Excited state proton transfer in the *Cinchona* alkaloid cupreidine†

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Photophysical properties of the organocatalyst cupreidine (**CPD**) and its chromophoric building block 6-hydroxyquinoline (**6HQ**) in protic and nonprotic polar solvents (methanol and acetonitrile) were investigated by means of UV-vis absorption, and steady state and time resolved fluorescence spectroscopy. The effects of the catalytically relevant interactions with electrophilic and hydrogen bonding agents (*p*-toluene sulfonic acid and water) on their spectral characteristics were studied. In neutral **CPD** in acetonitrile, quenching of fluorescence occurs due to electron transfer from the quinuclidine nitrogen to the excited quinoline chromophore. Protonation suppresses this process, while complexation with water leads to enhanced excited state proton transfer from the 6′-OH group to the quinuclidine nitrogen, and emission occurs from the anionic form of the chromophore. The weakly emitting zwitterionic form of the hydroxyquinoline chromophore is readily formed in methanol, but not in acetonitrile.

Introduction

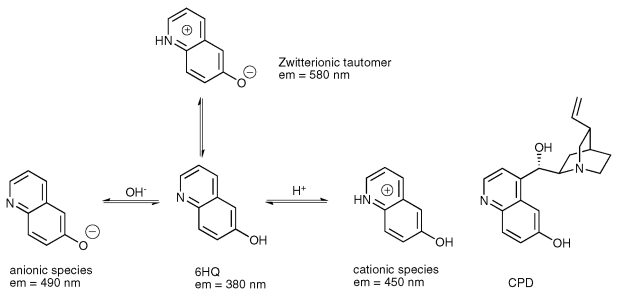
For centuries, *Cinchona* alkaloids were the traditional drugs to treat malaria.[1] Recently, the exploitation of *Cinchona* derivatives as catalysts and chiral resolving agents has attracted extensive attention.[2] Increasing efforts have been made to unravel conformational properties and the mechanism of the catalytic effect of *Cinchona* alkaloids on some organic reactions by NMR spectroscopy[3,4] and theoretical studies.[5]

Fluorescence methods have proven to be useful tools in many fields of science and technology,[6] but have rarely been applied to mechanistic investigation of organic catalytic reactions. In principle, the intrinsic fluorescence of *Cinchona* alkaloids could be exploited to advance the understanding of their catalytic mechanisms, and aid the design of new catalysts. Interestingly, although there are numerous papers about the photophysical properties of *Cinchona* alkaloids in aqueous media,[7] there are very few papers in which organic solvents were used.[8,9] Many organocatalytic reactions are carried out in organic solvents. Therefore, knowledge and understanding of the essential photophysical properties of *Cinchona* alkaloids in organic solvents is a prerequisite for the fruitful use of fluorescence techniques for the study of catalysis by this class of compounds.

Cinchona alkaloids have a quinoline chromophore connected with a quinuclidine unit *via* a chiral carbon atom. It is generally recognized that both the hydroxyl group(s) and the quinuclidine nitrogen play key roles in the catalysis of the organic reactions by *Cinchona* alkaloids.[10] We have chosen cupreidine (**CPD**) as the subject for the present study because it is readily available and has both the 6′-OH group at the quinoline and the quinuclidine nitrogen.

The photophysical properties of 6-hydroxyquinoline (**6HQ**) and 6-methoxyquinoline (**6MQ**) have been studied in different solvents under different conditions.[11–15] In organic solvents, **6HQ** shows the emission of the neutral species at ~380 nm, while small amounts of water in alcohol solvents resulted in a red-shifted emission peak of the zwitterionic tautomeric form, caused by excited state proton transfer[13,14] (ESPT). The different protonation states of **6HQ** are shown in Scheme 1.[12]

Among the most important interactions in organocatalysis are hydrogen bonding and acid/base or electrophile/nucleophile interactions.[5] In the present paper we describe the response of the absorption and emission spectra of **CPD** to acid and water, in protic and non-protic polar solvents. Acid and water are the simplest electrophilic and hydrogen-bonding agents, which model the interactions of **CPD** with reagents during catalysis. The results show that (1) although the quinoline moiety is the chromophore, the quinuclidine unit plays an important role in the photophysical properties of *Cinchona* alkaloids as an electron donor and proton acceptor; (2) the effects of acid and of water on the emission spectra of **6HQ** and **CPD** are different for the protic and nonprotic polar organic solvents methanol and acetonitrile.



