Complete resolution of the reaction Rates of flavylium Networks. The role played by 2-phenyl-2H-chromen-4-ol and the hydroxyl attack to the quinoidal Base

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Abstract Complete analytical resolution of the network of chemical reactions involving the flavylium compounds was achieved by means of the Laplace transform, general partial fraction theorem and Vieta's formulae. The kinetic model includes basic and acid catalysis of the hydration and tautomerization reactions. The formation of phenyl-2H-chromen-4-ol (B_4) and the role it plays in the kinetics in the case of compounds lacking of the hydroxyl substituents was also accounted for. In all cases four kinetic steps could be individualized and the pH dependent mole fraction distribution of the several species monitored as a function of time, the last one leading to the equilibrium. It is worth of note the role of B_4 in the network, which like the quinoidal base is a kinetic product that retards the formation of Ct. The evolution of B_4 is also dependent on the existence or not of the *cis-trans* isomerisation barrier. Application of the model to the data of flavylium networks previously reported in literature, predicts with great accuracy the respective behavior.

1 Introduction

2-phenyl-1-benzopyrylium (Flavylium) constitutes a big family of compounds including anthocyanins, the natural dyes responsible for the color of many flowers and fruits.

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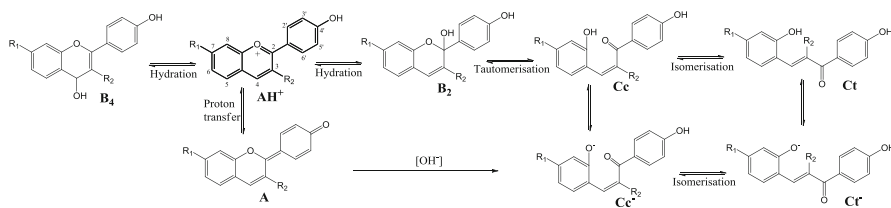
Scheme 1 A general chemical reactions network of anthocyanins, flavylium and naphthoflavylium compounds

Anthocyanins are derivative of the flavylium compounds possessing glucose or another sugar substituent at position 3 or 3 and 5 [1]. Natural Anthocyanins are involved in acid-base type of equilibrium between flavylium cation and essentially the "basic" species quinoidal base (proton releasing from flavylium cation) and hemiketal (hydration of flavylium cation), which determines the pH dependent color. In anthocyanins the chalcones are minor products. In contrast synthetic flavylium compound without substituent in position 3 [2] can be involved not only in proton transfer and hydration reactions, but also into a ring-chain tautomeric reaction producing a *cis*-chalcone from the hemiketal and isomerisation leading to *trans*-chalcone. In spite of these differences all flavylium derived compounds follow the same network of chemical reactions. The kinetics of the reversible reactions network of the and the thermodynamics depends on the substituents of the flavylium core. The network is thus a complex system that could respond to various stimuli such as pH, light, (photoinduced *trans-cis* isomerisation) solvents and presence of surfactants, metal cation, gels, ionic liquids within others [3,4].
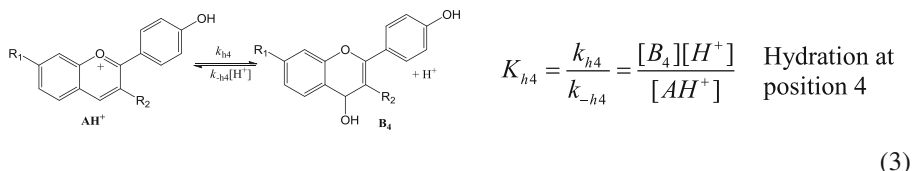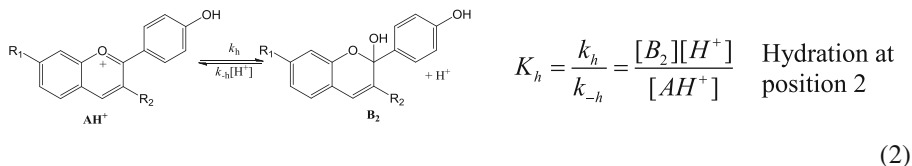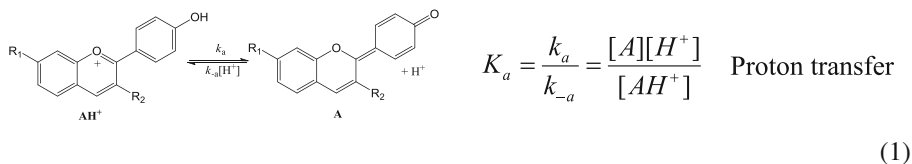
The study of the flavylium network of chemical reactions has been put together in several steps complemented or corrected consecutively during the course of many decades. [5] The work from Brouillard and Dubois [6], and McClelland [7] shaped the perception that we have of the network. In particular the achievements of McClelland introducing the basic and acid catalysis were of primordial importance. However, up to now a complete resolution of the kinetic equations including the acid and basic catalysis as well as the possibility of **B₄** formation was not accomplished. A complete resolution of thermodynamic and kinetic behavior of such a network of chemical reactions will provide a better understanding of the behavior of those systems giving important information for the synthesis of the compounds with desired properties, in particular for the model systems for optical memories. [8]

2 Theory

2.1 Thermodynamic behavior

Scheme 1 reports a typical flavylium network of reactions.

Flavilium cation **AH⁺** is the most stable species at significantly low pH values. When the pH is raised, three competitive reactions occur:

$$K_a = \frac{k_a}{k_{-a}} = \frac{[A][H^+]}{[AH^+]} \quad \text{Proton transfer}$$

(1)

$$K_h = \frac{k_h}{k_{-h}} = \frac{[B_2][H^+]}{[AH^+]} \quad \begin{array}{l}\text{Hydration at} \\ \text{position 2}\end{array}$$

(2)

$$K_{h4} = \frac{k_{h4}}{k_{-h4}} = \frac{[B_4][H^+]}{[AH^+]} \quad \begin{array}{l}\text{Hydration at} \\ \text{position 4}\end{array}$$

(3)

The proton transfer reaction Eq. (1) is very fast (process ends in less than a millisecond) and the quinoidal base **A** is formed almost instantaneously. However, often other basic species are more stable than quinoidal base and thus it disappears partially or completely during the pseudo equilibration process (see below). Usually flavylium cation have smaller positive charge at position 4 than at position 2 and as a consequence the hydration reaction at position 4 Eq. (3) is slower and leads to a less stable product than at position 2 Eq. (2). For the flavylium compounds possessing a hydroxyl group substituent ordinary the **B$_4$** species is not experimentally observed. That is why two different general models could be constituted—one for flavylium compounds bearing hydroxyl susbtituents, which form the quinoidal base **A**, but not **B$_4$** and another for compounds lacking of the hydroxyl group forming **B$_4$**, but not **A** (see below). The hemiketal **B$_2$** (chromene) is involved in a ring-chain tautometic process Eq. (4) leading to the formation of *cis*-chalcone **Cc**.

