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A highly efficient dinuclear Cu(II) chemosensor for colorimetric and fluorescent detection of cyanide in water

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Abstract

A novel dinuclear copper chemosensor selectively binds cyanide over a wide range of inorganic anions, enabling it to detect cyanide in water up to 0.02 ppm which is 10 times lower than the EPA standard for drinking water.

Cyanide is known as a fast acting and potentially deadly chemical species to humans, posing a severe threat to public health, the environment, and homeland security.[1] The toxicity of cyanide is due to its high affinity to bind with iron in cytochrome *c* oxidase which leads to the inhibition of oxygen utilization, resulting in *hypoxia* – a fatal medical condition.[2] Furthermore, the exposure to a high concentration of cyanide can result in thyroid toxicity due to the inhibition of iodine uptake.[3] According to the United States Environmental Protection Agency, the maximum acceptable level of cyanide is 0.2 ppm in drinking water,[4a] while the safe limit is 0.05 and 0.07 ppm set by the European Union[4b] and the World Health Organization, respectively.[4c] Nevertheless, it is used as a critical reagent in a number of industries including gold mining, electroplating, plastic manufacturing, and the petroleum industry, leading to unavoidable pollution of the environment.[1a] There have been several techniques for the detection of cyanide, including chromatography, potentiometry, capillary electrophoresis and ion chromatography, *etc*.[5] However, these techniques require expensive instruments and laborious sample preparation. Consequently, there is a widespread need to develop readily available and effective molecular probes for the detection of cyanide, particularly at low concentration in water.

In recent years, a number of synthetic receptors for cyanide have been reported;[6] the majority of them are primarily based on the utilization of H-bond donors.[6a] Therefore, their application is restricted primarily in non-aqueous solvents due to the poor solubility of such receptors and/or lessened tendency to form hydrogen bonds in aqueous medium. Other receptors that exhibit colorimetric or fluorometric response to cyanide require either a pure

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organic solvent or an organic-water mixture, making them less effective for practical applications.[7] Because of the high solvation energy of cyanide (-339 kJ mol^{-1}),[6g] it is often difficult to achieve high selectivity for cyanide in the presence of other anions like fluoride, sulphate, acetate, *etc.*[6] Alternatively, macrocycle-based dinuclear metal complexes are used to bind anions through Lewis-acid/base interactions in water.[8] Such complexes have been shown to bind a wide variety of anions including halides,[8c,d] phosphates,[8e] nucleosides,[8f] dicarboxylates,[8g] and oxalates.[8h] Although dinuclear metal compounds form cascade-type complexes[9] with a cyanide anion bridging two metal ions in a macrocycle, to the best of our knowledge, they have not been evaluated for cyanide binding in solution yet. One powerful approach, however, is a fluorescence technique based on an indicator displacement assay, providing a rapid and cost-effective way for the fluorescence turn-on sensing of an anion in a solution at very low concentration.[10] Herein, we report a simple macrocycle-based dinuclear Cu(II) complex (**L**) for the fluorescent sensing of cyanide in water at neutral pH, providing a sharp colour change up to 0.02 ppm level in the presence of an external dye (Eosin Y or Fluorescein). The sensing mechanism of **L** toward cyanide is illustrated in Scheme 1.

The free macrocycle **1** and **L** were prepared following the method as reported previously.[11] The macrocyclic dinuclear copper complex **L** was synthesized from the reaction of **1** with two equivalents of anhydrous $CuBr_2$ in H_2O. The blue powder thus obtained was dissolved in 2 mL of water-methanol mixture (1:1, v/v) and recrystallized by slow evaporation of the solution, providing X-ray quality crystals.‡ Single crystal X-ray analysis confirmed the formation of **L**·Br_2·H_2O with a space group of *Pn* (see ESI).