Scheme 1 Chemical structures of compounds studied and differently protonated species of **6HQ** with their emission wavelengths in water.[12]

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Experimental details

Materials

CPD was available in the laboratory.[16] *p*-Toluenesulfonic acid monohydrate (*p*TsOH, >98.5%) and 6-hydroxyquinoline (**6HQ**, 95%) were purchased from Sigma-Aldrich. **6HQ** was recrystallized from ethyl acetate before use (mp = 192–194 °C, lit. 192–193 °C).[17] Acetonitrile (MeCN) and methanol (MeOH) were of spectroscopic grade. MeCN was distilled from CaH_2. MeOH was dried overnight with $MgSO_4$ and then distilled and stored over 4 Å molecular sieves before use;[18] the water content was less than 200 ppm. Doubly distilled water was used.

Spectral measurements

An accurately weighed amount of **CPD** or **6HQ** was dissolved in 25 mL MeOH or MeCN to obtain a stock solution. 30 μL of the stock solution was added to a 1 cm cuvette. 3 mL of the corresponding solvent was added to the cuvette after MeOH or MeCN was evaporated. Absorption measurements were performed with a Varian Cary 300 spectrophotometer and fluorescence spectra were recorded on a SPEX Fluorolog 3 fluorescence spectrophotometer. All the experiments were performed at 23 °C using non-degassed samples. The titration experiments with acid were carried out by adding small quantities (less than 60 μL) of a stock solution of *p*TsOH (~15 mM) to 3 mL of the solution of interest.

For the measurements of fluorescence quantum yields quinine bisulfate in 0.5 M H_2SO_4 (λ_{ex} = 320, Φ_f = 0.55) was used as the standard.[19]

Time-resolved fluorescence data were acquired using the time-correlated single-photon counting (SPC) technique with an excitation wavelength of 323.5 nm. The measurements were performed with an in-house assembled SPC setup, which has been described elsewhere.[20]

The fluorescence decay curves were fitted (Igor Pro 6.0, Wave Metrics, Inc., Lake Oswego, OR 97035, USA) to a sum of 1 to 3 exponential functions, convolved with the instrument response function, which was measured by Raman scattering of water. For global analysis we used Fluofit version 4.4 from Picoquant Gmbh, Berlin, Germany.

Quantum chemical calculations were performed using the Gaussian 03 program.[21] The B971 functional[22] was used because of its good reputation for the description of hydrogen bonds.[23] The solvent (MeCN) was described using the Polarizable Continuum Method.[24]

Results and discussion

Effect of protonation on the spectral characteristics of 6HQ and CPD in MeCN

The effects of protonation on the absorption spectra of **6HQ** and **CPD** in MeCN are shown in Fig. S1 (ESI†) and Fig. 1, respectively. Acid induces similar changes of the spectra of both compounds. **6HQ** has two absorption peaks (centered at about 320 and 332 nm, respectively, Fig. S1, ESI†). Upon the addition of acid (*p*TsOH), two new peaks in the absorption spectrum appeared (314 and 346 nm) and developed at the expense of the original bands, yielding two isosbestic points (323 and 334 nm), which indicates that there are two species, namely, neutral and cationic **6HQ** in the ground state. These results are similar to those obtained in aqueous solution.[12] Compared with **6HQ**, **CPD** has the same chromophore but it has a hydroxymethyl quinuclidine substituent at the 4-position. The UV-vis spectrum shows insignificant changes when the ratio of [*p*TsOH] to [**CPD**] is less than 1 (not shown); beyond this value, it evolves gradually with the absorption maxima shifting from 325 and 336 nm to 317 and 358 nm (Fig. 1), respectively. Apparently isosbestic points at 324 and 341 nm can be seen, but they are not perfect, possibly due to the change of the population of different conformations upon protonation.[4]

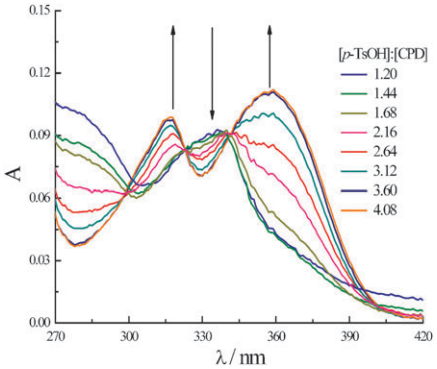

Fig. 1 Effect of added acid on the absorption spectrum of **CPD** (27 μM) in MeCN.

At the ratio of [*p*TsOH] to [**CPD**] above 3.60, further addition of *p*TsOH had no effect on the UV-vis spectrum of **CPD**. The different effects of acid on the spectra of **6HQ** and **CPD** are obviously due to the presence of the strongly basic quinuclidine unit in **CPD**, which is protonated before the quinoline nitrogen. As a result, the first equivalent of acid has little effect on the absorption spectrum of **CPD**. In contrast to the case of **6HQ**, in order to achieve full protonation of the quinoline unit in **CPD** an excess of *p*TsOH is needed, probably because of electrostatic repulsion.