$$K_t = \frac{k_t}{k_{-t}} = \frac{[Cc]}{[B_2]} \quad \text{Tautomerization}$$

(4)
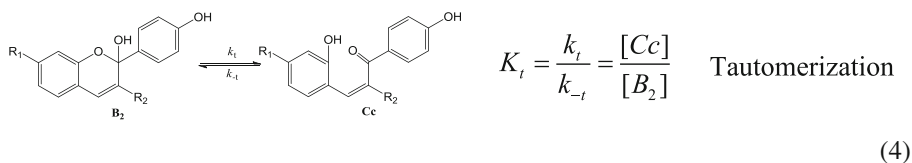
Both tautomeric reactions direct and reverse are catalyzed by H^+ and OH^{-7}. In fact observed rate constants of the tautomeric reaction k_t and k_{-t} are not constants as a function of pH, but functions of proton and hydroxyl concentration as follows:

$$k_t' = k_t + k_t^H[H^+] + k_t^{OH}[OH^-]; \quad k_{-t}' = k_{-t} + k_{-t}^H[H^+] + k_{-t}^{OH}[OH^-]$$

However, it was experimentally observed that the thermodynamic constant K_t is not function of pH, the effect of proton and hydroxyl being considered as a catalytic effect: the following relation is valid:

$$K_t = \frac{k_t}{k_{-t}} = \frac{k'_t}{k'_{-t}} = \frac{k_t^H}{k_{-t}^H} = \frac{k_t^{OH}}{k_{-t}^{OH}} \tag{5}$$

The most stable species at higher pH values in synthetic flavylium or naphthoflavy-lium networks is generally the *trans*-chalcone **Ct** formed trough the isomerisation of **Cc** Eq. (6).

$$K_i = \frac{k_i}{k_{-i}} = \frac{[Ct]}{[Cc]} \qquad \text{Isomerisation}$$

$$\tag{6}$$
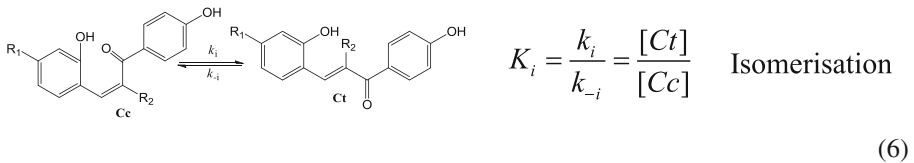
Often, especially when a substituent in position 7 is not presented and substituent at position 2' or 4' is −OH or −OCH$_3$ group, a *cis-trans* isomerisation barrier is high and the isomerisation reaction is much slower that the other three. In this case pseudo equilibrium between **AH$^+$** and **A, B** and **Cc** species, prior to significant formation of **Ct**, can be experimentally observed according to Eqs. (1–4). The system can be simplified in one single acid base type equation involving **AH$^+$** and **CB$^\wedge$**, see Eq. (7):

$$AH^+ \overset{K_a^\wedge}{\rightleftarrows} CB^\wedge + H^+ \tag{7}$$

$$\text{Where}: [CB^\wedge] = [Cc] + [B_2] + [B_4] + [A] \tag{8}$$

$$\text{and } K_a^\wedge = K_a + K_h + K_{h4} + K_h K_t = \frac{[CB^\wedge][H^+]}{[AH^+]} \tag{9}$$

The mole fraction of the species at pseudo equilibrium (7) can be calculated as follows:

$$\chi_{AH^+} = \frac{[H^+]}{[H^+] + K_a^\wedge} \tag{10}$$

$$\chi_A = \frac{K_a}{[H^+] + K_a^\wedge} \tag{11}$$

$$\chi_{B_2} = \frac{K_h}{[H^+] + K_a^\wedge} \tag{12}$$

$$\chi_{B_4} = \frac{K_{h4}}{[H^+] + K_a^\wedge} \tag{13}$$

$$\chi_{Cc} = \frac{K_h K_t}{[H^+] + K_a^\wedge} \tag{14}$$

By analogy with pseudo equilibrium the final equilibrium on the system can be presented as:

$$AH^+ \overset{K_a'}{\rightleftarrows} CB + H^+ \tag{15}$$

$$\text{Where : } [CB] = [Ct] + [Cc] + [B_2] + [B_4] + [A] \tag{16}$$

$$\text{and } K_a' = K_a^\wedge + K_h K_t K_i = \frac{[CB][H^+]}{[AH^+]} \tag{17}$$

The mole fraction of the species at equilibrium (15) can be calculated as follows:

$$\chi_{AH^+} = \frac{[H^+]}{[H^+] + K_a'} \tag{18}$$

$$\chi_A = \frac{K_a}{[H^+] + K_a'} \tag{19}$$

$$\chi_{B_2} = \frac{K_h}{[H^+] + K_a'} \tag{20}$$

$$\chi_{B_4} = \frac{K_{h4}}{[H^+] + K_a'} \tag{21}$$

$$\chi_{Cc} = \frac{K_h K_t}{[H^+] + K_a'} \tag{22}$$

$$\chi_{Ct} = \frac{K_h K_t K_i}{[H^+] + K_a'} \tag{23}$$
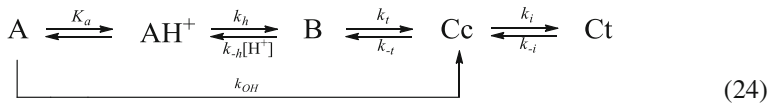
2.2 Kinetic behavior and mathematical resolution

The resolution of the kinetic Scheme 1, Eqs. (1–6) for direct pH jumps, reverse pH jumps and flash photolysis experiments is based on the Laplace transformation, general partial fraction theorem and Vieta's formulae. Mathematical reasoning was maid previously in great details elsewhere [9] and here only the main properties of the solutions and the specific details for these particular cases are presented. The general algorithm of the solution can be written as follows:

1. A set of differential equation describing the chemical processes in the system is written
2. By using the Laplace Transform property to transform a differential equation in linear one the system is transformed into linear system of equations.
3. The obtained system of linear equations is solved for the new variables in Laplace space
4. The solutions can be presented as: $x(s) = \frac{P_1(s)}{s.P_2(s)}$,
   where: $x(s)$ is the new variable in Laplace space, $P_1(s)$ and $P_2(s)$ are polynomials. The degree of the polynomial P_1 is smaller or equal to the degree of the polynomial P_2.
   The roots of the polynomial $P_2(s)$ depend on all the rate constants of the system as well as $[H^+]$ and are the observed rate constants i.e. positive real numbers. Polynomial $P_2(s)$ is the characteristic equation of the presented system [10]. The denominator $s. P_2(s) = 0$ have an obvious root $s = 0$. This is a so-called stationary solution—all of the observed constants are equal to zero and it represents the system in equilibrium.