The receptor was found to be soluble in water, showing an absorption band at 610 nm (Fig. S5). The addition of cyanide ion to **L** (1×10^{-3} M) resulted in a blue shift, showing a corresponding color change from blue to faint red (Fig. S6). In contrast, the band was almost unchanged in the present of other anions except in phosphate, which provided a red shift. Since the sensitivity of free **L** to detect cyanide was low, the sensing ability of the dinuclear copper complex (**L**) for anions was investigated by an indicator displacement assay (IDA) using two different fluorescent indicators: Eosin Y (EY) and fluorescein (FL), which are known as effective dyes providing both excitation and emission wavelengths in the visible region with high quantum yield.[8f] Upon the incremental addition of **L** (2.0×10^{-4} M) to a solution of FL (2.0×10^{-6} M) buffered at pH 7.0 (20 mM HEPES), the fluorescence band (λ_{max}) at 512 nm was gradually quenched (Fig. 1a), resulting in an almost complete quenching of the emission with 5 equivalents of **L** (fluorescence OFF). Similar quenching was also observed when EY was titrated with L at λ_{max} = 536 nm (Fig. 2a). Such quenching is the result of an ion-pair formation between **L** and the anionic dye, as reported in the literature for related systems.[8e,8f] The change in the fluorescence intensity gave the best fit to a 1:1 binding model,[12] yielding the binding constants, log *K*= 5.68 and log *K*= 6.69 for FL and EY, respectively, which are consistent with reported values.[8f,10b] The 1:1 binding was further confirmed by a Job plot analysis (ESI).

‡Crystal data for **L**·Br_2·H_2O: $C_{26}H_{42}Br_2Cu_2N_6$•2Br•H_2O, M = 903.39, monoclinic, a = 7.9296(10) Å, b = 9.0949(12) Å, c = 22.638(3) Å, α = 90.00°, β = 99.403(7)°, γ = 90.00°, V= 1610.7(4) $Å^3$, T = 100(2) K, space group *Pn*, Z = 2, 16571 reflections measured, 7656 independent reflections (R_{int} = 0.0668). R_1 = 0.0491 ($I > 2\sigma(I)$). CCDC: 1020837.

The receptor-dye complexes were studied for cyanide in a competitive binding approach. Since the addition of two equivalents of **L** to a dye (FL or EY) gave an appreciable quenching, we have chosen the **L**:dye (FL or EY) ratio as 2:1 (mol/mol). Upon the addition of CN^- to **L**·FL or **L**·EY (**L**/dye = 2:1) solution, the fluorescence band was found to increase (Fig. 1b and 2b), indicating the successful competitive binding of CN^- and the removal of the dye from the receptor-dye complex (fluorescence ON) to the solution as proposed in Scheme 1. The titration profile gave the best fit to a 1:1 binding model,[12] presumably forming a cyanide-bridged complex, with a cyanide linking to both copper ions in the macrocycle (Scheme 1).[9] The calculated binding constants (log *K*) of **L**·FL and **L**·EY for the anion were estimated to 5.59 and 5.56, respectively.

The selectivity of the receptor-dye complexes for cyanide was examined for a number of inorganic anions including F^-, Cl^-, Br^-, I^-, NO_3^-, HCO_3^-, ClO_4^-, SO_4^{2-}, and PO_4^{3-} under identical conditions. As shown in Fig. 3, with the exception of PO_4^{3-}, the addition of other anions to a receptor-dye complex, did not result in any significant change of the fluorescent band even after the addition of 50 equivalents of anions. However, CO_3^{2-} was previously reported to bind with macrocycle-based copper(II) complexes.[13]

For phosphate, a moderate revival of the fluorescence was observed. The estimated binding constants (log *K*), as calculated from the titration experiments with PO_4^{3-} (Figs. S7 and S8 in ESI), are 3.86 and 3.92 for **L**·FL and **L**·EY, respectively. These values are much lower than those found with CN^-, suggesting that the receptor has a strong selectivity for cyanide in water. In an earlier work, a thiophene-based dinuclear copper(II) complex was found to bind PO_4^{3-} with a binding constant of 4.1 (log *K*) in water in the presence of EY.[8e]

