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Selective, sensitive and reversible "turn-on" fluorescent cyanide probes based on 2,2′-dipyridylaminoanthracene–Cu²⁺ ensembles†

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2,2′-Dipyridylamine and anthracene units were linked to afford highly emissive compounds whose Cu²⁺ ensembles were developed as effective fluorescence turn-on CN⁻ probes.

Although cyanide is extremely toxic to living organisms,[1] it has been widely used in industrial processes including gold mining, electroplating and plastic production.[2] Misuse of cyanide has occasionally led to environmental pollution making urgently necessary the development of an effective and practical signaling system for cyanide detection.[3]

Among several sensing strategies, fluorescence sensing is a valuable technique which has advantages such as high sensitivity, rapid response and ease of application.[4] In particular, fluorescence "turn-on" type probes are highly desirable but are still rather rare.[4] For fluorescent cyanide sensing, methods have been developed based on various mechanisms, including nucleophilic addition, hydrogen-bonding, and metal complex ensemble displacement.[5] Among these approaches to sensing cyanide, use of copper–cyanide affinity has attracted special attention.[6] Cu(II) complexes of fluorescent chromophores are usually non-fluorescent due to the paramagnetic quenching effect. Cyanide is known to react with the copper ions in such complexes to form very stable $[Cu(CN)_x]^{n-}$ species, and fluorescence of the chromophores can be recovered.[6b,d,7] Thus, a few turn-on fluorescent CN⁻ probes have been developed based on Cu(II) ensembles.[7] In designing such probes, fluorophores with high quantum yields are required in order to improve the signal-to-noise ratio. In addition, a receptor with a high affinity towards Cu²⁺ should be incorporated to ensure that fluorescence quenching occurs upon addition of Cu²⁺.

Based on these considerations and our previous work on related systems,[7a,8] compounds **1–3** were designed and synthesized. In these compounds, a strongly emissive anthracene unit was selected as the reporting group, and a typical Cu²⁺ chelating 2,

2′-dipyridylamine (2,2′-dpa) moiety[9] was used as the recognition group. **1–3** are strongly emissive compounds, with the Φ_f values in ethanol determined to be 0.69, 0.68 and 0.68, respectively, using anthracene as the reference[10] (Fig. S1, ESI†). We envisioned that the combination of strongly emissive anthracene fluorophore and copper-chelating 2,2′-dpa in **1–3** would assure rapid fluorescence quenching in the presence of Cu²⁺, and that the fluorescence could be recovered by the cyanide displacement approach. Thus, coordination ensembles of **1-Cu²⁺–3-Cu²⁺** act as highly selective and sensitive fluorescence turn-on CN⁻ probes with a detection limit of 2×10^{-7} M for **2-Cu²⁺**.

Compounds **1–3** were synthesized by Sonogashira and Ullmann coupling reactions (Scheme 1) and characterized by ¹H NMR, ¹³C NMR, and HRMS (Fig. S2–S14, ESI†).

Titrations of Cu²⁺ with solutions of **1** and **2** led to substantial changes in UV-Vis and fluorescence spectra. As shown in Fig. 1a, upon the addition of Cu²⁺ to a MeOH–H₂O solution of **1**, the peaks at 403 and 425 nm gradually decreased with a new peak developing at 447 nm. Appearance of isosbestic points indicates the formation of a well defined complex between **1** and Cu²⁺. Also, fluorescence was almost completely quenched upon addition of 4 equiv. of Cu²⁺ (Fig. 1b). In contrast, addition of other divalent cations such as Zn²⁺, Cd²⁺, Hg²⁺, Ni²⁺, Mn²⁺, and Ca²⁺ caused only slight quenching of the fluorescence (Fig. S15, ESI†),
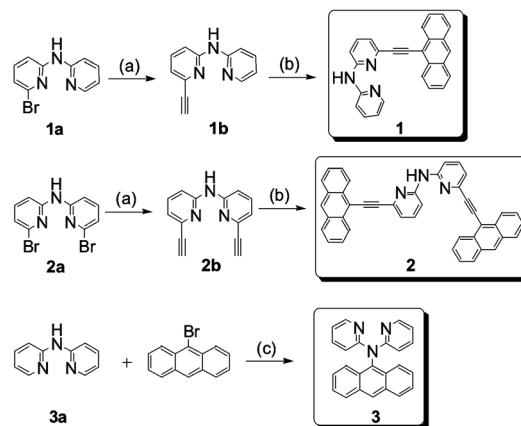
Scheme 1 Syntheses of **1–3**. Reaction conditions: (a) (i) TMSA, Pd(PPh₃)₂Cl₂, CuI, Et₂NH, (ii) *n*-Bu₄NF, THF; (b) 9-bromoanthracene, Pd(PPh₃)₂Cl₂, CuI, i-Pr₂NH,THF; (c) CuSO₄, K₂CO₃, 18-crown-6, Ph₂O.