5. Finally the mole fractions of all chemical species as a function of time are obtained after Inverse Laplace transform by means of the general partial fraction theorem as it described in a previous paper [9]. The final solution can be presented in a form: $S(t) = \sum_{x=\alpha,\beta,\gamma,\delta} C_x^S e^{-xt}$

System I: Hydroxyl substituent is present and quinoidal base species **A** is formed, **B**$_4$ is not formed. The general scheme of the reaction network can be written as:

$$A \underset{}{\overset{K_a}{\rightleftarrows}} AH^+ \underset{k_{-h}[H^+]}{\overset{k_h}{\rightleftarrows}} B \underset{k_{-t}}{\overset{k_t}{\rightleftarrows}} Cc \underset{k_{-i}}{\overset{k_i}{\rightleftarrows}} Ct$$

$$\xrightarrow{k_{OH}}$$

$$\tag{24}$$

The following assumptions have been made:

– **AH$^+$/A** are in fast equilibrium and behaves like one component:
– **B$_4$** is not formed due to thermodynamic and kinetic reasons
– Reaction **A → Cc** is not reversible
– Ionized species **Cc$^-$** and **Ct$^-$** are not formed

It is worth of note that in moderately acidic solutions neither **B2** nor **Cc** are formed from **A** as reported in the paper of Brouillard and Dubois [6].

The set of differential equation describing kinetic behavior of the system (24) are:

$$\frac{d[AH^+ + A]}{dt} = -\left(k_h \frac{[H^+]}{[H^+ + Ka]} + k_{OH} \frac{K_a}{[H^+ + Ka]}\right)[AH^+ + A]$$
$$+ k_{-h}[H^+][B] \tag{25}$$

$$\frac{d[B]}{dt} = k_h \frac{[H^+]}{[H^+] + K_a}[AH^+ + A] - (k_{-h}[H^+] + k_t)[B] + k_{-t}[Cc] \tag{26}$$

$$\frac{d[Cc]}{dt} = k_{OH} \frac{K_a}{[H+] + K_a}[AH^+ + A] + k_t[B]$$
$$- (k_{-t} + k_i)[Cc] + k_{-i}[Ct] \tag{27}$$

$$\frac{d[Ct]}{dt} = k_i[Cc] - k_{-i}[Ct] \tag{28}$$

Mass balance of the system:

$$[AH^+ + A] + [B] + [Cc] + [Ct] = C_0 \tag{29}$$

For purposes of simplicity the following substitution are made:

$$k'_h = k_h \frac{[H^+]}{[H^+] + K_a} \tag{30}$$

$$k'_{-h} = k_{-h}[H^+] \tag{31}$$

$$k'_{OH} = k_{OH} \frac{K_a}{[H^+] + K_a} \tag{32}$$

$$k'_t = k_t + k_t^H[H^+] + k_t^{OH}[OH^-] \tag{33}$$

$$k'_{-t} = k_{-t} + k_{-t}^H[H^+] + k_{-t}^{OH}[OH^-] \tag{34}$$

After Laplace transformation of Eqs. (25–28) [11]:

$$ah(s) + a(s) = \left(\begin{matrix} k'_{-h}\left(s(ah_0+b_0)(s+k_i+k_{-i})+k'_{-t}(s-ct_0s+k_{-i})\right) \\ +ah_0s(s\left(s+k'_{-t}+k_i\right)+k'_t(s+k_i)+k_{-i}\left(s+k'_t+k'_{-t}\right)) \end{matrix} \right) \Big/ s.P(s) \tag{35}$$

$$b(s) = \left(\begin{matrix} s(s+k_i+k_{-i})\left(k'_h(ah_0+b_0)+b_0\left(s+k'_{OH}\right)\right) \\ +\left(k'_h(s-ct_0s+k_{-i})+k_{-i}\left(s-ah_0s+k'_{OH}\right)\right) \\ +s\left(s(b_0+cc_0)+k'_{OH}(1-ct_0)\right))k'_{-t} \end{matrix} \right) \Big/ s.P(s) \tag{36}$$

$$cc(s) = \left(\begin{matrix} s(s+k'_h)(cc_0s+(cc_0+ct_0)k_{-i})+s((ah_0+cc_0)s \\ +(1-b_0)k_{-i})k'_{OH}+k'_{-h}(k_{-i}((cc_0+ct_0)s+k'_{OH})+s(cc_0s \\ +(1-ct_0)k'_{OH}))+(k'_h((1-ct_0)s+k_{-i})+k_{-i}(s-ah_0s+k'_{OH}) \\ +s((b_0+cc_0)s+(1-ct_0)k'_{OH}))k'_t \end{matrix} \right) \Big/ s.P(s) \tag{37}$$

where:

s is a new varable in Laplace space

ah_0, b_0, cc_0 and ct_0 are mole fraction of the corresponding species at $t = 0$

$$P(s) = A.s^3 + Bs^2 + Cs + D = (s + \alpha)(s + \beta)(s + \gamma) \tag{38}$$

where α, β, γ are the roots of $P(s)$ and observed rate constant of the processes for the system Eq. (24).

The coefficients of the $P(s)$ Eq. (38) are:

$$A = 1 \tag{39}$$

$$B = k'_h + k'_{-h} + k'_t + k'_{-t} + k_i + k_{-i} + k'_{OH} \tag{40}$$

$$C = k'_h\left(k'_t + k'_{-t} + k_i + k_{-i}\right) + k'_{-h}\left(k'_{-t} + k_i + k_{-i}\right) + k'_t k_i + k_{-i}\left(k'_t + k'_{-t}\right)$$
$$+ k'_{OH}\left(k'_{-h} + k'_t + k'_{-t} + k_i + k_{-i}\right) \tag{41}$$

$$D = k'_h\left(k_i k'_t + k_{-i}\left(k'_{-t} + k'_t\right)\right) + k'_{OH}\left(k'_{-h}(k_{-i} + k_i) + k'_{-h}k'_{-t}k_{-i} + k'_t k_i\right.$$
$$\left. + k_{-i}\left(k'_t + k'_{-t}\right)\right) \tag{42}$$

As reported previously [9], the observed rate constants of the system Eq. (24) α, β, γ can be claculated through Vieta's formulas or by solving the 3rd degree polynomial Eq. (38) applying Cardano's formulae [12].

$$\alpha + \beta + \gamma = B \tag{43}$$

$$\alpha.\beta + \alpha.\gamma + \beta.\gamma = C \tag{44}$$

$$\alpha.\beta.\gamma = D \tag{45}$$

After α, β, γ were obtained, we can perform an inverse Laplace transform and gain a formulae for the mole fraction variation of the components as a function of time.