The dinuclear complex was further tested for the colorimetric detection of cyanide anion in water. Fig. 4 shows the colour change of **L**·FL for various anions in water buffered with 20 mM HEPES at pH 7.0 under (A) visible and (B) UV light at 365 nm. The dark golden colour of the **L.**FL solution turned to yellow green after the addition of 10 equivalents of cyanide anion, while other anions did not produce any significant change in colour under visible light. However, under the UV lamp at 365 (Fig. 4B), the colour change of **L.**FL was clearly noticeable (dark green to spring green) for cyanide as well as for phosphate, agreeing with the results from fluorescence titrations. Colorimetric studies were also performed on **L**.EY for anions under identical conditions, showing a sharp colour change for cyanide under visible (deep magenta to pale orange) and UV light at 365 nm (pale purple to green yellow (Fig. S15 in ESI). The fluorescence ratio (I/I_o) shows a linear dependency with cyanide in the range of 0.5 to 5 μM, allowing us to estimate the lowest detection limit up to 0.01 ppm (Fig. S16 and S17 in ESI). The concentration dependent colorimetric titrations, as shown in Fig. 5, clearly demonstrate that cyanide is detectable up to 0.02 ppm simply by colour change under the UV light at 365 nm in water.

In order to understand the interactions of cyanide with the copper atoms of the receptor, theoretical calculations based on density functional theory (DFT) were performed with the M06L meta-GGA functional with a polarized 6-31g(d,p) basis set. Extensive previous work has shown that the M06L semi-local functional can accurately predict binding energies in both organometallic compounds[14] as well as noncovalent interactions for large systems.[15]

Atomic coordinates from the crystal structure (CCDC 1020837) were used as initial geometries to optimize the structures. Fully unconstrained geometry optimizations were carried out on both the isolated receptor as well as several cyanide-bound complexes (see Fig. 6 and Figs. S18-S19). For each of the optimized geometries, the average binding energy per cyanide ion was calculated with the expression $E_{average} = (E_{receptor} + n \cdot E_{CN} - E_{complex})/n$, where n is the number of cyanide ions bound in the complex. We optimized three different binding motifs consisting of (1) a single cyanide ion bridging across the copper atoms inside the receptor, (2) two cyanide ions, each bound to a separate copper atom within the interior of the receptor (Fig. S18), and (3) two cyanide ions, each bound to a separate copper atom outside the receptor (Fig. S19). For each of the above three configurations, we obtained average binding energies of 203.53, 158.23, and 150.18 kcal/mol, respectively; demonstrating that a 1:1 binding is energetically more favorable than a 1:2 binding. Since the single cyanide ion configuration possesses the largest average binding energy, we carried out an additional charge decomposition analysis of this configuration. Due to its high symmetry, the DFT calculations predict an equal positive charge of +0.58 on each of the copper atoms in the isolated receptor (Fig. S20). In contrast, the cyanide ion has an asymmetric electron distribution with the carbon more negatively charged than the nitrogen atom (Fig. S21). Consequently, the binding of the cyanide ion breaks the electrostatic symmetry of the receptor, resulting in an asymmetric charge distribution between the two copper atoms (+0.53 vs +0.71).

