# Tetrathiafulvalene Derivatives Recognition of Copper with High Selectivity

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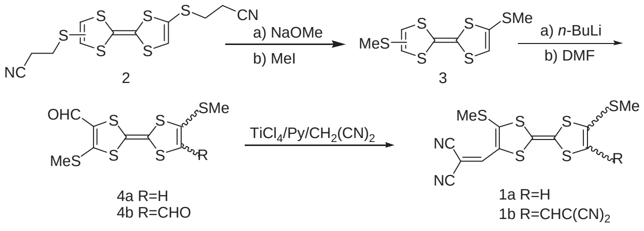
New sensors based on D–A type tetrathiafulvalene derivatives are reported. These sensors can detect $Cu^{2+}$ with high selectivity in the presence of other metal ions, including $Fe^{2+}$, $Co^{2+}$, $Ni^{2+}$, and $Zn^{2+}$ etc., which usually interfere the detection of $Cu^{2+}$.

There is a growing interest in the development of new methods for heavy metal detection, because a) heavy metals pose severe risks for human health and environment; b) some heavy metals play important roles in biological systems. Copper, as a kind of heavy metal, is not only a significant metal pollutant due to its widespread use, but also an essential trace element in all living organism where it serves as a co-factor in at least 30 important enzymes.[1] Though copper toxicity to human is rather low comparing with other heavy metals, if as little as 2 grams of a copper salt are ingested, usually with suicidal intent, the resulting copper-induced hemolytic anemia and kidney damage are generally fatal.[2] On the other hand, defective copper metabolism in body can cause neurological disorders, such as Menkes syndrome and Wilson's disease.[3] Furthermore, it has also been demonstrated that cancer produces a significant alteration of copper metabolism and distribution in the body.[4] To date, many methods have been established to detect copper, but most of them have limitations in selectivity, because of the interference with other metal ions $Zn^{2+}$, $Ni^{2+}$, $Fe^{2+}$, and $Co^{2+}$ etc. Tetrathiafulvalene (TTF) and its derivatives, as strong donors, have been widely used in material chemistry.[5] Based on the redox property of TTF unit, TTF and its derivatives also find application in sensors.[6] Usually, these sensor systems incorporate TTF units into macrocyclic or supramolecular structures and detect analytes by electrochemical method. Like other type of sensors, the TTF type sensors also have limitations in selectivity (interference with other transition metal ions) and/or physical properties changing undistinguishable after complexation of analyte. Herein we report two D–A type TTF-based sensors **1a** and **1b** which can detect $Cu^{2+}$ with high selectivitity by colorimetric method.

The structures of **1a** and **1b** are shown in Scheme 1. Compounds **1a** and **1b** are D–$\pi$–A type molecules. Since donor and acceptor are connected by conjugated bridge in **1a** and **1b**, when **1a** and **1b** coordinate with metal ions, the electron donating ability of the donor part or the electron withdrawing ability of the acceptor part will change, and this will lead to the physical properties changing of **1a** and **1b**, that is our idea to design the molecules.

The synthesis of **1a** and **1b** was outlined in Scheme 1. Compound **2** was synthesized according to the literature.[7] **3** was obtained by removing $CH_2CH_2CN$ protection groups under basic conditions and followed by treatment with MeI. **3** reacted with BuLi and DMF at −78 °C to give the aldehyde derivatives **4a** and **4b**. Then **1a** and **1b** was obtained by reacting **4a** and **4b** with malononitrile in the presence of $TiCl_4$ and pyridine.[8] Pure *cis*- and *trans*-isomers of **4b** were obtained by chromatography, and single crystal of *cis*-**4b** was grown by slow solvent volatilising. The crystal structure of *cis*-**4b** showed dimer structure in the molecular packing. The center-to-center distance between the $C_3S_2$ five-membered rings of two adjacent *cis*-**4b** monomers was about 3.77 Å, suggesting $\pi$–$\pi$ stacking interactions within the dimers. The dimers linked to each other through weak hydrogen bonds between –HC(10)=O(2) and –SC(9)$H_3$, extending the molecular packing into an interesting 1D supermolecular array along the *b*-axis (Figure 1). Because of the reactive aldehyde function groups, **4b** will be an useful intermediate with exactly configuration for TTF chemistry. An attempt to separate the *cis*- and *trans*-isomers of **1a** and **1b** was failed.