For AH^+/A, Eq. (35), after inverse Laplace transform:

$$[AH + A](t) = \frac{k'_{-h}k'_{-t}k_{-i}}{\alpha\beta\gamma} + \frac{e^{-\alpha t}C_\alpha^{AH}}{\alpha(\alpha - \beta)(\alpha - \gamma)}$$
$$+ \frac{e^{-\beta t}C_\beta^{AH}}{\beta(\alpha - \beta)(\beta - \gamma)} + \frac{e^{-\gamma t}C_\gamma^{AH}}{\gamma(\gamma - \alpha)(\gamma - \beta)} \tag{46}$$

where

$$C_x^{AH} = \begin{pmatrix} k'_{-h}\left(-x(ah_0 + b_0)(x - k_{-i} - k_i) + (x(1 - ct_0) - k_{-i})k'_{-t}\right) + \\ +ah_0 x \left(x^2 - x(k_i + k'_{-t}) + (k_i - x)k'_t + k_{-i}(k'_t + k'_{-t} - x)\right) \end{pmatrix}$$
$$x = \alpha, \beta, \gamma \tag{47}$$

It is easy to be seen that:

$$[AH^+](t) = \frac{[H^+]}{[H^+] + K_a}[AH + A](t) \tag{48}$$

$$[A](t) = \frac{K_a}{[H^+] + K_a}[AH + A](t) \tag{49}$$

From Eq. (36), after inverse Laplace transform:

$$[B](t) = \frac{\left(k'_h + k'_{OH}\right)k'_{-t}k_{-i}}{\alpha\beta\gamma} + \frac{e^{-\alpha t}C_\alpha^B}{\alpha(\alpha - \beta)(\alpha - \gamma)}$$
$$+ \frac{e^{-\beta t}C_\beta^B}{\beta(\beta - \alpha)(\beta - \gamma)} + \frac{e^{-\gamma t}C_\gamma^B}{\gamma(\gamma - \alpha)(\gamma - \beta)} \tag{50}$$

where

$$C_x^B = \begin{pmatrix} x(x - k_i - k_{-i})\left(b_0(x - k'_{OH}) - k'_h(ah_0 + b_0)\right) + \left(k'_h(x(1 - ct_0) - k_{-i}) - \\ -k_{-i}\left(x(ah_0 - 1) + k'_{OH}\right) + x\left((1 - ct_0)k'_{OH} - x(b_0 + cc_0)\right)\right)k'_{-t} \end{pmatrix}$$
$$x = \alpha, \beta, \gamma \tag{51}$$

From Eq. (37), after inverse Laplace transform
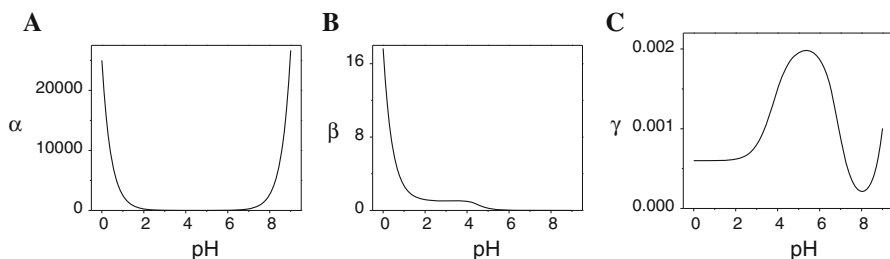
A   **B**   **C**

Fig. 1 Observed rate constants in (s^{-1}) for simulated system with: $k_h = 1, k_{-h} = 25{,}000, k_t = 0.6, k_{-t} = 1, k_i = 0.01, k_{-i} = 0.0006, k_t^H = 10, k_t^{OH} = 10^9, k_{OH} = 100, K_a = 10^{-4}$. The values were chosen to be close to the experimental values obtained for 4',7-dihydroxy flavylium [13] which was used as a model compound. **a** α, **b** β, **c** γ as defined in Eqs. (43–45)

$$[Cc](t) = \frac{\left(k'_{-h}k'_{OH} + k'_t\left(k'_h + k'_{OH}\right)\right)k_{-i}}{\alpha\beta\gamma} + \frac{e^{-\alpha t}C_\alpha^{Cc}}{\alpha(\alpha - \beta)(\alpha - \gamma)}$$
$$+ \frac{e^{-\beta t}C_\beta^{Cc}}{\beta(\alpha - \beta)(\beta - \gamma)} + \frac{e^{-\gamma t}C_\gamma^{Cc}}{\gamma(\gamma - \alpha)(\gamma - \beta)} \tag{52}$$

where

$$C_x^{Cc} = \begin{pmatrix} x(x - k'_h)(xcc_0 + (ah_0 + b_0 - 1)k_{-i}) - x(x(ah_0 + cc_0) \\ +(b_0 - 1)k_{-i})k'_{OH} + k_{-h}(-k_{-i}(x(ah_0 + b_0 - 1) + k'_{OH}) \\ +x((1 - ct_0)k'_{OH}) - xcc_0) + (k'_h(x(1 - ct_0) - k_{-i}) \\ -k_{-i}((ah_0 - 1)x + k'_{OH}) + x((1 - ct_0)k'_{OH} - x(b_0 + cc_0)))k'_t \end{pmatrix}$$
$$x = \alpha, \beta, \gamma \tag{53}$$

and finally [Ct](t) can be calculated from the material balance of the system:

$$[Ct](t) = 1 - ([AH + A](t) + [B](t) + [Cc](t)) \tag{54}$$

The representation of the rate constants as a function of pH is a complex process and in most of the cases it is not possible to be observed in a single experiment all the nuances of the system, as reported in Fig. 1. Moreover, the faster process needs a stopped flow instrument. In some cases it is not possible to separate the three kinetic processes.