In summary, we have reported a unique probe that is capable of colorimetric detection of cyanide in water up to 0.020 ppm, which is much lower than the acceptable limit of 0.20 ppm set by EPA for drinking water. The readily available chemosensor has been successfully explored in an indicator displacement approach using two different commercially available dyes to selectively and strongly bind cyanide over a wide range of common inorganic anions. The results from DFT calculations further suggest that the cyanide anion is bridged between two copper ions of the host through strong electrostatic interactions. This strategy provides an insight into the rational design of selective optical sensors for other anions of environmental and biological relevance.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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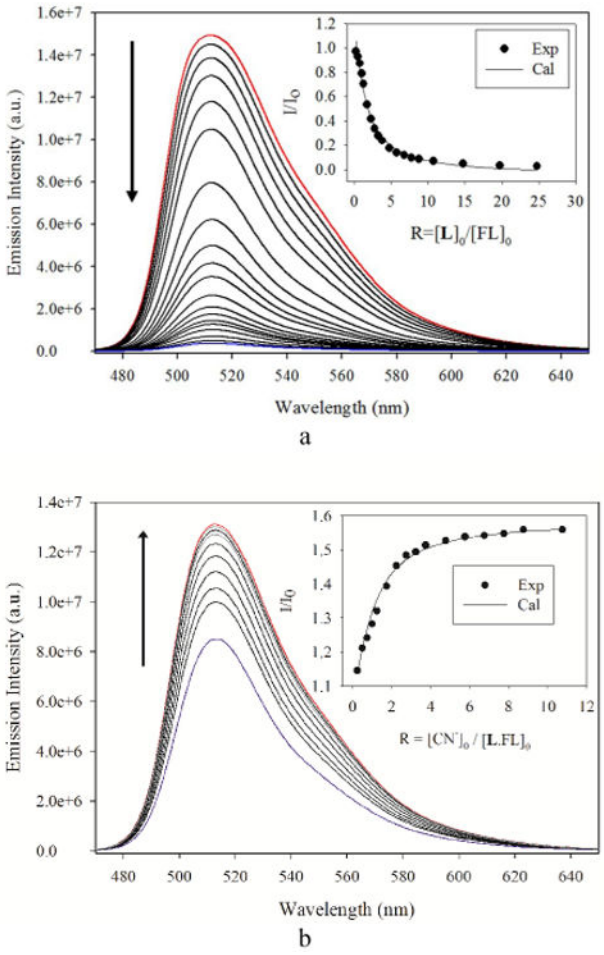


Fig. 1.

(a) Decrease of fluorescence intensity of FL upon the gradual addition of **L** ($[FL]_o = 2 \times 10^{-6}$ M, $[\mathbf{L}]_o = 2 \times 10^{-4}$ M), and (b) the enhancement of fluorescence intensity of [**L**·FL] (**L**/FL = 2:1) upon the addition of KCN ($[FL]_o = 2 \times 10^{-6}$ M, $[KCN]_o = 2 \times 10^{-4}$ M) in water buffered with 20 mM HEPES at pH 7.0. λ_{ex} = 450 nm, λ_{em} = 512 nm, d_{ex} = 2.5, d_{em} = 2.5. Insets show the titration plots of I/I_o against equivalents of added guests at a wavelength of 512 nm.

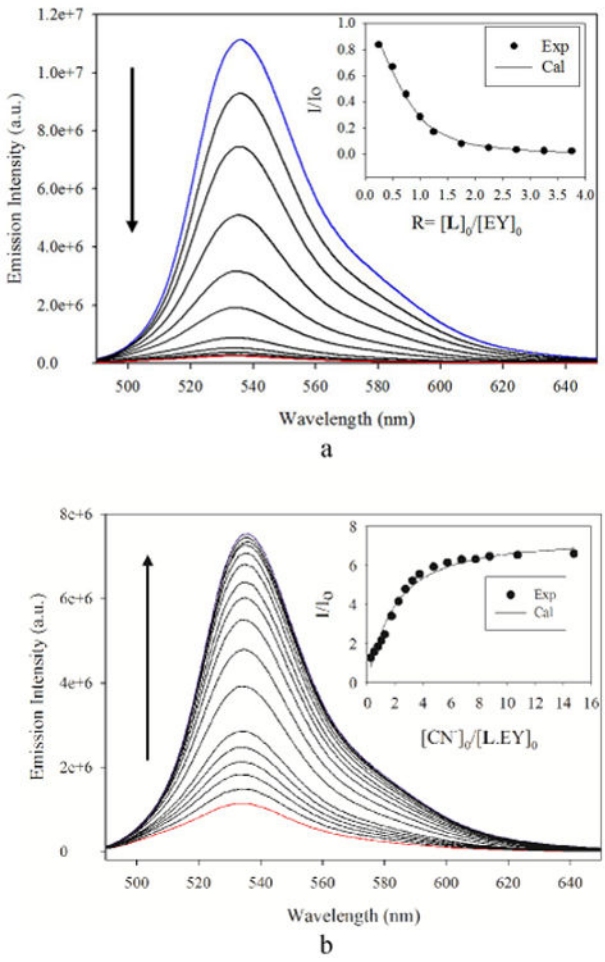


Fig. 2.

