting feature of this system is, however, its photochromism. When the ionic liquid phase containing **Ct** at pH = 6.8 (measured in the upper aqueous phase) is irradiated, the photochemical product $\mathbf{AH^+}$ appears. More interestingly, the system reverts back to **Ct** after ca. 11 h in the dark, at 22 °C, Fig. 15.

A similar system is obtained when 7,4′-dihydroxyflavylium is incorporated in the same ionic liquid, Fig. 16 [48].

Table 3
Micelle effects in 7,4′-dihydroxyflaylium.[a]

	Water	CTAB	AOT reverse micelles
pK_a	4.0	4.0	3.0
pK_a'	3.0	0.2	1.7
Φ	0.5	0.79	0.94

[a] Aqueous solutions 25 °C, unless otherwise noted.

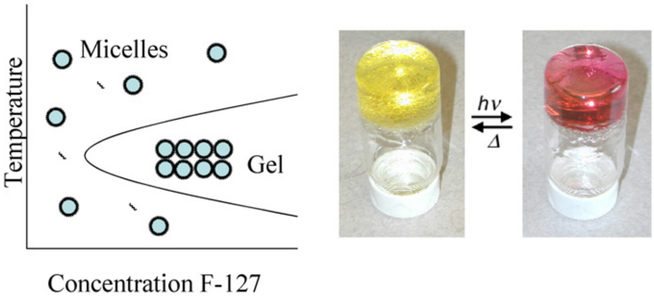


Fig. 13. Schematic phase diagram of Pluronic F-127 aqueous solutions and example of the photochromic effect.

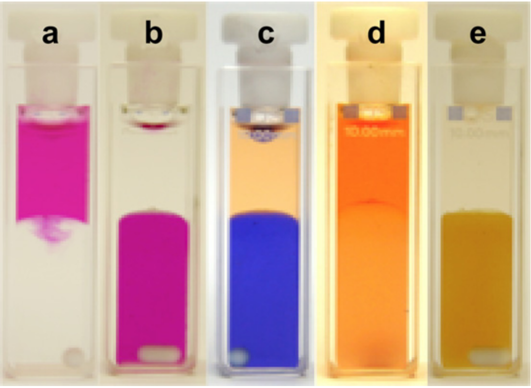


Fig. 14. Behavior of 7-(*N,N*-diethylamino)-4′-hydroxyflavylium tetrafluoroborate in biphasic systems constituted by aqueous solution (upper phase) and 1-*n*-butyl-3-methyl-imidazolium hexafluorophosphate, [bmim][PF_6] (lower phase), upon pH jumps in the aqueous phase. a) pH = 1.0 in the aqueous phase, $\mathbf{AH^+}$ species, before shaking; b) after shaking, $\mathbf{AH^+}$ completely transfers to the ionic liquid; c) upon addition of base and shaking for 2 min; d) upon 10 min (shaking); e) upon addition of acid and shaking [46].

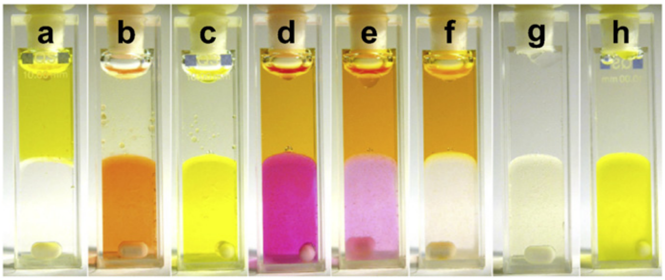


Fig. 16. a) 1-*n*-butyl-3-methyl-imidazolium hexafluorophosphate, [bmim][PF_6] (lower phase), 4′,7-dihydroxyflavylium perchlorate in 0.01 M HCl (upper phase), $\mathbf{AH^+}$ species; b) after moderate shaking, **A** species; c) after vigorous shaking, $\mathbf{A}H^+$ species; d) after alkalinization of the aqueous phase (pH = 12) with minimum shaking, $\mathbf{A}^-$ bottom, $\mathbf{Ct^{2-}}$ up; e) after moderate shaking, f) after vigorous shaking, $\mathbf{Ct^{2-}}$ species, g) after reacidification of the aqueous phase and vigorous shaking, **Ct** species, h) after irradiation of the ionic liquid phase at 366 nm, $\mathbf{A}H^+$ species [48].

The aqueous solution of the compound at pH 1 was introduced in the upper phase of the system, a). A moderate shaking leads to the dissolution of all the flavylium cation in the ionic liquid in its orange–brown quinoidal base form, **A**, b). However, upon *ca.* 1 min of vigorous shaking, the bottom ionic liquid solution becomes yellow, indicating that **A** was protonated to form the $\mathbf{A}H^+$ species, c). The flavylium cation dissolved in the ionic liquid phase is the thermodynamically stable situation, which is reached without shaking but it takes several hours. A cycle to write–read–erase can be obtained from this point. Fig. 16d–f, show three stages obtained upon a pH jump from 1 to 12 carried out in the aqueous phase. The final equilibrium in this step is obtained with the $\mathbf{Ct}^{2-}$ species completely dissolved into the aqueous phase, Fig. 16f. The next step of the cycle consists of a pH jump in the aqueous phase, back to pH = 1.0, followed by vigorous mixing of the two phases. This procedure allows the **Ct** species formed in the water phase to dissolve completely in the ionic liquid. The equilibrium species at this pH value ($\mathbf{AH^+}$) is formed with a slow rate (after 1 h at 40 °C, less than 2% of flavylium cation was formed), showing that, in contrary to the behavior in water, the **Ct** species of this compound in the ionic liquid exhibits a very large kinetic barrier that prevents rapid *cis–trans* isomerization, a necessary requirement to a “memory” model. Irradiation of **Ct** incorporated in the ionic liquid phase at pH = 1.0 leads spontaneously to the yellow $\mathbf{AH^+}$ (via **Cc** and **B**) write step. Now the information ($\mathbf{AH^+}$ can be red at a wavelength where **Ct** does not absorb. To erase the system a pH jump to basic media forms $\mathbf{Ct^{2-}}$, and to enable for the next cycle another pH jump back to acid leads the system into **Ct** (meta-stable state).

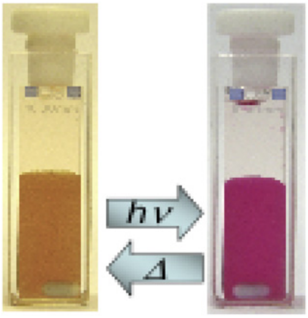


Fig. 15. Photochromic system of 7-(*N,N*-diethylamino)-4′-hydroxyflavylium in water/ionic liquid [bmim][PF_6] biphasic systems [46].

12. Conclusions and future prospects

The extension of the flavylium photochromism into systems such as gels or ionic liquids promises new applications beyond the models for optical memories. In fact, the primary photochemical steps when **Ct** is excited to the singlet state are optimized in those systems in such a way that the photochromic effect is enhanced. It was shown recently that the photochromism could be employed to change the rheological properties of a gel [49]. Therefore, flavylium compounds can be used in photoresponsive smart materials in which a macroscopic physical property (such as viscosity) is changed after irradiation with light. To achieve such effects one must select carefully the substituents in the flavylium cation in order to use them on a given material.

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