Figure 1 represents the pH dependence of the three rate constants. Figure 1a exhibits the characteristic U shape of a process where the left branch regards the hydration Eq. (2), and the right one the hydroxyl attack to the quinoidal base. An example of this reaction is given in Fig. 2a. Figure 1b, has also two components the one of the left when the kinetic process is controlled by the tautomerization Eq. (4), and the other when the control is made by the hydration. Figure 2b shows an experimental case. Finally, Fig. 1c represents the slower step which is controlled by the *cis-trans* isomerisation Eq. (6) at lower pH values and by the hydration at higher pH values, being the final raising due to the reaction of the quinoidal base (a kinetic product) with the hydroxyl. Figure 2c shows an experimental case. Regarding the bell shape curve, Fig. 1c, and neglecting the final raising which take place at more basic pH values, the maximum
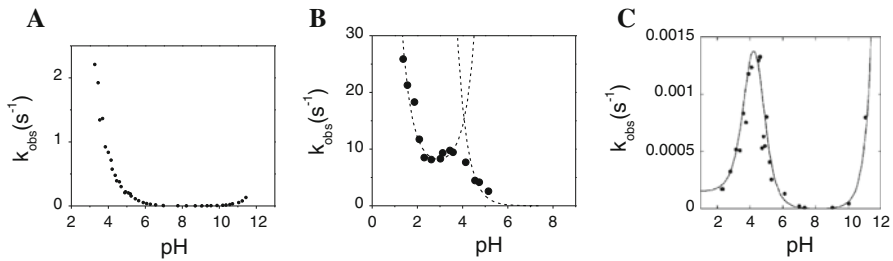
Fig. 2 Observed rate constants for 3 different compounds: type and behavior are the same as predicted, **a** 4'-hydroxyflavilium compound [14], **b** 4'-hydroxynaphthoflavylium [15], **c** observed rate constant for 7-Hydroxy-2-(4-hydroxystyryl)-1-benzopyrylium chloride [16]. Reprint with permission from ref. [16] Copyright 2009, American Chemical Society
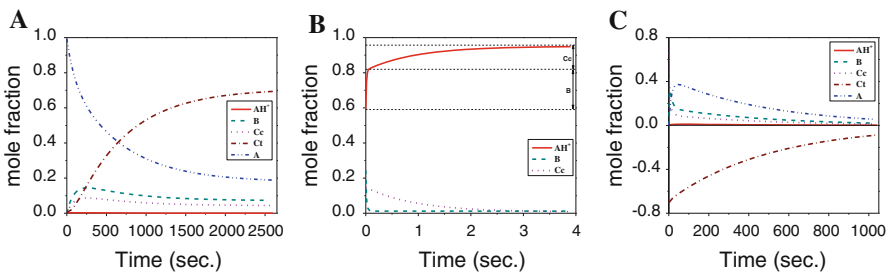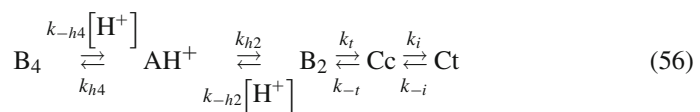

Fig. 3 Observed mole fraction changes as a function of time for simulated system with: $k_h = 1$, $k_{-h} = 25,000$, $k_t = 0.6$, $k_{-t} = 1$, $k_i = 0.01$, $k_{-i} = 0.0006$, $k_t^H = 10$, $k_t^{OH} = 10^9$, $k_{OH} = 100$, $K_a = 10^{-4}$. **a** After direct pH jump from 1 to 6.5. **b** After reverse pH jump from 6.5 to 2.5. **c** Flash photolysis experiment at pH = 5.5 made with assumption that all of the **Ct** available at equilibrium is instantaneously converted into **Cc**

of the curve is given by Eq. (55), and the minimum of the curve at very low pH trends to k_{-i}.

$$H_{MAX} \approx \frac{K_a k_{-i} + \sqrt{K_a k_h k_{-i}((K_a + K_h K_t K_i) - k_i K_t)}}{k_h - k_{-i}} \tag{55}$$

The model can be generalized to account for not only direct pH jumps starting from flavylium cation (Fig. 3a), but also reverse pH jumps where equilibrated solutions at higher pH values are made more acidic (Fig. 3b). In addition it is possible to fit the data form a flash photolysis experiments. In this last case **Ct** is irradiated leading to **Cc** and according to the pH give spontaneously (or not) **AH$^+$** and **A** (Fig. 3c).

System II: **B$_4$** is presented:

$$\text{B}_4 \underset{k_{h4}}{\overset{k_{-h4}[\text{H}^+]}{\rightleftarrows}} \text{AH}^+ \underset{k_{-h2}[\text{H}^+]}{\overset{k_{h2}}{\rightleftarrows}} \text{B}_2 \underset{k_{-t}}{\overset{k_t}{\rightleftarrows}} \text{Cc} \underset{k_{-i}}{\overset{k_i}{\rightleftarrows}} \text{Ct} \tag{56}$$

Differential equations for system (56) could be written in a form:

$$\frac{d[B_4]}{dt} = k_{h4}[AH^+] - k_{-h4}[H^+][B_4] \tag{57}$$

$$\frac{d[AH^+]}{dt} = k_{-h4}[H^+][B_4] - (k_{h2} + k_{h4})[AH^+] + k_{-h2}[H^+][B_2] \tag{58}$$

$$\frac{d[B2]}{dt} = k_{h2}[AH^+] - (k_{-h2} + k_t)[B_2] + k_{-t}[Cc] \tag{59}$$

$$\frac{d[Cc]}{dt} = k_t[B_2] - (k_{-t} + k_i)[Cc] + k_{-i}[Ct] \tag{60}$$

$$\frac{d[Ct]}{dt} = k_i[Cc] - k_{-i}[Ct] \tag{61}$$

Mass balance of the system:

$$[B_4] + [AH^+] + [B_2] + [Cc] + [Ct] = C_0 \tag{62}$$

As before:

$$k'_{-h2} = k_{-h2}[H^+] \tag{63}$$

$$k'_{-h4} = k_{-h4}[H^+] \tag{64}$$

$$k'_t = k_t + k_t^H[H^+] + k_t^{OH}[OH^-] \tag{65}$$

$$k'_{-t} = k_{-t} + k_{-t}^H[H^+] + k_{-t}^{OH}[OH^-] \tag{66}$$

After Laplace Transform of Eqs. (57–61):

$$b4(s) = -\left(\begin{array}{c} k'_{-h2}(s(-b4_0s + (cc_0 + ct_0 - 1)k_{h4})(s + k_{-i} + k_i) \\ + (k_{h4}((ct_0 - 1)s - k_{-i}) - b4_0s(s + k_{-i}))k'_{-t}) \\ + s(-b4_0(s + k_{h2}) + (b2_0 + cc_0 + ct_0 - 1)k_{h4}) \\ (s(s + k_i + k'_{-t}) + (s + k_i)k'_t + k_{-i}(s + k'_{-t} + k'_t)) \end{array}\right) \Bigg/ P_1(s) \tag{67}$$

$$ah(s) = \left(\begin{array}{c} k'_{-h2}(s((a_0 + b2_0)s - (cc_0 + ct_0 - 1)k'_{-h4})(s + k_{-i} + k_i) \\ + (k'_{-h4}(s - ct_0s + k_{-i}) + s((ah_0 + b2_0 + cc_0)s \\ + (1 - b4_0)k_{-i}))k'_{-t}) + s(ah_0s + (ah_0 + b4_0)k'_{-h4}) \\ (s(s + k_i + k'_{-t}) + (s + k_i)k'_t + k'_{-t}(s + k'_{-t} + k'_t)) \end{array}\right) \Bigg/ P_1(s) \tag{68}$$

$$b2(s) = \left(\begin{array}{c} s(s + k'_{-h4} + k_{h4})(b2_0s(s + k_{-i} + k_i) + ((b2_0 + cc_0)s \\ + (1 - ah_0 - b4_0)k_{-i})k'_{-t}) + k_{h2}(s((ah_0 + b2_0)s \\ - (cc_0 + ct_0 - 1)k'_{-h4})(s + k_{-i} + k_i) + (k'_{-h4}(s - ct_0s + k_{-i}) \\ + s((ah_0 + b2_0 + cc_0)s + (1 - b4_0)k_{-i}))k'_{-t}) \end{array}\right) \Bigg/ P_1(s) \tag{69}$$