(a) Decrease of fluorescence intensity of EY upon the gradual addition of **L** ($[EY]_o = 2 \times 10^{-6}$ M, $[\mathbf{L}]_o = 2 \times 10^{-4}$ M), and (b) the enhancement of fluorescence intensity of [**L**·EY] (**L**/EY = 2:1) upon the addition of KCN ($[EY]_o = 2 \times 10^{-6}$ M, $[KCN]_o = 2 \times 10^{-4}$ M) in water buffered with 20 mM HEPES at pH 7.0. $\lambda_{ex} = 470$ nm, $\lambda_{em} = 536$ nm, $d_{ex} = 2$, $d_{em} = 3$. Insets show the titration plots of I/I_o against equivalents of added guests at a wavelength of 536 nm.

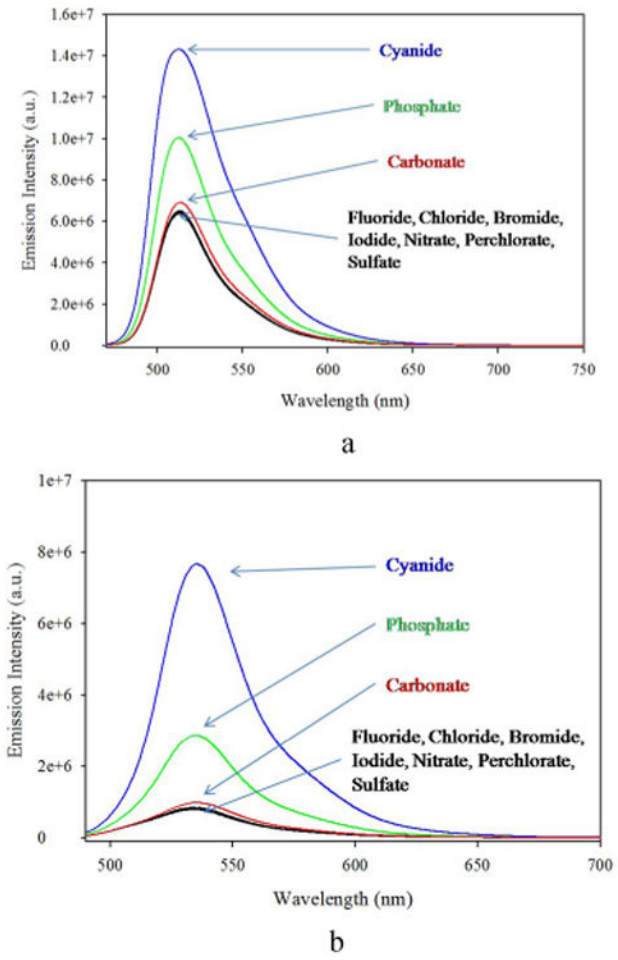


Fig. 3.

Change in fluorescence intensity of (a) **L**·FL (**L**:FL = 2:1, $[FL]_o = 2 \times 10^{-6}$ M, λ_{ex} = 450 nm, λ_{em} = 512 nm), and (b) **L**·EY (**L**:EY = 2:1, $[EY]_o = 2 \times 10^{-6}$ M, λ_{ex} = 470 nm, λ_{em} = 536 nm) upon addition of 50 equivalents different anions in 20 mM HEPES buffer at pH 7.0