In MeCN, **6HQ** (fluorescence quantum yield[8] Φ_f = 0.087) shows a single emission peak at ~360 nm (Fig. S2a, ESI†), which is attributed to the locally excited (LE) state emission. With increasing *p*TsOH concentration, the fluorescence intensity of **6HQ** at 360 nm is significantly reduced, and a much stronger red-shifted emission ($\lambda_{max} \approx$ 450 nm) is observed, with an isoemissive point at 395 nm. The new emission peak at 450 nm is assigned to the cationic species of **6HQ** that results from the protonation of the quinoline nitrogen.

CPD in MeCN has two weak emission bands (Φ_f = 0.047) at about 360 nm and 520 nm, corresponding to emissions from the LE state and an intramolecular charge transfer (ICT) state, respectively.[8] The intensity of the LE emission increases, while that of the ICT band decreases when the ratio of [*p*TsOH] to [**CPD**] changes from 0 to ~1 (Fig. 2a); above this range, a new emission band at about 450 nm forms and develops at the expense of the LE emission band (360 nm, Fig. 2b). The nearly isoemissive point at 411 nm reveals the clean formation of a

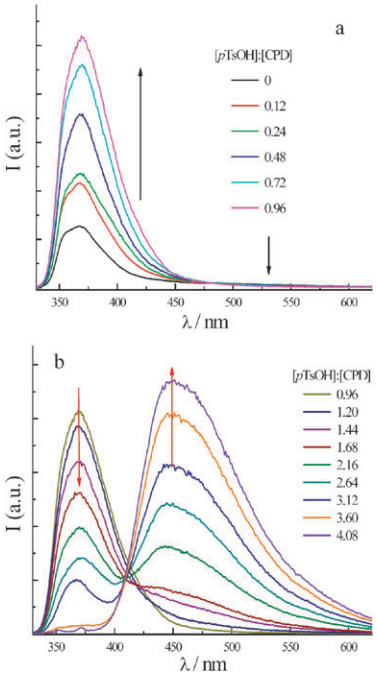

Fig. 2 Effect of acid on the emission spectrum of **CPD** (27 μM) in MeCN (excited at 320 nm).

new emitting species in which the chromophore is protonated in agreement with the absorption spectra. The lower fluorescence quantum yield of **CPD** in MeCN is attributed to electron transfer from the tertiary amine to the quinoline fluorophore.[8] Addition of up to 1 eq. of acid restores the LE emission because the electron donating group is effectively removed by protonation of the quinuclidine nitrogen.

Effect of protonation on the spectral characteristics of 6HQ and CPD in MeOH

In methanol, the addition of acid leads to similar changes in the absorption spectra as in acetonitrile: two new peaks of the protonated quinoline chromophore cleanly grow in, while the original band decreases (Fig. S3, ESI†).

The changes of the emission spectra of **CPD** in MeOH (Φ_f = 0.114) upon the addition of *p*TsOH (Fig. 3) reflect the sequential protonation of the quinuclidine and quinoline units. In the absence of acid, an LE band can be seen at 380 nm, but there are also weak emissions at ~490 nm and ~580 nm, attributable to the anionic form (proton transfer to the quinuclidine) and the zwitterionic tautomer, respectively. The LE band (red-shifted compared to that in MeCN) and the zwitterionic emission are also observed in **6HQ** (Fig. S2b, ESI†).

The fluorescence intensity at ~380 nm increases clearly when the ratio [*p*TsOH]/[**CPD**] changes from 0 to 1.05 (Fig. 3a) because proton transfer to the quinuclidine nitrogen is suppressed. Beyond 1 equivalent of acid, the LE emission decreases gradually as the quinoline becomes protonated (Fig. 3b). At the same time, the peak at 580 nm increases in intensity. The emission peak of the cationic species (~450 nm) appears only at higher proton concentration