$$ct(s) = \left(\begin{array}{c} sk_{-h2}(s + k'_{-h4} + k_{h4})((cc_0 + ct_0)k_i + ct_0(s + k'_{-t})) \\ + s((s + k_{h2})(s + k'_{-h4}) + sk_{h4})((cc_0 + ct_0)k_i + ct_0(s + k'_{-t})) \\ + (s(s + k'_{-h4} + k_{h4})(ct_0s + (b2_0 + cc_0 + ct_0)k_i) \\ + k_{h2}(ct_0s(s + k'_{-h4}) + ((1 - b4_0)s + k'_{-h4})k_i))k'_t \end{array}\right) \Bigg/ P_1(s) \tag{70}$$

$$P_1(s) = s(A.s^4 + Bs^3 + Cs^2 + Ds + E) = s(s+\alpha)(s+\beta)(s+\gamma)(s+\delta) \tag{71}$$

$$A = 1 \tag{72}$$

$$B = k_{h2} + k'_{-h2} + k_{h4} + k'_{-h4} + k'_t + k'_{-t} + k_i + k_{-i} \tag{73}$$

$$C = (k_{h4} + k'_{-h4})(k'_{-t} + k_{-i} + k_i) + k'_{-t}k_{-i} + k'_{-h2}(k'_{-h4} + k_{h4} \tag{74}$$

$$+ k_{-i} + k_i + k'_{-t}) + (k'_{-h4} + k_{h4} + k_{-i} + k_i)k'_t$$

$$+ k_{h2}(k'_{-h4} + k_{-i} + k_i + k'_{-t} + k'_t) \tag{75}$$

$$D = k'_{-h2}((k'_{-h4} + k_{h4})(k_{-i} + k_i) + (k'_{-h4} + k_{h4} + k_{-i})k'_{-t})$$

$$+ (k'_{-h4} + k_{h4})(k_i k'_t + k_{-i}(k'_{-t} + k'_t)) + k_{h2}(k_i k'_t + k_{-i}(k'_{-t} + k'_t))$$

$$+ k'_{-h4}(k_{-i} + k_i + k'_{-t} + k'_t))$$

$$E = k'_{-h2}k'_{-t}k_{-i}(k'_{-h4} + k_{h4}) + k_{h2}k'_{-h4}(k_i k'_t + k_{-i}(k'_{-t} + k'_t)) \tag{76}$$

Roots of (71) are observed rate constants $\alpha, \beta, \gamma, \delta$ and

$$\alpha + \beta + \gamma + \delta = B \tag{77}$$

$$\alpha\beta + \alpha\gamma + \alpha\delta + \beta\gamma + \beta\delta + \gamma\delta = C \tag{78}$$

$$\alpha\beta\gamma + \alpha\beta\delta + \beta\gamma\delta = D \tag{79}$$

$$\alpha\beta\gamma\delta = E \tag{80}$$

Roots can be found numerically of by solving Eq. (71) analytically [17].
  After inverse Laplace transform:

$$[B4](t) = \frac{k_{h4}k'_{-h2}k'_{-t}k_{-i}}{\alpha\beta\gamma\delta} + \frac{e^{-\alpha t}C_\alpha^{B4}}{\alpha(\alpha-\beta)(\alpha-\gamma)(\alpha-\delta)} + \frac{e^{-\beta t}C_\beta^{B4}}{\beta(\beta-\alpha)(\beta-\gamma)(\beta-\delta)}$$

$$+ \frac{e^{-\gamma t}C_\gamma^{B4}}{\gamma(\gamma-\alpha)(\gamma-\beta)(\gamma-\delta)} + \frac{e^{-\delta t}C_\delta^{B4}}{\delta(\delta-\alpha)(\delta-\beta)(\delta-\gamma)} \tag{81}$$

$$\text{where} : C_x^{B4} = \begin{pmatrix} k'_{-h2}(-b4_0 x(x(x - k'_{-t} - k_i) + k_{-i}(k'_{-t} - x)) \\ + k_{h4}(k_{-i}((cc_0 + ct_0 - 1)x + k'_{-t}) \\ + x((cc_0 + ct_0 - 1)(k_i - x) + (ct_0 - 1)k'_{-t}))) \\ - x(-b4_0 x + b4_0 k_{h2} - (b2_0 + cc_0 + ct_0 - 1)k_{h4}) \\ (x(x - k'_t - k'_{-t}) + k_i(k'_t - x) + k_{-i}(k'_t + k'_{-t} - x)) \end{pmatrix} \tag{82}$$

$$[AH](t) = \frac{k'_{-h4}k'_{-h2}k'_{-t}k_{-i}}{\alpha\beta\gamma\delta} + \frac{e^{-\alpha t}C_\alpha^{AH}}{\alpha(\alpha-\beta)(\alpha-\gamma)(\alpha-\delta)} + \frac{e^{-\beta t}C_\beta^{AH}}{\beta(\beta-\alpha)(\beta-\gamma)(\beta-\delta)}$$

$$+ \frac{e^{-\gamma t}C_\gamma^{AH}}{\gamma(\gamma-\alpha)(\gamma-\beta)(\gamma-\delta)} + \frac{e^{-\delta t}C_\delta^{AH}}{\delta(\delta-\alpha)(\delta-\beta)(\delta-\gamma)} \tag{83}$$

where:

$$
C_x^{AH} = \begin{pmatrix} k'_{-h2}(k'_{-h4}(k_{-i}((cc_0 + ct_0 - 1)x + k'_{-t}) + x((cc_0 + ct_0 - 1)(k_i - x)) \\ + (ct_0 - 1)k'_{-t})) + x(x((ah_0 + b2_0)(k_i - x) + (a_0 + b2_0 + cc_0)k'_{-t}) \\ + k_{-i}((ah_0 + b2_0)\alpha - (1 - b4_0)k'_{-t}))) + x(ah_0 x - (ah_0 + b4_0)k'_{-h4}) \\ (x(x - k'_{-t} - k'_t) + k_i(k'_t - x) + k_{-i}(k'_{-t} + k'_t - x)) \end{pmatrix}
$$

$$(84)$$

$$
[B2](t) = \frac{k'_{-h4} k_{h2} k'_{-t} k_{-i}}{\alpha\beta\gamma\delta} + \frac{e^{-\alpha t} C_\alpha^{B2}}{\alpha(\alpha-\beta)(\alpha-\gamma)(\alpha-\delta)} + \frac{e^{-\beta t} C_\beta^{B2}}{\beta(\beta-\alpha)(\beta-\gamma)(\beta-\delta)}
$$
$$
+ \frac{e^{-\gamma t} C_\gamma^{B2}}{\gamma(\gamma - \alpha)(\gamma - \beta)(\gamma - \delta)} + \frac{e^{-\delta t} C_\delta^{B2}}{\delta(\delta - \alpha)(\delta - \beta)(\delta - \gamma)}
$$

$$(85)$$

where:

