Organic & Biomolecular Chemistry

COMMUNICATION

Click synthesized dianthryl–TTFV: an efficient fluorescent turn-on probe for transition metal ions†

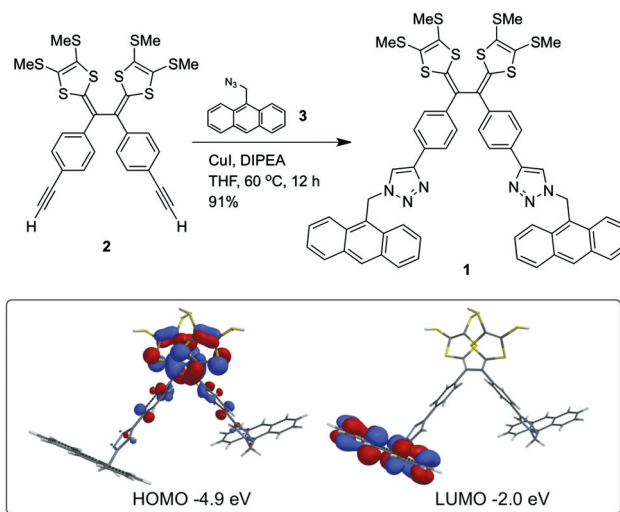Karimulla Mulla, Prateek Dongare, David W. Thompson and Yuming Zhao*

Tetrathiafulvalene vinylogue (TTFV) was functionalized with two anthryl fluorophores *via* Cu(I)-catalyzed alkyne–azide [3 + 2] cycloaddition, forming a dianthryl–TTFV hybrid to show fluorescent turn-on sensing behaviour for Cu²⁺, Fe²⁺, and Cd²⁺ ions in THF with remarkably low detection limit down to the sub-ppm level.

Cu-catalyzed alkyne–azide cycloaddition (CuAAC)[1] has been widely used as a facile and efficient ligation tool for preparation of molecular sensory systems, wherein the click product, 1,2,3-triazole, acts as a structural (linkage) and/or functional (ligand/receptor) component.[2] Numerous recent reports have demonstrated that 1,2,3-triazole can form stable complexes with various metal cations,[3] anions,[4] and certain biomolecules,[5] which renders it an appealing synthon for ligand and receptor design. In view of the versatile metal complexation behaviour, we have recently set out to explore some new "click" chemosensors utilizing click reaction-generated 1,2,3-triazole as an integral part to achieve improved and modfied sensor properties.[6]

In this communication, we report the facile click synthesis of a dianthryl–tetrathiafulvalene vinylogue (TTFV) derivative (**1**, Scheme 1) and its selective and sensitive fluorescent turn-on sensing behaviour towards certain transition metal ions, including Cu²⁺, Fe²⁺, and Cd²⁺. It is worth noting that detection of these metal ions is of great interest in respect to environmental remediation, biological studies, and industrial applications.[7] The molecular structure of click sensor **1** consists of three essential parts for a fluorescent chemosensor: (1) a central TTFV core as electron donor,[8] (2) two anthryl groups as fluorogenic units, and (3) two triazole rings as both linkages and receptors. The synthesis of compound **1** was accomplished by a two-fold CuAAC reaction between dialkynyl–TTFV precursor **2**[8a–c] and azido-anthracene **3** in the presence of CuI as catalyst and diisopropyl-ethylamine (DIPEA) as base. The reaction was carried out in THF at elevated temperature overnight to afford compound **1** in a high yield.

