Quantum dot/cyclodextrin supramolecular systems based on efficient molecular recognition and their use for sensing†

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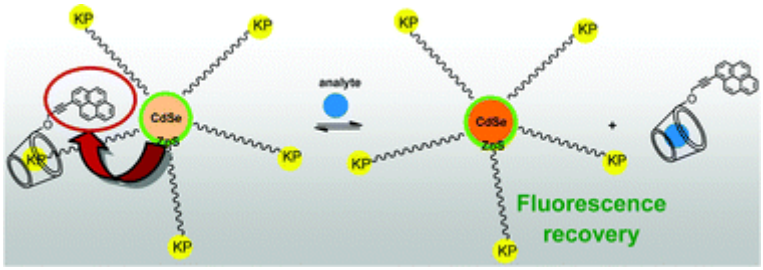
Abstract

A supramolecular system based on ketoprofen functionalised CdSe/ZnS nanoparticles and pyrene-modified β-CD was prepared and successfully used for molecular sensing of different analytes. In addition, a strategy for the individual recovery of all the components of the sensing assay is reported.



Core–shell CdSe/ZnS quantum dots (QDs) are highly fluorescent systems, which makes them of interest for biological, medical, and engineering applications.[1–4] The ZnS shell plays a crucial role in their emission properties and enhances the chemical- and photo-stability of the QDs. CdSe/ZnS nanoparticles are further passivated with organic ligands which allow them to remain stable as colloidal solutions in organic solvents and water and provide the desired surface functionality.[5] The application of QDs for biosensing is quite advanced, while their use as optical probes for molecular recognition has hardly been developed.[6]

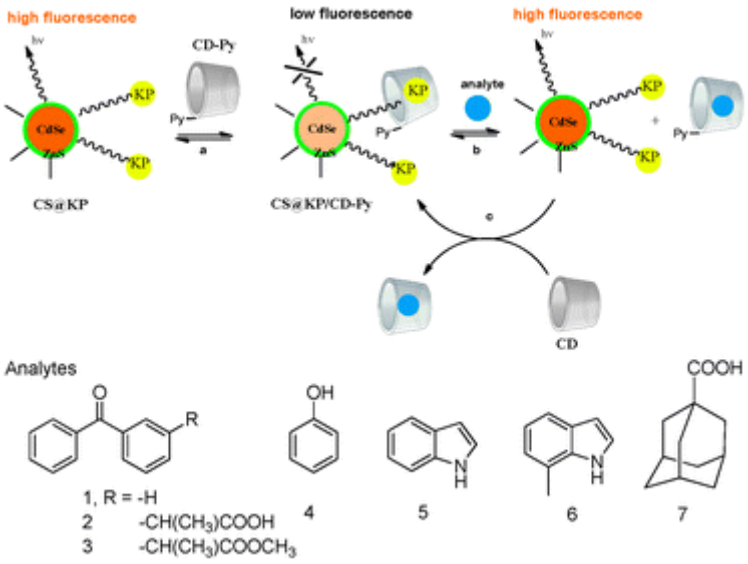
β-Cyclodextrin (CD) is a cyclic oligosaccharide comprising seven D-glucopyranose units linked by α-(1 → 4) bonds. It possesses a relatively rigid thorus-shaped structure, which defines an inner hydrophobic cavity rimmed by two hydrophilic openings which are different in diameter, the narrower containing the primary hydroxy groups located on the C-6 of the glucopyranose units and the wider containing the secondary groups located on positions C-2 and C-3 (Fig. S1,

ESI†). As a consequence, CD forms inclusion complexes in aqueous solution with a large variety of organic molecules of hydrophobic nature and of suitable size and geometry.[7–10] In addition to other applications, this feature has been explored for the design and construction of molecular sensors in which the inclusion of the guest molecule triggers a macroscopic signal which can be detected and quantified.[11] Both quantum dots and cyclodextrins have been used in Supramolecular Chemistry.[11–13]

Chemical sensing systems based on cyclodextrin-coated QDs have been recently designed.[6,14,15] For example, water-soluble CdSe/ZnS QDs have been prepared by association of the QDs with natural cyclodextrins helped by a sonochemical procedure; subsequent addition of phenols quenches the QD emission.[15] In addition, CD-capped CdSe/ZnS QDs have been prepared *via* covalent binding of an aminophenylboronic-functionalised QD to CD and used for optical sensing of different substrates by means of a fluorescence resonance energy transfer or an electron transfer mechanism.[6]

In this communication, we focus on a new strategy to obtain an easy-to-prepare and effective sensor, based on the molecular recognition between a QD and a CD that exhibits an enhanced fluorescence in response to different analytes.