$$
C_x^{B2} = \begin{pmatrix} x(x - k'_{-h4} - k_{h4})(x(b2_0(x - k_i) - (b2_0 + cc_0)k'_{-t}) \\ + k_{-i}((b2_0 + cc_0 + ct_0)k'_{-t} - b2_0 x)) + k_{h2}(k'_{-h4} \\ (k_{-i}((cc_0 + ct_0 - 1)x + k'_{-t}) + x((cc_0 + ct_0 - 1)(k_i - x) \\ + (ct_0 - 1)k'_{-t})) + x(x((ah_0 + b2_0)(k_i - x) \\ + (ah_0 + b2_0 + cc_0)k'_{-t}) + k_{-i}((ah_0 + b2_0)x - (1 - b4_0)k'_{-t}))) \end{pmatrix}
$$

$$(86)$$

$$
[Ct](t) = \frac{k'_{-h4} k_{h2} k_i k_t}{\alpha\beta\gamma\delta} + \frac{e^{-\alpha t} C_\alpha^{Ct}}{\alpha(\alpha - \beta)(\alpha - \gamma)(\alpha - \delta)} + \frac{e^{-\beta t} C_\beta^{Ct}}{\beta(\beta - \alpha)(\beta - \gamma)(\beta - \delta)}
$$
$$
+ \frac{e^{-\gamma t} C_\gamma^{Ct}}{\gamma(\gamma - \alpha)(\gamma - \beta)(\gamma - \delta)} + \frac{e^{-\delta t} C_\delta^{Ct}}{\delta(\delta - \alpha)(\delta - \beta)(\delta - \gamma)}
$$

$$(87)$$

where:

$$
C_x^{Ct} = \begin{pmatrix} -x k'_{-h2}(x - k'_{-h4} - k_{h4})(-(cc_0 + ct_0)k_i + ct_0(x - k'_{-t})) \\ + x(x - k'_{-h4} - k_{h4})(ct_0 x(x - k'_{-t} - k'_t) \\ + k_i(-(cc_0 + ct_0)x + (b2_0 + cc_0 + ct_0)k'_t)) \\ - k_{h2}(k'_{-h4}(k_i((cc_0 + ct_0)x - k'_t) + ct_0 x(k'_{-t} + k'_t - x)) \\ + x(ct_0 x(x - k'_{-t} - k'_t) + k_i((1 - b4_0)k'_t - (cc_0 + ct_0)x))) \end{pmatrix}
$$

$$(88)$$

The shape of the different rates as function of pH is given in Fig. 4. The simulation is made considering that **B₂** is formed 3 times faster than **B₄**. Figure 4a regards the rate constant of the hydration/dehydration involving **B₂**, Eq. (2) and tautomerization Eq. (4), while Fig. 4b an identical process involving **B₄**, Eq. (3). The difference of the two figures at higher pH values is a result from the fact that **B₄** is a kinetic product not evolving to **Cc** and **Ct**, while **B₂** can be involved into two different types of reactions.

Figure 4c is similar to Fig. 1b the left branch being controlled by tautomerization and the right by hydration of **B₂** in competition with **B₄** formation. Finally the slowest process presented on Fig. 4d is still an asymmetric bell shape curve where at higher pH values the rate determining step is the formation of **Ct** in this precise simulation
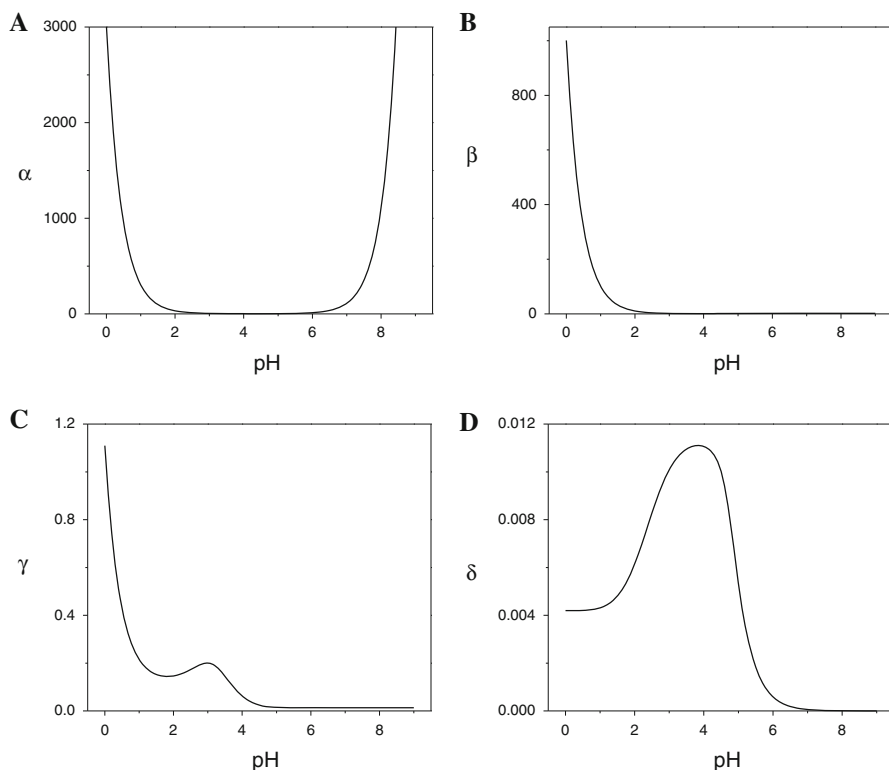
Fig. 4 Observed rate constants in (s^{-1}) for a simulated system defined in Eq. (56) with: $k_{h2} = 1$, $k_{-h2} = 3,000$, $k_{h4} = 0.8$, $k_{-h4} = 1,000$, $k_t = 1$, $k_{-t} = 0.1$, $k_i = 0.01$, $k_{-i} = 0.0042$, $k_t^H = 10$, $k_t^{OH} = 10^9$. **a** α, **b** β, **c** γ, **d** δ

controlled from the reservoir of **B$_4$**. On Fig. 5a, b the experimental case of processes shown on Fig. 4c, d is presented.

As in the previous case (*System I*) the mole fraction variation after reverse pH jumps and flash photolysis experiment were reported on Fig. 6.