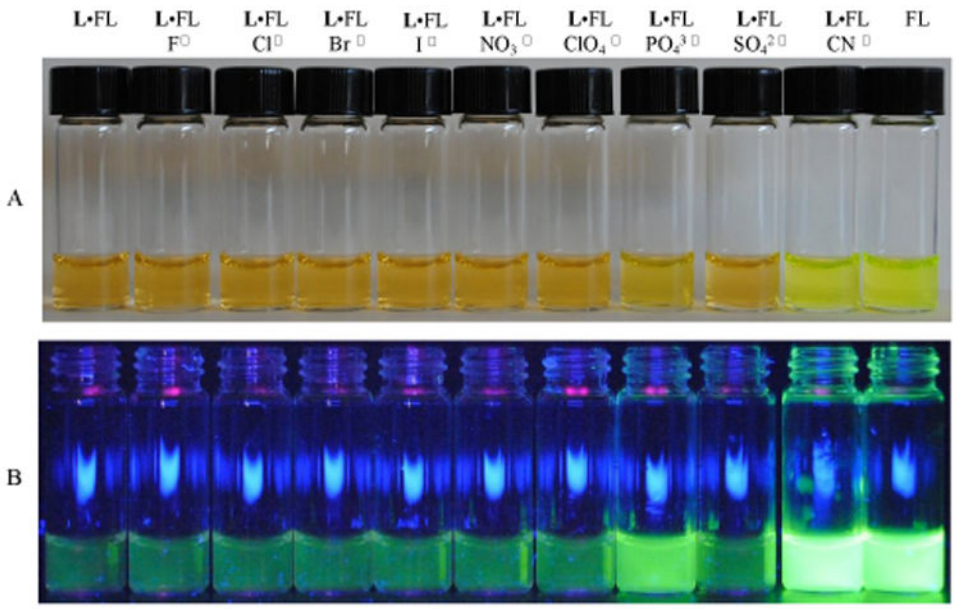


Fig. 4.

Colorimetric detection of cyanide against various anions (F^-, Cl^-, Br^-, I^-, NO_3^-, ClO_4^-, SO_4^{2-}, and PO_4^{3-}) with **L**·FL (**L**:FL = 2:1, $[FL]_0 = 2\times10^{-5}$ M) in water at pH 7.0. A: visible light; B: UV light at 365 nm; 10 equivalents of anion were added to the solution of **L**·FL.

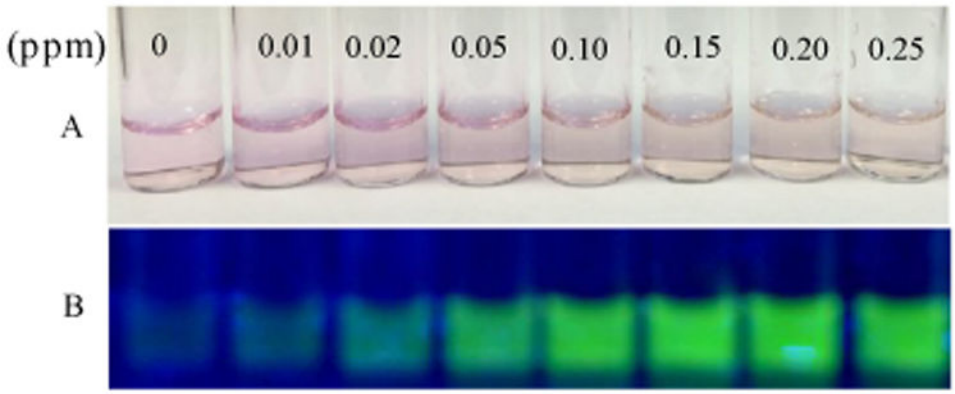


Fig. 5.

Progressive colour change with an increasing amount of cyanide in the range of 0 to 0.25 ppm to [**L**·EY] (**L**:EY = 2:1, $[FL]_o$ =4×10^{-6} M) in water at pH 7.0. A: visible light; B: UV light at 365 nm.