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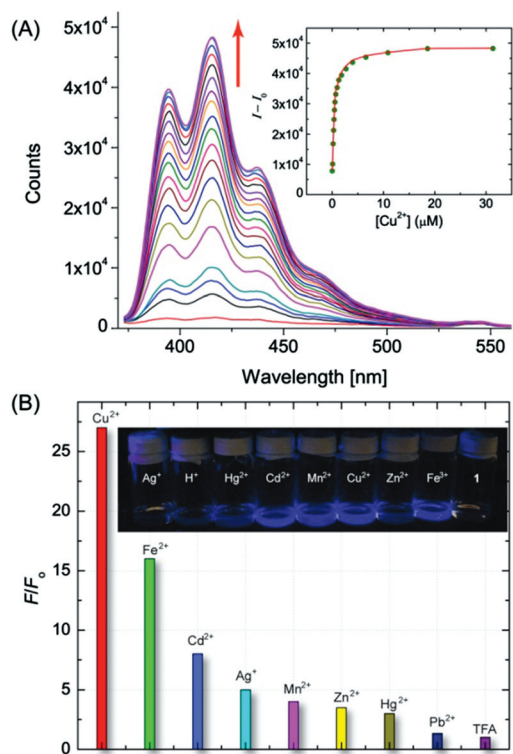
Scheme 1 Synthesis and FMO properties of diathryl–TTFV **1**.

The molecular structure and electronic properties of dianthryl–TTFV **1** were investigated by density functional theory (DFT) calculations at the B3LYP/6-31G* level.[9] In the optimized geometry of **1** (bottom of Scheme 1), the TTFV unit shows a pseudo-*cis* conformation. The HOMO is distributed at the central TTFV core, while two degenerated LUMOs are solely located at the two anthryl groups. Such spatially separated FMO characters together with the low oxidation potential of TTFV[10] suggest that photoinduced electron transfer (PET) quenching of the fluorophore would provide a mechanistic basis for sensing function.[11] Indeed, compound **1** was found to show very weak fluorescence (Φ = 0.009 in THF). In view of the good ligand abilities of the triazole rings, compound **1** was predicted to bind significantly to various transition metal ions. In principle, complexation with metal ions would reduce the electron-donating ability of the TTFV unit, which in turn attenuates the PET process to give rise to fluorescence enhancement (turn-on).

To test the anticipated sensory performance, dilute solutions of dianthryl–TTFV **1** in THF at μM concentrations were titrated with eight different transition metal ions. Of the metal ions tested, Cu²⁺, Fe²⁺, and Cd²⁺ give very significant fluorescence enhancement. Fig. 1A illustrates the fluorescence spectral changes of **1** in titration with Cu²⁺. The titration results clearly

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Fig. 1 (A) Fluorescence titration of **1** (5.55 μM) with Cu(OTf)$_2$ in THF at 298 ± 3 K, λ_{ex} = 350 nm. Inset: Stern–Volmer plot calculated from emission at λ = 415 nm. (B) Fluorescence enhancement (λ = 415 nm) at the endpoint of titration. F_o and F refer to the fluorescence intensities at the initial and ending points of titration. Inset: photographic images of solutions of **1** with various transition metal ions and TFA in THF under irradiation of a UV lamp.

show that with increasing addition of Cu^{2+}, an emission band of anthracene at 395 nm and vibronic progressions at 415, 440, and 470 (sh) nm grow in as a function of [Cu^{2+}]. At the endpoint of the titration, the fluorescence intensity is increased by 26-fold at 415 nm (detection limit: 0.26 μM). Note that the substantial fluorescence enhancement of **1** contrasts markedly the fluorescence quenching effect of Cu^{2+} on an anthryl–triazole sensor recently reported by Varazo et al.[12] Taken together, the TTFV donor must play a pivotal role in the fluorescence turn-on mechanism.

Besides Cu^{2+} ions, compound **1** also shows a considerable degree of fluorescence enhancement in response to the titration of Fe^{2+} and Cd^{2+} (see Fig. 1B). The detection limits are determined to be 0.48 μM for Fe^{2+} and 0.86 μM for Cd^{2+} respectively. For comparison, the titration of **1** with a strong protic acid, trifluoroacetic acid (TFA) was also performed. Fig. 1B clearly shows that the sensitivity of **1** towards the tested cations exhibits a decreasing trend as follows: Cu^{2+} > Fe^{2+} > Cd^{2+} > Ag$^+$ > Mn^{2+} > Zn^{2+} ~ Hg^{2+} > Pb^{2+} > H$^+$. To further quantify the binding properties of dianthryl–TTFV **1** with various metal ions, the fluorescence titration data were subjected to *SPECFIT* global analyses,[13] using the Levenberg–Marquardt nonlinear regression minimization procedure. The detailed binding stoichiometry and binding constants are listed in Table 1.