3 Results and discussion

Figure 7 illustrates how the model can contribute to the comprehension of the kinetic details in such a complex network of chemical reactions. It is possible to distinguish three steps occurring in more or less separated scales of time. In the faster step (Fig. 7a) the mole fraction of **B$_4$**, **B$_2$** and **Cc** increase at the expenses of **AH$^+$**, which mole fraction drops almost to zero. The relative amount depends on the ratio of the mole fraction defined in Eqs. (10–14) and from the initial and final pH. In a slower step **Ct** is formed through **B$_2$** and **Cc**, and a new pseudo-equilibrium is reached involving these three species. It is worth noting that **B$_4$** is still trapped during this step. The final equilibrium (Fig. 7c) is attained through the conversion of **B$_4$** into **Ct**, **Cc** and **B$_2$**. This result
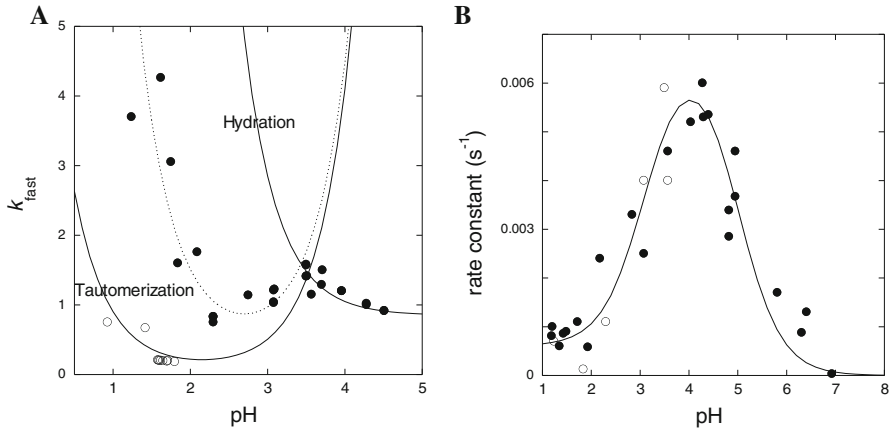
Fig. 5 Observed rate constants of Naphthoflavylium compouns [18]. **a** Constant γ, **b** constant δ. Reprint with permissions from ref. [18], Copyright 2009, Elsevier
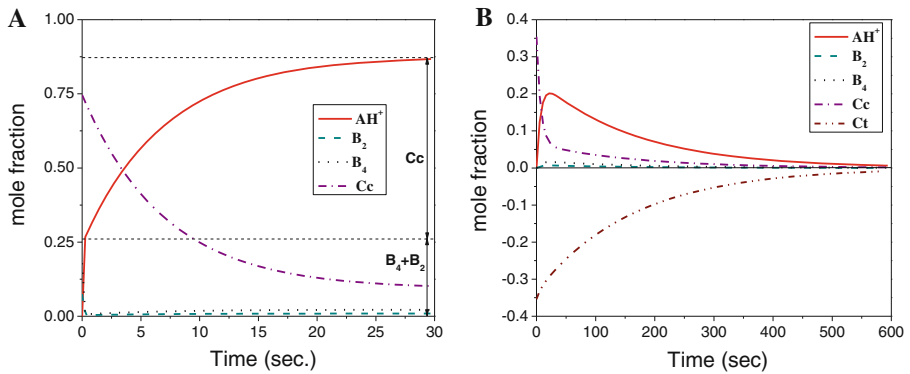

Fig. 6 Simulated—mole fraction of the components. **a** After reverce pH jump from pseudo equilibrium; **b** after flash photolysis experiment at pH = 2. $k_{h2} = 1$, $k_{-h2} = 3,000$, $k_{h4} = 0.8$, $k_{-h4} = 1,000$, $k_t = 1$, $k_{-t} = 0.1$, $k_i = 0.01$, $k_{-i} = 0.0042$, $k_t^H = 10$, $k_t^{OH} = 10^9$
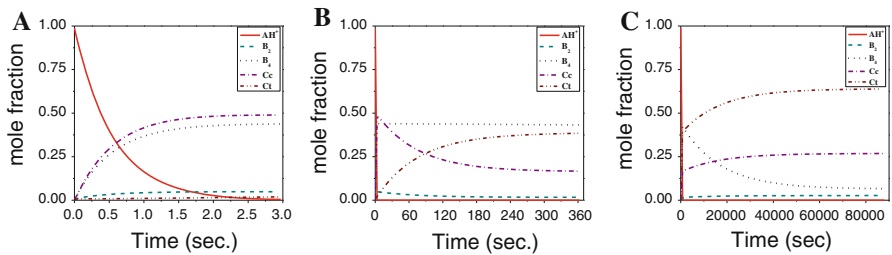

Fig. 7 Direct pH jump 0 to 7 for a system with: $k_{h2} = 1$, $k_{-h2} = 3,000$, $k_{h4} = 0.8$, $k_{-h4} = 1,000$, $k_t = 1$, $k_{-t} = 0.1$, $k_i = 0.01$, $k_{-i} = 0.0042$, $k_t^H = 10$, $k_t^{OH} = 10^9$. The three different equilibrations steps
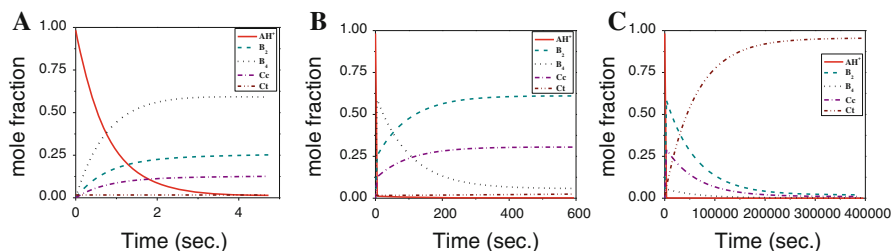
Fig. 8 Direct pH jump from 1 to 7 for a system with: $k_{h2} = 0.47$, $k_{-h2} = 14,000$, $k_{h4} = 0.81$, $k_{-h4} = 2.6 \times 10^5$, $k_t = 0.23$, $k_{-t} = 0.46$, $k_i = 5.0 \times 10^{-5}$, $k_{-i} = 5.0 \times 10^{-7}$, $k_t^H = 19.5$, $k_t^{OH} = 7.0 \times 10^9$

is observed whenever the compound does not present a kinetic barrier, as recently reported. [18]

In contrast in the case of the existence of a high barrier as in 4'-methoxyflavylium [19] the first kinetic process corresponds to the formation of **B₄**, **Cc** and **B₂**, the second process is the conversion of **B₄** in more **Cc** and **B₂**, and only after this step the **Ct** is formed in a much longer timescale (see Fig. 8).

4 Conclusions

The complete resolution of the kinetic equations of the network of chemical reactions involving flavylium compounds was achieved. The model following the initial proposal of McClelland [7,19] is general and could be applied for those flavylium compounds bearing hydroxyl substituents that give rise to quinoidal bases or those lacking of the hydroxyl substituent where in alternative the species **B₄** is formed. The acid and basic catalysis in both hydration reactions and tautomerization was included. The model predicts with great accuracy the behavior of previously reported flavylium systems and can be used to fit the experimental data and thus recover the respective rate constants. Moreover, it can fit the data from the direct and reverse pH jumps as well as the flash photolysis experiments. In addition, the pH dependent mole fraction distributions at the equilibrium as well as at the pseudo-equilibrium are easily obtained. The developed model is applicable not only to the flavylium systems, but to all of the chemical and biochemical reactions following the same pathway [20].

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