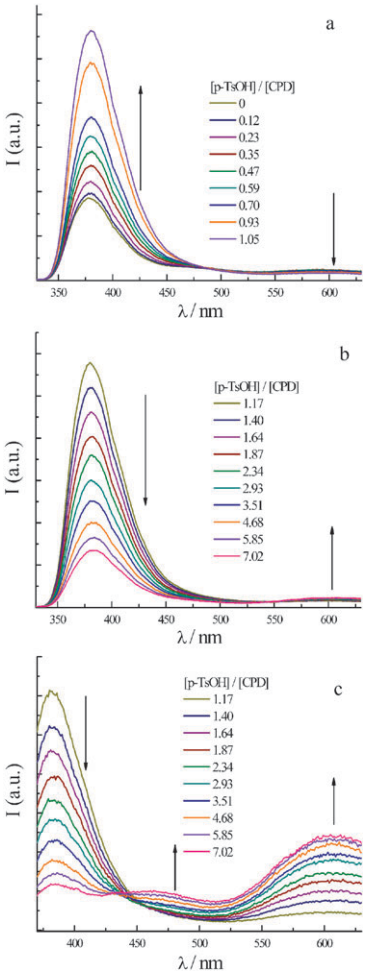

Fig. 3 Protonation effect on the emission spectra of **CPD** (40 μM) in MeOH excited at 320 nm (a, b) and 360 nm (c).

([*p*TsOH]/[**CPD**] > 2) when excited at 360 nm, where the cation is excited selectively (Fig. 3c).

When the quinuclidine nitrogen is not completely protonated ([*p*TsOH]/[**CPD**] < 1) the zwitterionic tautomer can be formed by transfer of the OH-proton to the quinuclidine, followed by protonation of the quinoline nitrogen by the solvent. When both nitrogens are protonated ([*p*TsOH]/[**CPD**] > 2), the OH-proton is transferred to the solvent rapidly after excitation.

Effect of water on the absorption and emission spectra of 6HQ and CPD

In MeOH and in MeCN, the shape of the absorption peak of **6HQ** shows no visible change upon the addition of water (Fig. S4, ESI†).

The fluorescence emission spectra of **6HQ** in methanol–water mixed solutions were already reported by Mehata *et al.*[13] Their results showed that with increasing water content, a strongly Stokes shifted new emission band at 580 nm developed, accompanied by a decrease of the LE emission (376 nm, in our case it is at ~372 nm, Fig. S5, ESI†) without noticeable wavelength change. No emission peak from the ionic species

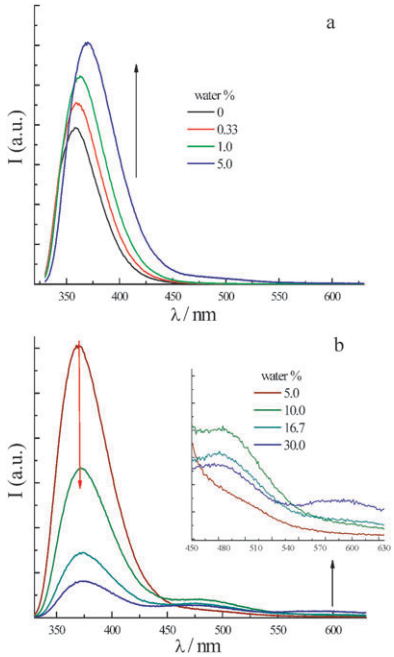

Fig. 4 Effect of water on the emission spectra of **6HQ** (48 μM) in MeCN (λ_{ex} = 320 nm).

($\lambda_{em} \approx$ 460 nm, cationic or anionic form)[12] was seen when exciting at 360 nm (data not shown).

The effect of water on the spectral properties of **6HQ** in MeCN is more complicated. The fluorescence intensity of the LE emission increases evidently with about 11 nm red shift upon the addition of water up to 5% (Fig. 4a). These spectral changes are probably a result of hydrogen bonding of water to the quinoline nitrogen and 6-hydroxy groups, without ESPT. Further addition of water leads to a slight further red shift (about 4 nm) and a distinct decrease in the intensity of the neutral LE emission. A shoulder at about 490 nm increases first and then decreases at water content >10%. This peak may be attributed to the anionic species (Fig. 4b). A third emission peak at about 580 nm appears simultaneously with decrease of the anion band (inset in Fig. 4b): when enough water is present, the zwitterionic tautomer can be formed.

The effects of water on the emission spectra of **CPD** in MeCN and MeOH are demonstrated in Fig. 5. In MeCN, the fluorescence intensity of the LE state decreases with increasing water content. The fluorescence intensity at ~520 nm first increases sharply, until the water content reaches 10%; then it decreases gradually. The long wavelength band shifts from ~520 nm to 490 nm upon addition of water (Fig. 5a). In the absence of water the emission presumably stems from the ICT state.[8] When a small quantity of water is present the emission is that of the anionic species. The emission band of the zwitterionic tautomer (~580 nm) is seen only at water content >70% (Fig. 5b).

In MeOH, the fluorescence intensities of neutral and anionic species decrease regularly upon water addition, accompanied with an increase in the fluorescence intensity at about 580 nm (zwitterionic form) and an isoemissive point at 494 nm (Fig. 5c).