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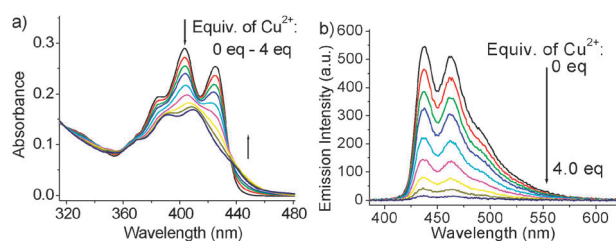
Fig. 1 (a) UV-Vis spectral changes during the titration of **1** (10 μM) with Cu^{2+} in MeOH–H$_2$O (4 : 1, v/v); (b) corresponding fluorescence emission spectral changes with λ_{ex} fixed at 360 nm (one of the isosbestic points).

indicating that **1** can be considered as a selective fluorescent "turn off" Cu^{2+} probe. Similar behaviour was also observed for **2** (Fig. S16 and S17, ESI†). A 1 : 1 binding mode is indicated by Job's plots for both **1-Cu^{2+}** and **2-Cu^{2+}** (Fig. S18 and S19, ESI†), with the corresponding association constants (K_{ass}) of 6×10^5 and 1×10^5 M^{-1}, respectively (Fig. S20 and S21, ESI†). Detection limits of **1** and **2** for Cu^{2+} were found to be 3×10^{-7} and 9×10^{-7} M, respectively (Fig. S22 and S23, ESI†). These values are comparable to some reported examples.[11]

Compared with **1** and **2**, a larger molar excess of Cu^{2+} is required to quench fluorescence (Fig. S24, ESI†) of **3**, indicating that coordination of **3** with Cu^{2+} is weaker. The association constant of Cu^{2+} with **3** was determined to be 2×10^3 M^{-1} (Fig. S25, ESI†). This observation is ascribed to intramolecular steric hindrance caused by the linkage between anthracene and the amino N atom of 2,2′-dpa, which is evidenced by the large dihedral angle of 35.2(1)° between the two pyridyl planes observed in the crystal structure of **3** (Fig. S26, ESI†), and it is consistent with the DFT calculation results, which give planar conformations for **1** and **2** (Fig. S27 and S28, ESI†), and a distorted conformation for **3** (Fig. S29, ESI†).

Considering the non-fluorescence of the Cu^{2+} ensembles and the strong affinity of CN$^-$ with Cu^{2+}, the Cu^{2+} ion in these ensembles may be removed by CN$^-$ to form stable [Cu(CN)$_x$]$^{n-}$ species with the concurrent recovery of the fluorescence of **1**, **2** and **3** (Scheme 2). Consequently, a "turn on" fluorescence was observed. For **1-Cu^{2+}**, addition of 12 equiv. of CN$^-$ caused almost complete recovery of the original fluorescence and UV-Vis spectrum of **1** (Fig. S30 and S31, ESI†).

Similar CN$^-$ sensing properties were also observed for **2-Cu^{2+}**, with 8 equiv. of CN$^-$ required to recover the fluorescence (Fig. S32, ESI†). The removal of Cu^{2+} by CN$^-$ from the complexes is observable by successive ^{1}H NMR titrations of **1** and **2** with Cu^{2+} and CN$^-$. The addition of Cu^{2+} to **1** and **2** in DMSO-d$_6$ resulted in broad peaks due to the paramagnetic effect of coordinated Cu^{2+}, while after addition of CN$^-$ the

original ^{1}H NMR signals of **1** and **2** were recovered (Fig. S33 and S34, ESI†). This is consistent with the removal of Cu^{2+} from **1-Cu^{2+}** and **2-Cu^{2+}** by CN$^-$. In the case of **3-Cu^{2+}**, a large quantity of CN$^-$ was required to remove excess Cu^{2+} and then react with **3-Cu^{2+}** to recover the fluorescence (Fig. S35, ESI†), so that the sensitivity is low.

Based on these measurements, detection limits of **1-Cu^{2+}** and **2-Cu^{2+}** for CN$^-$ were calculated[12] to be 3×10^{-7} and 2×10^{-7} M, respectively (Fig. S36 and S37, ESI†). These values lie well below the limit of 1.9 μM for cyanide in drinking water set by WHO,[13] indicating that these probes may be sensitive enough for practical applications.