The protocol used in the present work was to add ketoprofen-capped CdSe/ZnS QDs (CS@KP) to a solution of a CD bearing a pyrene unit on its secondary face (CD-Py, Fig. S1 in ESI†). CD-Py was selected because of the considerable association constant (K_a*ca.* 3000 M^{-1})[16] of CD with ketoprofen, and the potential capacity of the 3-(pyren-1-yl)prop-2-ynyl moiety to act as a quencher of the QD emission. The effective capping of CS@KP QDs by CD-Py led to QD/CD supramolecular systems (CS@KP/CD-Py, Scheme 1a, Fig. S2, ESI†), which were soluble in aqueous solvents. In the presence of the analyte, competitive association would recover the QD emission by moving the quencher (pyrene) away from the QD surface (Scheme 1b).



Scheme 1 Structures of CS@KP/CD-Py and of the analytes and protocol for the molecular recognition studies.

The CD-Py synthesis and characterisation is described in the ESI.†CD-Py exhibited red-shifted UV-absorbance bands compared to those of pyrene (Fig. S3, ESI†) and was soluble in water, DMF, and DMSO. The CS@KP QDs were synthesised by reaction of the bifunctional KP-SH ligand (ester of ketoprofen and 11-mercaptoundecanol) with either commercially available amine-capped CdSe/ZnS QDs from different sources (Evident, CS1; Ocean, CS2) or homemade QDs capped with trioctylphosphine oxide (CS3 and CS4), see experimental details in the ESI.† Table S1 (ESI†) shows the features [average diameter, the maximum of the first exciton (λ_{abs}) and of the emission (λ_{em}) peaks, as well as the fluorescence quantum yield (Φ_f)] of the initial core–shell QDs and that of the CS@KP QDs. ^{1}H NMR spectra proved that the ligand exchange reactions took place (Fig. S4, ESI†).[17]

The supramolecular systems were prepared by adding 20 µL of a toluene solution of the QD to 3 mL of an acetonitrile/water (3/1) solution of CD-Py (QD/CD-Py = 1/1000) and the system was stabilised over 15 minutes at room temperature (see UV-visspectra in Fig. S5, ESI†). The significant quenching of the QD emission evidenced formation of the CS@KP/CD-Py with the pyrene unit pointing toward the QD surface (Fig. 1A, Table S2, ESI†). Comparatively, the emission of the CS@KP QDs remained unchanged or even increased slightly upon addition of the natural CD (Fig. S6A, ESI†). Moreover, the supramolecular system exhibited a blue-shifted QD emission when compared to that of CS@KP and CS@KP/CD. The exact quenching mechanism is currently

under investigation, but electron transfer reactions involving the 1-pyrenethynyl units and the QD are most likely to be responsible for such a process.[18] Remarkably, the emission of the non-ketoprofen functionalised CS QDs was hardly influenced by capping with CD-Py (Table S2, ESI†), suggesting that the association of the CD to the ketoprofen units is essential to stimulate the quenching of the QD fluorescence.

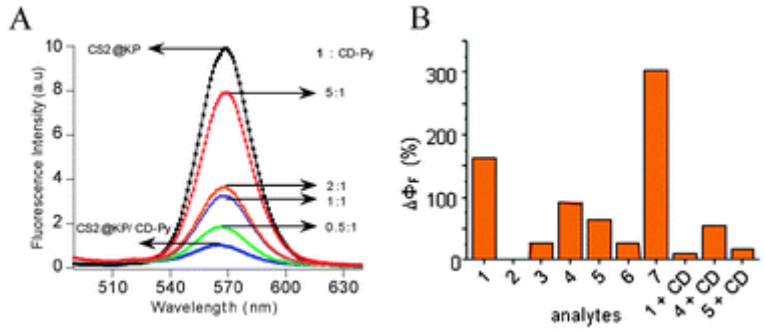


Fig. 1 (A) Fluorescence spectra (λ_{ex} = 450 nm) of deaerated acetonitrile/water (3/1) solutions of CS2@KP (5×10^{-9} M, ■), and CS2@KP/CD-Py (CD-Py/QD molar ratio of 1000), before (●) and after addition of **1**: **1/**CD-Py molar ratios of 0.5 :1 (▲), 1 :1, ▼), 2 :1 (○) and 5 :1 (□). (B) Effect of the addition of different analytes (**1** to **7**, 6×10^{-5} M) on the fluorescence (λ_{ex} = 450 nm) of the solutions of CS2@KP/CD-Py. Competitive effect of CD on analytes **1**, **4** and **5** is also shown. The luminescence of all the samples was recorded after 10 min ultrasound exposure.