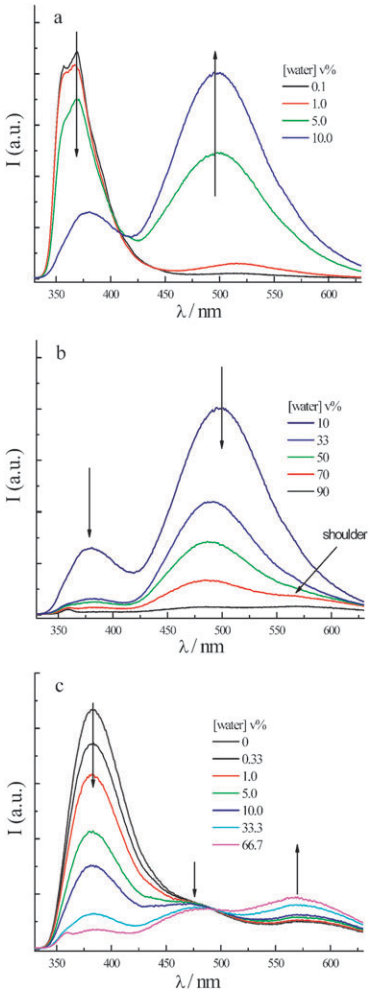

Fig. 5 Effect of water on the emission spectra of **CPD** in MeCN (27 μM, a and b) and MeOH (40 μM, c) (excited at 320 nm).

Time-resolved fluorescence spectroscopy

The fluorescence decays for the normal, cationic and zwitterionic emissions of **6HQ** and **CPD** in MeOH and MeCN were studied in order to get some insight into the dynamic nature of the proton transfer processes.

The fluorescence transients of **6HQ** in MeCN and MeOH solutions as a function of acid concentration were measured at wavelengths characteristic of the three different emitting species, and fitted in a global analysis. In MeOH, a tri-exponential function was used to fit the decay at all three emission wavelengths. The component with a decay time of 1.56 ns (1.45 ns in ref. 12) is dominant at 380 nm, and hardly changes its amplitude with the acid concentration (Fig. 6a and Fig. S6a, ESI†). This shows that the decrease in the emission intensity with increasing acid concentration is due to the lower concentration of the neutral form, not due to a quenching process.

At 450 nm, some emission of the neutral LE species is still observed, but a shorter component with decay time of about 0.05 ns appears and becomes more pronounced at higher acid concentrations (Fig. 6b and Fig. S6b). The shorter time can be ascribed to the cationic species, which is consistent with the very weak emission at ~450 nm.

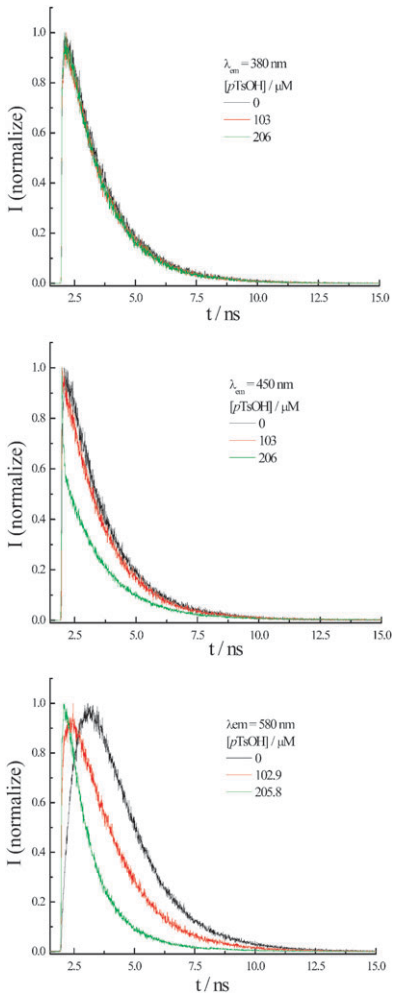

Fig. 6 Effect of acid on the fluorescence decay of **6HQ** (105 μM) in MeOH at different emission wavelengths. Traces were scaled to the same maximum.

The zwitterionic tautomer emission (580 nm) in the absence of acid shows a bi-exponential time profile with a rise time of 0.85 ns and a decay time of 1.56 ns, with opposite amplitudes (Fig. 6c and S6c, ESI†). Apparently, the neutral LE state is the precursor of the zwitterionic tautomer, which decays with a time constant of 0.85 ns. The decay time is similar to that reported for aqueous solutions.[11e] In the absence of acid the ESPT process involves transfer of a proton from methanol to the quinoline N-atom, and deprotonation of the OH-group. If the cation is an intermediate in this process it will go unnoticed because of its very rapid decay. With the addition of acid, the amplitude of the rise time decreases and finally no rise time can be detected at [*p*TsOH] $>$ 171 μM (about 1.64 eq.). In the presence of acid, the zwitterion can be formed simply by OH-deprotonation of the highly acidic quinolinium ion. When the zwitterion is formed from the protonated species, the fluorescence intensity curve rises with a time constant of 0.05 ns, and decays with 0.85 ns. When both neutral and cation precursors are present, complicated time profiles result, but they can still be fitted with the same three time constants. Fig. 7 shows the ESPT processes of **6HQ**.