The *SPECFIT* analyses indicate that compound **1** can bind with transition metal and proton ions to form both 1 : 1 and 1 : 2 complexes, while the binding constants vary substantially.

Table 1 Binding constants of **1** with select transition metal ions and TFA and standard electrode potentials ($E°$)[14] of the cations

Cation	log($\beta_{11} \times M^1$)	log($\beta_{12} \times M^2$)	$E°$ (298 K, V)
Cu^{2+}	7.12 ± 0.7	12.1 ± 0.8	+0.34 (Cu^{2+} → Cu^0)
Cd^{2+}	5.22 ± 0.6	9.75 ± 0.6	−0.40 (Cd^{2+} → Cd^0)
Zn^{2+}	4.78 ± 0.2	8.59 ± 0.3	−0.76 (Zn^{2+} → Zn^0)
Fe^{2+}	4.62 ± 0.4	10.8 ± 0.2	−0.44 (Fe^{2+} → Fe^0)
Mn^{2+}	4.58 ± 0.1	7.56 ± 0.1	−1.19 (Mn^{2+} → Mn^0)
Ag$^+$	3.57 ± 0.1	6.67 ± 0.1	+0.80 (Ag$^+$ → Ag^0)
Hg^{2+}	2.72 ± 0.2	4.47 ± 0.2	+0.79 (Hg^{2+} → Hg^0)
Pb^{2+}	1.72 ± 0.2	2.46 ± 0.3	−0.12 (Pb^{2+} → Pb^0)
H$^+$	1.63 ± 0.5	2.95 ± 0.6	+0.00 (H$^+$ → H$_2$)
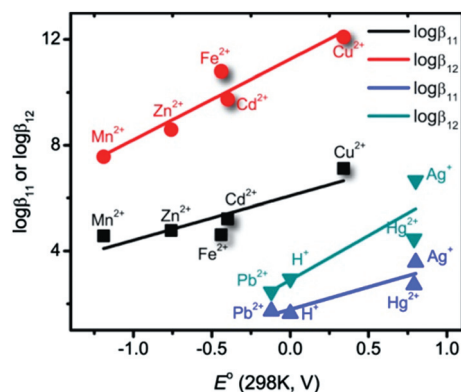
Fig. 2 Linear correlations of binding constants (log β) and standard electrode potentials ($E°$) of transition metal and proton ions.

Plotting the binding constants (log β_{11} and log β_{12}) of these cations against standard electrode potentials of the metal ions ($E°$) turns out to be very informative. As shown in Fig. 2, the cations fall in two distinct groups in terms of linear correlation between log β and $E°$. Group I consists of Cu^{2+}, Cd^{2+}, Zn^{2+}, Fe^{2+}, and Mn^{2+} ions, which afford considerably larger binding constants than those of Group II, which includes Ag$^+$, Hg^{2+}, H$^+$, and Pb^{2+} ions. These observations are in line with expectations based on hard–soft acid–base (HSAB) theory. The three metal ions (Cu^{2+}, Fe^{2+}, and Cd^{2+}) that cause sizeable fluorescence enhancement of sensor **1** share two common features: (1) they belong to Group I, and (2) their relatively high $E°$ values facilitate charge transfer from TTFV to metal ions, which efficiently attenuates the PET process from TTFV to anthracene. Overall, the relationships revealed in Fig. 2 are instructive for further design and fine-tuning of the selectivity and sensitivity of chemosensors with analogous molecular architectures.