In addition, the fluorescence of the pyrene unit of CD-Py was only slightly affected after formation of CS@KP/CD-Py (Fig. S6B, ESI†).

The influence of the polarity of the medium on the formation of pyrene radical cations is already known.[19] Therefore, to confirm the location of the pyrene moieties when CD-Py is capping the QDs, we performed transient absorption measurements of the pyrene systems (CD-Py, CS@KP/CD-Py, and CS/CD-Py). Laser flash photolysis (Nd/YAG, 355 nm) of CD-Py led to the formation of the pyrene triplet (λ_{max} at 430 nm, τ *ca.* 6 µs) and pyrene radical cation (λ_{max} at 490 nm, τ *ca.* 31 µs), see Table 1 and Fig. S7 and S8 (ESI†). Pyrene radical cation yield and lifetime diminished considerably, while the pyrene triplet yield and lifetime increased, in the case of the supramolecular system. These data are in agreement with the location of the pyrene moieties of CD-Py within the organic capping ligand of the CS@KP QDs, pointing toward the QD surface.

Table 1 Lifetimes of the pyrene triplet (^{3}Py) and pyrene radical cation (Py^+) of the pyrene systems in CH_3CN/water (3/1)

	^{3}Py τ^a/μs	Py $^+\tau^b$/μs
CD-Py	6.0 ± 0.8	31 ± 1
CS2@KP/CD-Py	24 ± 1	10 ± 2
1 + CS2@KP/CD-Py[c]	6.4 ± 0.9	27.4 ± 0.6
CS2@KP/CD	5.6 ± 0.2	22 ± 1

a Measured at 430 nm. b Measured at 490 nm. c 2 : 1 molar ratio.

Similar experiments were performed with CS/CD-Py and evidenced that the QD had considerably less effect on the yield and lifetime of the pyrene transients (Table 1). This might be attributed to a capping of the QD mainly by the primary face of CD-Py, *i.e.*, with its pyrene units located in the aqueous solution.

Subsequently, we studied the capacity of CS2@KP/CD-Py in molecular sensing, using benzophenone (**1**), ketoprofen (**2**), ketoprofen methyl ester (**3**), phenol (**4**), indole (**5**), 7-methylindole (**6**), and adamantane carboxylic acid (**7**) as analytes; Scheme 1b outlines the protocol for the assay.

The initial fluorescence of CS2@KP (Φ_f = 0.51) was quenched by addition of CD-Py (Φ_f = 0.11; QD/CD-Py molar ratio of 1/1000). Addition of CD had slight effect on the emission properties of CS2@KP/CD-Py (not shown). By contrast, addition of **1** to CS2@KP/CD-Py led to a 5 nm red shift of the λ_{em} and a remarkable enhancement of the QD fluorescence nearly recovering the fluorescence of CS2@KP when using a **1**/CD-Py molar ratio of 5 : 1 (see Fig. 1A for different molar ratios), *i.e.*, formation of the host–guest complexes between CD-Py and the analyte caused the release of the cyclodextrin from the QD surface. Consequently, laser flash photolysis experiments showed that the yield and lifetime of the pyrene transients upon addition of **1** to

CS2@KP/CD-Py (analyte/supramolecular system molar ratio of 2 : 1, Table 1) were similar to those of CD-Py in CH_3CN/H_2O (3/1).

Fig. 1B shows the emission response of CS2@KP/CD-Py (QD/CD-Py molar ratio of 1/1000) to a fixed amount (6×10^{-5} M, CD-Py/analyte molar ratio of 1/2) of the different analytes, demonstrating that the sensing systems can be implemented for many substrates provided that they associate to the cyclodextrin with a binding constant that allows the displacement of the ketoprofen units of the QD. The effect of the addition of CD on the emission of CS2@KP/CD-Py/analyte was also analysed. The emission of the QD decreased because of the competitive formation of analyte/CD and analyte/CD-Py host–guest complexes (Fig. 1B).

The pyrene-functionalisation of the cyclodextrin secondary face plays a role in its binding ability. Thus, for example, the relative sensitivity of the supramolecular system emission to the presence of analyte**1***vs.*analyte **2** was considerably larger than the ratio between the association constants of these analytes with natural CD.[16,20]

A preliminary assay showed that the presence of a given concentration of benzophenone did not cause an appreciable effect on indole response (Fig. S9, ESI†).