The cyclic voltammogram (CV) of **1a** showed two reversi-



**Scheme 1.**

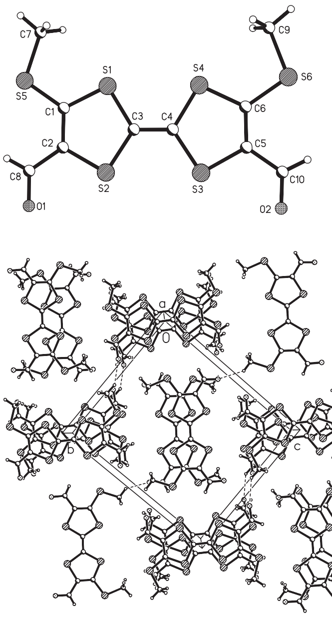


**Figure 1.** Molecule structure of *cis*-**4b** (top) and a packing diagram of the unit cell of *cis*-**4b** looking down the *a*-axis (bottom).

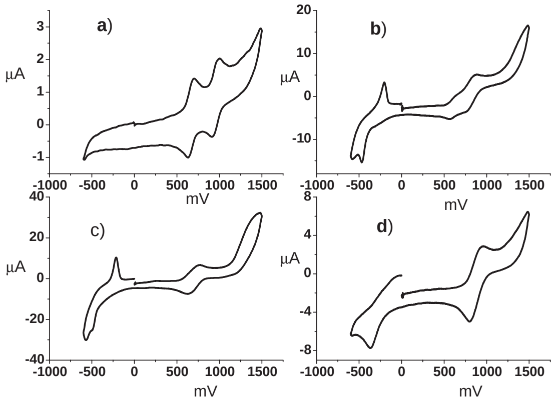


**Figure 2.** Cyclic voltammograms were measured as follows: $TBAPF_6$ as supporting electrolyte, Ag/AgCl as standard electrode, Pt as working and counter electrodes, scan rate: $40\,mV\,s^{-1}$. a) **1a** ($2 \times 10^{-4}$ mol/L); b) **1a** + 2 equiv. $Cu^{2+}$; c) **1a** + 2 equiv. $Cu^{2+}$ + 2 equiv. IMIS(each vs **1a**); d) $Cu^{2+}$ ($5 \times 10^{-4}$ mol/L).

ble peaks ($E^1_{1/2} = 0.68\,V$, $E^2_{1/2} = 0.97\,V$) for TTF and an irreversal peak ($E_{1/2} = -0.69\,V$) for CN in $CH_3CN$ (Figure 2). When 2 equiv. of $Cu^{2+}$ was added to a $CH_3CN$ solution of **1a**, a new redox peak was observed at −0.20 V with the disappearance of CN redox peak. The change of the redox peaks for TTF part could not be identified due to the overlay of $Cu^{2+}$.[9] The new peak (at −0.20 V) arose from the coordination of **1a** with $Cu^{2+}$. Since i) the cyclic voltammogram of $Cu(NO_3)_2$ showed no redox peak for $Cu^{2+}$ in $CH_3CN$ at −0.20 V (Figure 2d), ii) when a strong ligand for $Cu^{2+}$ (potassium salt of 2,2′-(anthracene-9,10-diyldimethylene)bis(malonic acid) was added to the solution of **1a** with $Cu^{2+}$, the peak at −0.20 V was cleared away. No peak appeared in the range of −0.5–0 V, while a solution of **1a** was treated with interference metal ions (IMIS). The IMIS included alkali and alkaline earth metal ions $Li^+$, $Na^+$, $K^+$, $Mg^{2+}$, $Ca^{2+}$, and $Ba^{2+}$; transition series metal ions $Cr^{3+}$, $Mn^{2+}$, $Fe^{2+}$, $Co^{2+}$, $Ni^{2+}$, $Y^+$, $Zn^{2+}$, $Cd^{2+}$, and $Hg^{2+}$ as well as $Pb^{2+}$. The selectivity of **1a** for $Cu^{2+}$ had been tested in the presence of IMIS. For a $CH_3CN$ solution of **1a**, the metal ions were added in any order ($Cu^{2+}$ first, then IMIS; or IMIS first, then $Cu^{2+}$), only one new redox peak was observed (at −0.2 V), and the peak was assigned to the complex of $Cu^{2+}$ with **1a**. Similar to that observed for **1a** and $Cu^{2+}$, compound **1b** also showed sensing of $Cu^{2+}$ over IMIS, with a new redox peak (at −0.21 V) emerging in the CV arising from the coordination of **1b** and $Cu^{2+}$.

