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# Steric hindrance-enforced distortion as a general strategy for the design of fluorescence "turn-on" cyanide probes†

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**For the rational design of fluorescence "turn-on" cyanide probes, a general strategy is developed by introducing a dicyanovinyl group at the sterically demanding position of a large π framework.**

Anion recognition chemistry has attracted intensive scrutiny in recent years.[1–3] Among various anions, cyanide poses continuing environmental contamination problems due to its high toxicity and widespread applications in industrial processes.[4–6] Thus, effective cyanide probes are highly desired. As a versatile probe technique, elicitation of fluorescence has the advantages of simplicity, high sensitivity, and low cost. However, probes that rely on fluorescence quenching suffer from inherent drawbacks including low signal-to-noise ratio and non-specific quenching so that "turn-on" type fluorescence probes are preferred,[7,8] and they have been designed utilizing various binding moieties based on various channels such as proton transfer, exciplex, intramolecular charge transfer (ICT), and metal coordination.[9–13] In this respect, the dicyanovinyl (DCV) unit has been widely employed due to the possible nucleophilic addition of $CN^-$ to the double bond, which results in either enhancement or quenching of fluorescence, although the predictability of the effect remains elusive.[11a,14] Hence, development of a general strategy towards rational design of fluorescence "turn-on" $CN^-$ probes would be advantageous. A good starting point for the rational development of fluorescence "turn-on" probes is the use of nearly non-fluorescent hosts[15] constructed from potential fluorophores. We envisioned that if DCV is introduced into a sterically demanding framework, such as the 9-anthryl moiety, it would be forced to twist out of the anthryl plane thus yielding a twisted intramolecular charge transfer (TICT) state and quenching of its fluorescence.[16] Furthermore, introduction of an additional electron donor into the π-framework may further attenuate fluorescence due to the possible TICT state associated with the donor.[17,18] Accordingly, **C1**, **C2** and **C3** were synthesized by introducing DCV to a 9-anthryl moiety, with an electron-donating group attached to the 10-position (Fig. 1).

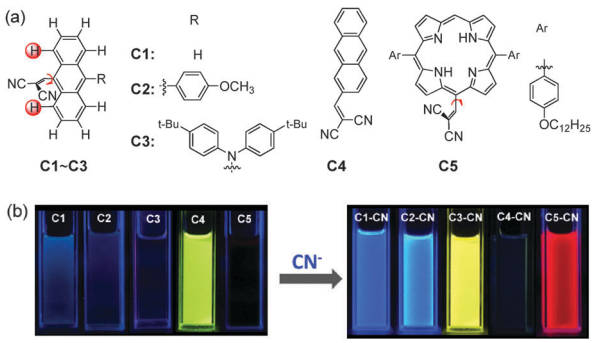


**Fig. 1** (a) Chemical structures of probes **C1–C5**. (b) Photographs of **C1–C5** (40 μM) in $CH_2Cl_2$ showing the fluorescence changes upon addition of 3 equiv. of $CN^-$ under a portable UV lamp.

As expected, these molecules are non-planar, exhibiting weak fluorescence which decreases in intensity with the increasing donating ability of the donor. Interestingly, the addition of $CN^-$ induced fluorescence enhancement by up to 242-fold. High selectivity and sensitivity to $CN^-$ can be realized with the advantages of low background fluorescence, tunable emission wavelengths (Fig. 1), and excellent "turn-on" behaviour in both $CH_2Cl_2$ and aqueous systems. To the best of our knowledge, this is the first demonstration of introduction of DCV into a sterically demanding framework opening a promising strategy for the rational design of fluorescence "turn-on" $CN^-$ probes.

**C1–C3** were readily synthesized by reactions between the respective 9-formyl anthracene derivatives and malononitrile (Scheme S1†), and fully characterized using $^1$H-NMR, $^{13}$C-NMR, and HRMS (Fig. S1–S3†). To our satisfaction, they exhibit rather weak fluorescence in $CH_2Cl_2$ with quantum yields of 0.49%, 0.42%, and 0.065%, respectively (Table S1†). Thus, we continued to estimate their probe

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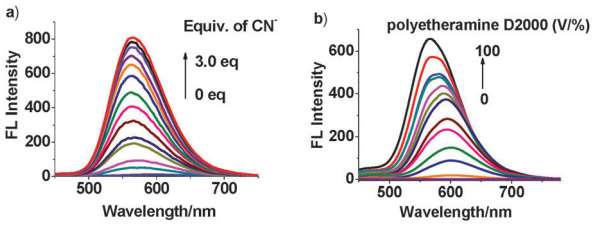


**Fig. 2** (a) Fluorescence changes upon addition of $CN^-$ to **C3** (20 μM, $\lambda_{ex}$ = 396 nm) in $CH_2Cl_2$. (b) Fluorescence changes with varying viscosity in a mixture of $CH_2Cl_2$–polyetheramine D2000 for **C3** (20 μM, $\lambda_{ex}$ = 401 nm).