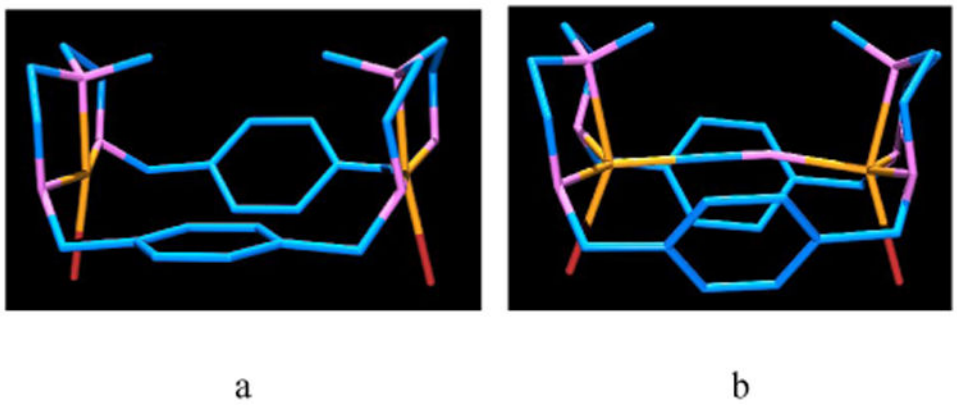
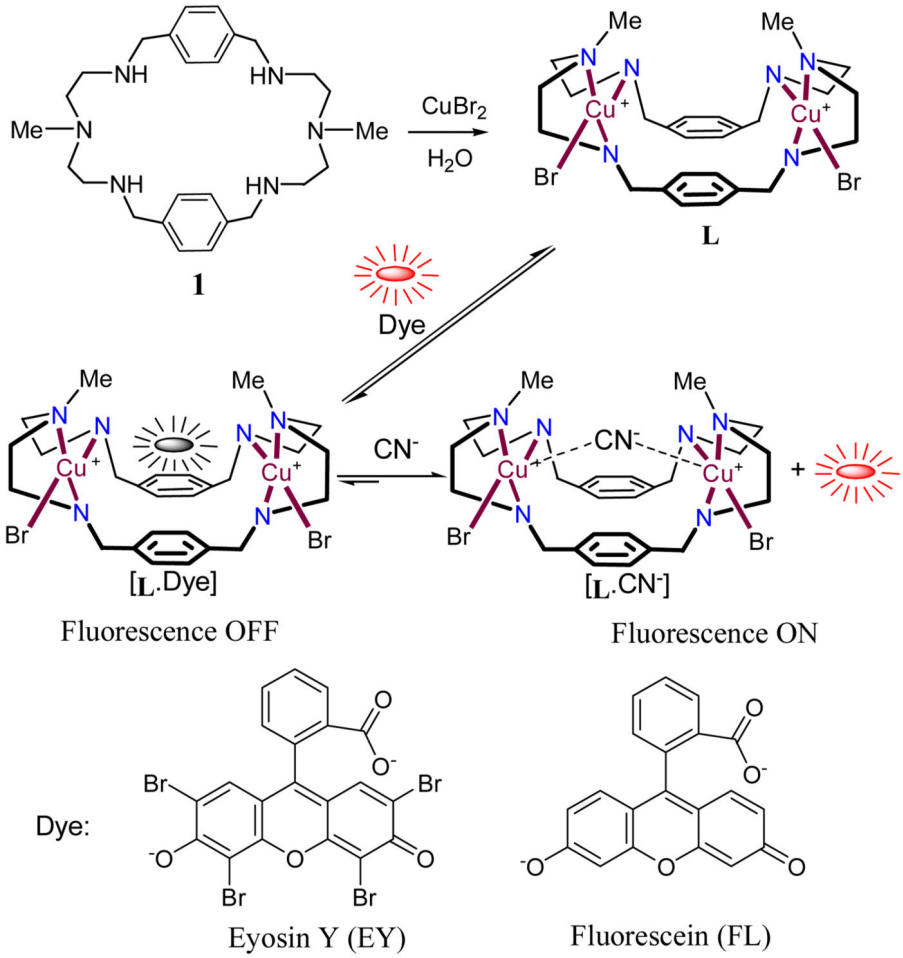


Fig. 6.

Optimized structures of (a) **L** and (b) [**L**(CN)]$^{-}$. Colour codes: blue = carbon, pink = nitrogen, orange = copper. Hydrogen atoms are not shown for clarity.



Scheme 1.

Synthetic pathway to **L** and its binding mechanism for cyanide in the presence of an external dye.