As we expected, when a solution of **1a** ($10^{-5}$ mol/L, $CH_3CN/H_2O = 4{:}1$, v/v) was treated with $Cu^{2+}$, based on the complexation between $Cu^{2+}$ and **1a**, the intensity of intramolecular charge-transfer (ICT) absorption in UV–vis spectra (590 nm) decreased with the addition of $Cu^{2+}$, which confirmed our idea for the molecule design. Similar to **1a**, the addition of $Cu^{2+}$ also resulted in the ICT absorption of **1b** ($10^{-5}$ mol/L, $CH_3CN$) intensity decreasing (Supporting Information).[10]

When a solution of **1a** ($10^{-5}$ mol/L, $CH_3CN/H_2O = 4{:}1$, v/v) was treated with 1 equiv. of $Cu(NO_3)_2$ (aqueous solutioin), the color of the solution changed from dark cyan to dark orange immediately, which could be identified by naked-eyes. The IMIS nearly led no color change to **1a**. While a solution of **1a** containing IMIS was treated with $Cu(NO_3)_2$ (aqueous soultion), the optical changes of the solution was identical to those observed for solutions containing only $Cu^{2+}$, this color change was suitable for a pH range of 1 to 8. Moreover, addition of water did not lead to the decomplexation of $Cu^{2+}$. Finally, we noted that the complex of **1a** and $Cu^{2+}$ converted back into **1a** via treatment with the sodium salt of EDTA. Similar to **1a**, **1b** also showed high selectivity for $Cu^{2+}$ in the presence of IMIS in $CH_3CN$ solution. When $Cu(NO_3)_2$ (aqueous solution) was added to a $CH_3CN$ solution of **1b**, the color of the solution changed from blue to orange.

In summary, TTF-based D–π–A type sensors **1a** and **1b** have been developed. These sensors show high selectivity for $Cu^{2+}$ by colorimetric methods. The color change of **1a**, after addition of $Cu^{2+}$, can be easily identified by naked-eyes in a wide pH range, its high selectivity for $Cu^{2+}$ is examined in the presence of IMIS, some of which usually interfere the detection of $Cu^{2+}$ and are concerned as environment pollutants. Pure isomers **4b**, an important intermediate with di-aldehyde function groups was obtained by careful chromatography, and the crystal of *cis*-**4b** shows that dimer is formed through π–π stacking interactions in the molecular packing, and the weak hydrogen bond between –CHO and –SMe from neighbouring dimers extends this structure into an interesting 1D supermolecular array.

## References and Notes

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9 The redox peak of $Cu^{2+}$ is broad, and it overlays the redox peaks of TTF part in **1a**.
10 An attempt to calculate the binding constants was failed because of the interference of large excess of $Cu^{2+}$ in the UV–vis titration profiles ($Cu^{2+}$ should be largely excess to calculate the binding constant by UV–vis titration).

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