It was also noted that when the solution of compound **1** was prepared at mM or higher concentrations in THF, significant precipitation took place upon addition of various metal ions. It is rationalized that at higher concentrations, metal–sulfur interactions become significant in addition to the metal–triazole interactions. As such, the resulting complexes would stay in the form of clusters or agglomerates,[15] which lead to substantial fluorescence quenching. These complexes are soluble in polar organic solvents such as acetonitrile, and the solutions of certain metal complexes (Cu^{2+}, Fe^{2+}, Cd^{2+}, and Pb^{2+}) in acetonitrile display visually distinct colours to enable straightforward colorimetric detection (see Fig. 3A). UV-Vis spectral analyses (Fig. 3B) clearly show that Cu^{2+}, Fe^{2+}, and Cd^{2+} ions when complexing with **1** at relatively high concentrations give pronounced
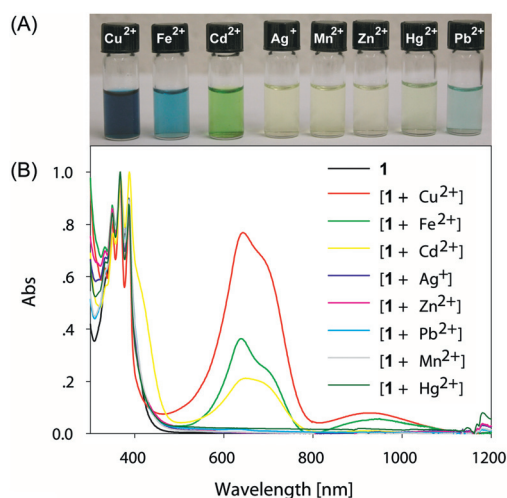
Fig. 3 (A) Photographic images of solutions of compound **1** and various transition metal ions in acetonitrile. (B) UV-Vis absorption spectra of compound **1** with various transition metal ions (*ca.* 11 mol equiv.) measured in acetonitrile at room temperature.

absorptions in the Vis-NIR region of the spectrum. Of particular note is the rise of a new band at *ca.* 500–800 nm, which is likely due to the formation of $[TTFV]^+$ and $[TTFV]^{2+}$ *via* TTFV-to-metal charge transfer.[8,16] In addition, a broad weak band ranging from *ca.* 800 to 1100 nm can be clearly seen in the Vis-NIR profiles of Cu^{2+} and Fe^{2+} complexes, which is tentatively assigned to $[TTFV]^+$. The UV-Vis data substantiate that at high concentrations the sulfur groups of **1** can also act as ligands to interact with oxidative metal ions, such as Cu^{2+}, Fe^{2+}, and Cd^{2+}, to form colourful charge-transfer complexes.

Experiments to elucidate the metal ion binding properties were undertaken by ^1H NMR titration between dianthryl–TTFV and select transition metal ions, Cu^{2+}, Cd^{2+}, and Ag^+ in THF-d_8. For the Cu^{2+} ion titration, pronounced line-broadening of all the NMR signals (see ESI†) and significant precipitation were observed. The results suggest strong interactions of Cu^{2+} with **1** and a considerable degree of aggregation for the resulting complexes in THF-d_8. For the titration of Cd^{2+} and Ag^+ ions, the formation of precipitate was not as notable as observed in the Cu^{2+} titration. In general, the ^1H NMR spectral responses of **1** to Cd^{2+} and Ag^+ ions were similar. In the case of Cd^{2+} titration, most of the aromatic protons do not shift with increasing $[Cd^{2+}]$, except for the triazolyl proton which shows a downfield shift from 7.60 to 7.73 ppm after *ca.* 7.0 molar equivalents of Cd^{2+} was added. The observation substantiates that the triazole units in compound **1** act as active ligands to coordinate with transition metals. It is also noted that the line-broadening of certain phenyl protons and the SMe protons (see ESI†) appear to be far more pronounced than that of the other protons. This unusual phenomenon suggests that ligand exchange is rapid on the NMR time scale, when specific metals are bound to sensor **1**.

In summary, click-generated dianthryl–TTFV **1** exhibits fluorescence turn-on sensing function towards Cu^{2+}, Fe^{2+}, and Cd^{2+} ions at μM concentrations in THF with excellent sensitivity, while at mM concentrations in acetonitrile it allows for colorimetric detection of these three metal ions. The investigation on metal-ion binding properties has shown that triazole linkers in

compound **1** serve as effective ligands (receptors) to coordinate with metal ions. To the best of our knowledge, compound **1** is the first example of TTFV-based "click sensors", and we believe it can be a useful design motif for the development of fluorophore-based molecular sensory and optoelectronic devices.

Acknowledgements

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