Finally, a control experiment was performed on the individual recovery of CD-Py, the QD, and the analyte once the assay of molecular recognition was complete (see Fig. 2). Vial I, containing a 5.25 mL acetonitrile/water (3/1) solution of CD-Py and CS2@KP (3.03×10^{-5} M and 3.03×10^{-8} M, respectively), mainly showed the blue-fluorescence of CD-Py. Vial II corresponded to the molecular recognition assay of analyte **7** (6.06×10^{-5} M, analyte dissolved in 57 µL of toluene).

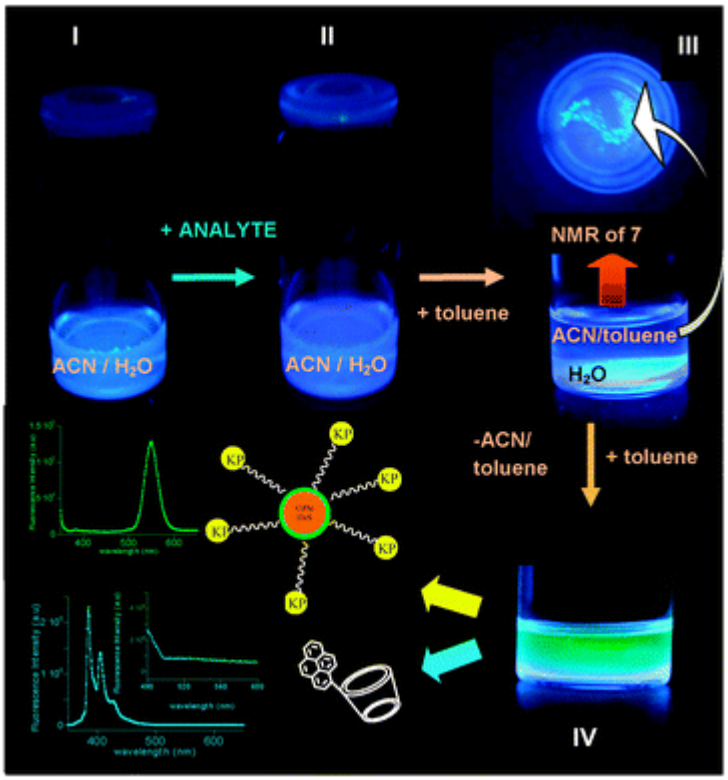


Fig. 2 Recovery of the QD, β-CD-Py, and **7**, once the assay of molecular recognition was complete.

Once the molecular recognition experiment was complete, the aim was to recover the three elements. Addition of toluene (250 µL) to vial II caused separation of the solution into two phases, migration of acetonitrile to the toluene phase, and separation of the QD in the interphase (see vial III, upper view picture), due to the low solubility of the QD in both the organic and the aqueous phases. Then, the organic phase was separated and the solvent evaporated; the ^{1}H NMR spectrum of the residue demonstrated the recovery of **7** (Fig. S10, ESI†). After separation of the organic phase from vial III, addition of 4 mL of toluene led to the QD transfer to the organic solution (vial IV). The fluorescence spectrum of the organic phase evidenced the recovery of CS2@KP (Fig. 2) while that of the aqueous phase showed the recovery of CD-Py (Fig. 2). The absence of **7** in the aqueous phase was corroborated by ^{1}H NMR and MS/GC. The experiment was also performed on a large scale (ten-fold) leading to similar results to those described above.

In summary, herein we report a simple preparation of supramolecular QD/CD systems based on the effective recognition between the QD periphery and a β-cyclodextrin with an appended

QD quencher (pyrene). The CD can be transferred in and out of the aqueous solution upon complexation and decomplexation with an analyte. The generality of the strategy is demonstrated using quantum dots from different sources (homemade and several commercially available). These studies demonstrate the impressive applicability of these supramolecular QD/CD systems as effective molecular sensors. Moreover, all the components of the assay (CS@KP, CD-Py, and the analyte) can be recovered individually, which is highly desirable both from the commercial and environmental points of view.

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Notes and references

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Footnote

1. † Electronic supplementary information (ESI) available: Additional absorption, emission, transient absorption and NMR spectra; photophysical properties of QD and lifetimes of the pyrene systems. Preparation and characterisation of β-CD-Py, KP-SH, home-made CS and CS@KP. See DOI: 10.1039/c1cc15312a