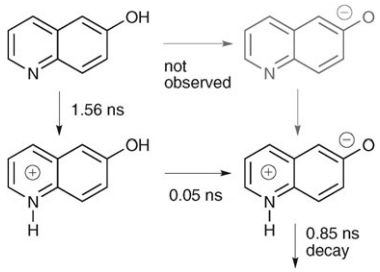

Fig. 7 Kinetics of ESPT processes of **6HQ** in MeOH/acid.

Different results are obtained in MeCN. In the absence of acid, the fluorescence decay of **6HQ** is mono-exponential with a lifetime of 1.33 ns in the emission wavelength range of 370–500 nm. The presence of acid did not induce a change in the fluorescence decay for the emission band at 370 nm. A bi-exponential function was used to fit the decay at 450 nm: in addition to the component of 1.33 ns corresponding to the neutral species, a much longer component (about 12 ns) is observed arising from the cationic species. The amplitude of the longer component increases with the addition of acid (Fig. S7, ESI†). In contrast to the situation in MeOH, the cation excited state is long-lived because the OH-deprotonation cannot occur.

The fluorescence decays of **CPD** are complicated (Tables 1 and 2) because of the involvement of multiple conformations and the additional ICT and PT states. The entire set of data at different wavelengths and different acid concentrations could not be fitted globally with 4 components, the maximum in the program available to us. Therefore a full analysis is beyond the scope of the present study. Some results, however, could be extracted. In MeCN, the decay has at least three components in all the wavelength ranges detected. The two shorter components may be due to the LE states with different conformations, while the longest component may be caused by the ICT state. The relative amplitude associated with the shortest one (0.037 ns) is dominant in the shorter wavelength range, and decreases with increasing emission wavelength. With the addition of acid, two shorter components become less important. The amplitude of the longest one increases clearly at 380 nm, accompanied by a new component (8.9 ns) that appears and becomes more important, due to the formation of the dicationic species.

The fluorescence decays of **CPD** in the presence of acid in MeOH are very complicated, but could be analyzed globally for each detection wavelength. The set of decays in the short wavelength region (380 nm, LE) with different concentrations of acid could be globally analyzed; the amplitude of a short-lived component (0.62 ns) decreased with added acid, a decay component of 1.54 ns increased in parallel. When the quinuclidine nitrogen is protonated, **CPD** resembles **6HQ**. At 450 nm, the emission of the protonated chromophore becomes more important at higher acid concentration. The set of decay curves at 9 different acid concentrations can be globally fitted with two time constants of 1.16 and 0.31 ns.

The time profiles at 560 nm as a function of acid are more complex. Four components were not enough for an adequate fit of this data set. At the stage where the quinuclidine is

Table 1 Relative amplitudes α_i of the four time components in the fluorescence decays of **CPD** (54 μM) in MeCN at three different emission wavelengths in the presence of different concentrations of *p*TsOH (λ_{ex} = 323.5 nm)

		380 nm				450 nm				560 nm			
[*p*TsOH]/μM	τ/ns	0.04	0.61	1.7	8.9	0.04	1.2	3.5	8.9	0.04	1.4	6.2	8.9
0		48	36	16		32	41	28		−52	22	26	
69		40	11	50		3	49	48	1	−33	21	43	4
137			7	42	51		11	−25	63	−5		−38	56

Table 2 Relative amplitudes α_i of the two time components in the fluorescence decays of **CPD** (81 μM) in MeOH at three selected emission wavelengths in the presence of different concentrations of *p*TsOH (λ_{ex} = 323.5 nm)

		380 nm		450 nm		560 nm	
[*p*TsOH]/μM	τ/ns	1.54	0.62	1.16	0.31	0.49	1.28
0		22	78	6	94	−27	72
69		34	66	11	89	−29	70
137		75	25	21	79	−35	64
172		88	12	26	74	−40	58

protonated but the quinoline is not, a decay curve is observed similar to that of **6HQ**, with a rise of 0.49 ns and a decay of 1.28 ns, corresponding to decay and formation of the zwitterionic tautomer, respectively.