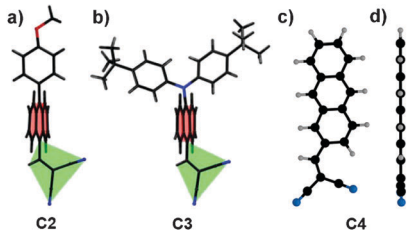


**Fig. 3** X-ray crystal structures of (a) **C2** and (b) **C3** showing the twisting between the anthryl framework and DCV. Optimized planar structure of **C4**. (c) Top view and (d) side view.

behaviour for $CN^-$. For example, in the case of **C3** only $CN^-$ induced a drastic colour change and an approximately 242-fold fluorescence enhancement amongst the various anions added to its $CH_2Cl_2$ solution (Fig. 2a and Fig. S4a†). Concomitant UV-vis spectral measurements revealed a clear isosbestic point at 396 nm (Fig. S4b†). For **C1** and **C2**, addition of $CN^-$ caused similar UV-vis spectral changes, with prompt fluorescence enhancements (Fig. S5–S8†) of approximately 29- and 54-fold, respectively.

For practical applications, it is essential that probes are available for operation in aqueous systems. Hence, we investigated the probe behaviour of **C1–C3** in a mixed solvent of THF–$H_2O$ (4 : 1 v/v) (Fig. S9–S11†). Interestingly, similar fluorescence "turn-on" behaviour was observed for **C1–C3** in the aqueous systems upon addition of $CN^-$. In addition, the presence of competing anions did not interfere significantly with $CN^-$ probing behavior, which is indicative of the excellent selectivity of these probes. The detection limit is also a key parameter based on the sensitivity of anion probes with fluorescence titration measurements yielding the detection limits[19] for **C1**, **C2** and **C3** for $CN^-$ of 2.46, 1.29, and 1.14 μM (Fig. S12†), respectively. The values for **C2** and **C3** lie well below the safe $CN^-$ levels in drinking water set by the World Health Organization (WHO).[20] In addition, the sensing systems can detect $CN^-$ in the solvents containing high proportions of water (Fig. S13†), showing good photostability (Fig. S14†), and they work well over a pH range of 9–14 (Fig. S15†). These results demonstrate that these probes are a promising prototype of highly selective and sensitive fluorescence "turn-on" $CN^-$ probes.

In order to understand the interaction of $CN^-$ with **C1–C3**, their addition products were isolated and characterized (Fig. S16–S18†). In the $^1$H-NMR spectrum of **C3–CN**, the vinylic proton signal of **C3** at 8.97 ppm disappeared and two new peaks emerged at 6.08 and 5.00 ppm (Fig. S3 and S18†). These results are in agreement with a nucleophilic addition mechanism.

As previously mentioned, the very weak fluorescence of **C1–C3** may be ascribed to energy loss caused by intramolecular rotation between the DCV and anthryl units in the nonplanar molecular structures. As clearly evidenced from X-ray single crystal structures (Fig. 3a and b), the dihedral angles between the DCV and anthryl units in the molecules of **C2** and **C3** are 65.6° and 59.5°, respectively. These large dihedral values clearly demonstrate twisting of the molecules to nonplanar structures, which facilitates intramolecular rotation and non-radiative relaxation of the excited state, resulting in the very weak fluorescence observed for **C1–C3**.

To further elucidate the effect of steric hindrance, the control compound **C4** was prepared by introducing DCV to the less sterically demanding 2-position of anthracene (Scheme S1 and Fig. S19†). As expected, the DCV and anthryl units have a small interplanar angle of 0.6° in the optimized conformation (Fig. 3c and d), adopting a nearly planar conformation. This conjugated planar conformation likely suppresses non-radiative energy loss expected due to torsional rotation. Thus, in contrast to **C1–C3**, **C4** exhibits very strong fluorescence with a high quantum yield of 64.1%. Moreover, the fluorescence of **C4** was drastically quenched upon addition of $CN^-$ (Fig. S20†). The rather strong fluorescence of **C4** further supports the postulation that twisting and rotation of the 9-anthryl and DCV units due to steric crowding is responsible for the weak fluorescence observed for **C1–C3**. Additionally, in more viscous solvents, intramolecular rotation can be suppressed, and the fluorescence will be recovered. For instance, fluorescences of **C1–C3** were significantly enhanced with increasing solvent viscosity in a mixed solvent of $CH_2Cl_2$ and polyetheramine D2000[21] (Fig. 2b, S21–S23†). In contrast, **C4** exhibited a totally different behaviour in that in a $CH_2Cl_2$ solution a broad intense excimer-based emission peak[22] was observed at 529 nm, probably arising from its highly planar structure. With increasing viscosity, the emission intensity of the 529 nm peak decreased, and peaks due to monomerically dispersed **C4** emerged at 419 and 401 nm (Fig. S24b†), which is in good agreement with reported systems.[23]