Both for **6HQ** and **CPD** in MeOH the cationic species has a short lifetime due to rapid OH-deprotonation, which is consistent with the weak emission at about 450 nm.

Discussion

The responses of the fluorescence of **6HQ** and **CPD** to acid and water can be summarized as follows:

(1) acid and water promote the appearance of the emission of the zwitterionic tautomer of **6HQ** (Fig. S2b, c and S5; ESI†) and **CPD** (Fig. 3b, c and 5c) in MeOH, while no or much weaker tautomeric emission can be seen in MeCN except at high water content (Fig. S2a, S4 and S5a, b, ESI†);

(2) anionic emission of **6HQ** appears only at relatively high water content in MeCN (Fig. 4b), whereas that of **CPD** can easily be seen at much lower water content in both solvents (Fig. 5a and c);

(3) the presence of small amounts of acid ([*p*TsOH]/[**CPD**] $\leq$ 1) results in the increase of LE emission intensity of **CPD** (Fig. 2a and 3a), while the presence of acid leads to the decrease in LE emission of **6HQ** (Fig. S2a and S2b, ESI†).

There are a proton donor (–OH) and a proton acceptor (quinoline nitrogen) in the fluorophore of both **CPD** and **6HQ**. The proton acceptor quinoline nitrogen has a pK_a of about 5.1.[12] The hydroxyquinoline chromophore has a slight "push–pull" character, the nitrogen containing ring being electron deficient and the hydroxy-substituted ring being electron rich. The protonation of the quinoline nitrogen strongly enhances this push–pull character, which causes a considerable bathochromic shift in absorption (+20 nm) and emission spectra (+80 nm). The cationic emission appears at ~450 nm for both compounds. On the other hand, the hydroxyl group in the quinoline ring can easily be deprotonated in the excited state (the pK_a* is more than 5 pH units lower than its pK_a).[12] If a suitable hydrogen bond network is offered, the excited state proton transfer from the hydroxy group in the fluorophore to the quinoline nitrogen can occur and the emission peak of the zwitterion will appear. The spectral behavior of **6HQ** in water–MeOH mixed solution was studied by Mehata and coworkers.[13] They explained that water and MeOH can form hydrogen bond bridges to facilitate the migration of a proton from the hydroxyl group to the quinoline nitrogen. But in the MeCN–water system, formation of hydrogen bond bridges is not possible. The $H_2O\cdots H_2O$ hydrogen bonds cannot easily form at lower water content because water molecules are separated from each other or from **6HQ** (**CPD**) molecules by MeCN molecules. Therefore, the emission peak of the tautomer can be seen only at relatively high water content (>16.7% and >50% for **6HQ** and **CPD**, respectively).

In MeOH, the addition of acid led to the formation of the zwitterionic tautomer in the excited state. In addition, the presence of water can make the proton migrate from the hydroxy group of **6HQ** in the excited state to the solvent. As a result, the emission peak of the anionic species is observed in MeCN at water content larger than 5% (Fig. 4b), but no such peak is seen in MeOH even in the presence of 16.7% water (Fig. S5, ESI†).

In the case of **CPD**, there is another proton acceptor as well as electron donor, quinuclidine nitrogen, which has a higher pK_a (9.7) than the quinoline nitrogen. Electron transfer can take place from the tertiary amine to the fluorophore and quench the LE fluorescence to a large extent (Φ_f of **CPD** is lower than that of **6HQ** in MeCN).[8] The protonation of the tertiary amine prevents the excited state electron transfer and leads to recovery of the fluorescence of the LE state. Further addition of acid results in the formation of ground state dicationic species caused by the protonation of the quinoline ring (emission at about 450 nm). The isoemissive point at 411 nm characterizes the transformation from monocationic species to the dicationic species. The anionic emission appearing in the presence of a small amount of water (<1% in MeCN and <200 ppm in MeOH) reveals that it is much easier for **CPD** than for **6HQ** to form anionic emissive species. The likely reason is that an intramolecular hydrogen bond can be formed between the hydroxyl group and tertiary amino group with water as a bridge. Fig. 8 shows a computed structure of such a complex in the ground state. A similar water-bridged complex is thought to be involved in fast proton transfer between acid and base in water.[25]

In order to gain further insight into the effects of solvents and substituents on the photophysical properties of **6HQ** and **CPD**, we have also studied the spectral characteristics of 6-methoxyquinoline (**6MQ**) and 10,11-dehydroquinidine

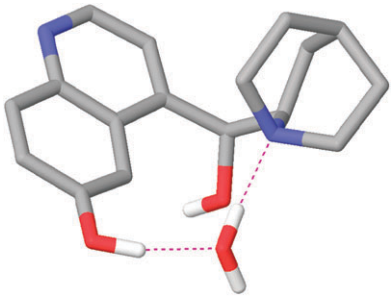

Fig. 8 Computed structure (B971/6-31G(d)) of a complex of **CPD** (without vinyl group) and water.

(**dHQD**), which lack the proton donating hydroxyl group in the quinoline ring.

For both compounds, the spectral changes induced by acid are solvent independent (Fig. S8–S11, ESI† and ref. 8): the addition of acid leads to the appearance of cationic absorption and emission peaks, while no tautomeric emission is observed: the excited state intramolecular proton transfer cannot take place in **6MQ** and **dHQD** because of the lack of a proton donor. Nevertheless, in organic solvent–water mixed systems, the emission spectra are somewhat solvent dependent (Fig. 9 and S12, ESI†).

In MeCN, the emission intensities of the neutral species of **6MQ** or **dHQD** increased steadily with a red shift at relatively low water content. The emission intensities of the LE state increased less in MeOH in the presence of a small amount of water.

At the same time, there are some differences in the spectral behavior between **6MQ** and **dHQD**. For **6MQ**, in the presence of a large amount of water, the original emission peak decreases its intensity while a second emission peak around 450 nm emerged and developed in both solvents which is caused by the protonation of quinoline nitrogen in the excited state. No dicationic emission peak is seen in the case of **dHQD** even in water. The existence of the protonated tertiary amine makes it much more difficult for nitrogen of the quinoline ring to be protonated in the excited state, so, the monocationic compound is the dominant species in the excited state. The same results are obtained in the case of **CPD**, namely, no dicationic species is observed in the presence of water, in agreement with the idea of the protonated tertiary amine inhibiting the protonation of quinoline nitrogen.

The above results reveal that the hydroxyl group in the quinoline ring leads to the solvent dependence of photophysical properties of **6HQ** and **CPD**.

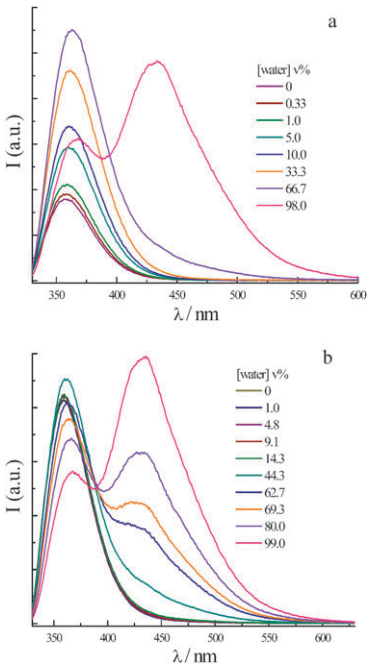

Fig. 9 Effect of water on the emission spectra of **6MQ** in (a) MeCN and (b) MeOH (excited at 320 nm).

Conclusions

The zwitterionic tautomer is the most stable form in the excited state of the **6HQ** fluorophore in protic solvents. In MeOH **6HQ** and **CPD** can form this tautomer *via* solvent-assisted proton transfer, but this occurs with only low efficiency. In MeCN proton transfer cannot occur at all, and only an emission of the neutral form ($\sim$360 nm) is observed for **6HQ**. **CPD** shows weak emission due to excited state electron transfer.

Protonation of the quinoline unit by a strong acid leads to the cationic form, which emits at about 450 nm in both MeOH and MeCN. In MeOH, the excited cation can donate the very acidic proton from the OH group to the solvent, giving rise to the zwitterionic tautomer. In MeCN, no proton acceptor is available, and only the strong cation emission is observed.

In MeOH the presence of water can promote the excited state intramolecular proton transfer due to the proton rearrangement within hydrogen bond clusters. The tautomer species in MeCN can be observed only at higher water content ($>$15% for **6HQ** and $>$50% for **CPD**). The presence of a small amount of water leads to the emission of the anionic form of **CPD** in both solvents due to an intramolecular water-bridge between the nitrogen of the quinuclidine and 6′-hydroxyl group, but a much larger amount of water is needed for the formation of the anionic species of **6HQ**.

The interactions with acid and water greatly affect the photophysics of the organocatalyst **CPD**, through the quinuclidine nitrogen and the quinoline 6′-OH group. Both functionalities are thought to play a key role in the catalytic pathways,[5] so it may be expected that the interactions with substrates of catalyzed reactions will affect the fluorescence. Binding of an electrophile to the quinuclidine nitrogen will have a particularly strong effect. Preliminary results indicate that this is indeed the case. In future work we will explore the modulation of the fluorescence of *Cinchona* organocatalysts by various electrophilic agents to gain insight into the kinetics and mechanisms of organocatalysis.

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