To demonstrate the general applicability of our above-mentioned strategy, we introduced DCV into another typical π-conjugated framework, that of porphyrin, at its sterically demanding *meso*-position to afford **C5** (Scheme S1 and Fig. S25†). As expected, **C5** exhibits weak fluorescence similar to that of **C1–C3**, with a quantum yield of 0.53% in $CH_2Cl_2$. Its fluorescence intensity was also significantly enhanced upon addition of $CN^-$ (Fig. S26†) or with increasing solvent viscosity (Fig. S27†). These results indicate that our design strategy is likely to have general applicability. It is noteworthy that the emission wavelengths of the probe–cyanide adducts can be modulated from blue to red (Fig. 1) by variation of the framework in combination with the introduction of different electron donors. As a matter of fact, the emission in the NIR wavelength range makes such probes suitable for applications in living systems.[24]

To gain further insights into the weak fluorescence of the probes, time-dependent density functional theory (TDDFT) calculations were carried out. In the lowest singlet excited state (LUMO) of **C1** and **C2**, the anthryl unit is nearly perpendicular to DCV (Fig. S28 and Table S2†), and the HOMO and LUMO are localized on these two units, respectively. For **C3**, the HOMO is localized on the diphenylamino group, and the LUMO is localized over the anthryl and DCV units. These results are

 

indicative of TICT states,[15a,16–18] associated with DCV in **C1** and **C2**, and with the diphenylamino moiety in **C3**, leading to the weak and decreasing fluorescence of **C1–C3**. Furthermore, their fluorescence decay curves were observed to be biexponential (Fig. S29†), with the slow decay component corresponding to the TICT states.[25] Upon addition of $CN^-$, the curves became monoexponential (Fig. S29†), concurrent with the disappearance of the TICT deactivation pathway, resulting in a decrease in the intensity of the charge-transfer peak and an increase in the intensity of the locally excited peak (Fig. S4b, S5a and c, S9a–S11a†) in their absorption spectra,[26] which correspond to the electronic transitions between HOMO − 1 and LUMO (Fig. S28†). Thus, fluorescence recovery was observed. In contrast, **C4** is nearly planar in both the ground state and the lowest singlet excited state. Addition of $CN^-$ can disrupt the large planar conjugation system, resulting in a distinct decrease in the excimer-originated fluorescence (Fig. S20†). Compared with **C1–C4**, **C5** has a relatively larger and more flexible porphyrin framework, which was also distorted by the steric hindrance associated with DCV (Fig. S30†), so that weak fluorescence could be observed. Addition of $CN^-$ disrupted the DCV group, leading to recovery of the planarity of the porphyrin macrocycle (Fig. S30†) resulting in drastic fluorescence enhancement. Meanwhile, the initially biexponential fluorescence decay curve for the distorted structure of **C5** becomes monoexponential for the planar structure of the cyanide adduct[27] (Fig. S29 and Table S3†). In addition, a sharper and blue-shifted Soret band was observed upon reaction with $CN^-$ (Fig. S26a†), indicating that the porphyrin aromaticity is increased with the improved molecular planarity although the conjugation size was reduced after disruption of the DCV group.[28]

In conclusion, a general strategy for the rational design of fluorescence ''turn-on'' cyanide probes has been developed by introducing a dicyanovinyl unit at a sterically demanding position of a large π framework. Such probes show very weak background fluorescence due to the distorted nonplanar molecular structure and intramolecular rotation with a potential TICT state. Addition of $CN^-$ can induce fluorescence enhancement up to a maximum of 242 fold for **C3**. By applying our design strategy for substituted anthracene probes to the porphyrin ring system, we have demonstrated the potential general applicability for the development of highly sensitive and selective fluorescence ''turn-on'' cyanide probes applicable in aqueous systems with low background fluorescence and tunable emission wavelengths.

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