Another major issue in the field of ion sensing is the selectivity toward the target ion. It is well known that detection of cyanide is usually complicated by interference from F$^-$, AcO$^-$ and H$_2$PO$_4^-$. To our delight, both **1-Cu^{2+}** and **2-Cu^{2+}** complexes show excellent selectivity for CN$^-$. As depicted in Fig. 2a, addition of CN$^-$ to a MeOH–H$_2$O solution of **1-Cu^{2+}** significantly enhanced its fluorescence by about 35-fold, whereas, other anions such as F$^-$, Cl$^-$, Br$^-$, I$^-$, AcO$^-$, H$_2$PO$_4^-$, CO$_3^{2-}$, SO$_4^{2-}$, SCN$^-$, and S^{2-} only slightly enhanced the fluorescence even after addition of 100 equiv. We performed competition experiments to further elucidate anion selectivity. When 100 equiv. of various anions were added separately to the solutions of **1-Cu^{2+}**, followed by the addition of 20 eq. of CN$^-$, sharp fluorescence "turn-on" could be detected (Fig. 2b), indicative of small interference by these anions. Similar to this observation, **2-Cu^{2+}** also shows high selectivity toward CN$^-$ (Fig. S38, ESI†). From these results, it can be concluded that **1-Cu^{2+}** and **2-Cu^{2+}** show very good selectivity for CN$^-$, and the competing anions do not interfere significantly with CN$^-$ sensing. These inspiring results suggest that **1-Cu^{2+}** and **2-Cu^{2+}** can be established as promising prototypes of fluorescence turn-on cyanide probes in aqueous media.

Considering the fact that addition of CN$^-$ to solutions of **1-Cu^{2+}** and **2-Cu^{2+}** leads to regeneration of **1** and **2**, we tested the reversibility of these cyanide sensing systems. The fluorescence could be turned off and on repeatedly with the alternate addition of Cu^{2+} and CN$^-$ ions (Fig. 3 and Fig. S39, ESI†), indicative of good reversibility of these probes.

Response time is an important practical parameter. Rapid response within a few seconds was observed for **1** and **2** (Fig. S40 and S41, ESI†). Furthermore, the sensing systems
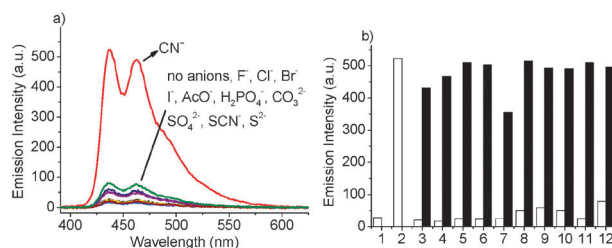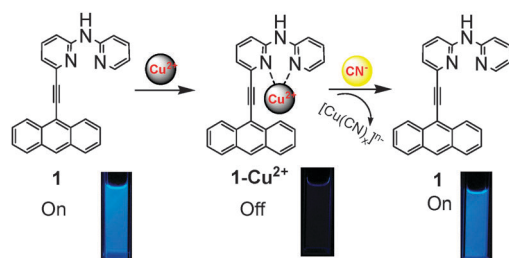

Fig. 2 (a) Changes in the emission spectrum of **1-Cu^{2+}** (10 μM) in the presence of various anions (CN$^-$: 20 equiv., other anions: 100 equiv.) in MeOH–H$_2$O (4 : 1, v/v); (b) white bars represent the addition of 100 equiv. of various anions (CN$^-$: 20 eq.). Black bars represent the addition of 100 equiv. of indicated anions, followed by 20 equiv. of CN$^-$ anions. 1–12: no anion, CN$^-$, F$^-$, Cl$^-$, Br$^-$, I$^-$, AcO$^-$, H$_2$PO$_4^-$, CO$_3^{2-}$, SO$_4^{2-}$, SCN$^-$ and S^{2-}.

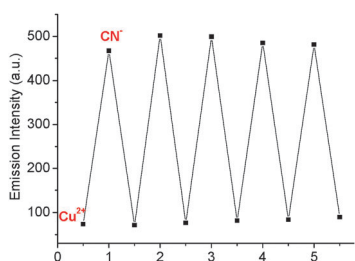**Scheme 2** Proposed sensing mechanism for compound **1**.

Fig. 3 Emission intensity of **1-Cu^{2+}** with alternate addition of CN$^-$ and Cu^{2+}.

work well over a wide pH range of 7–10 (Fig. S42 and S43, ESI†), which makes them more applicable in practical systems.

In summary, we have synthesized a new prototype of highly fluorescent compounds **1−3** by linking a strongly emissive anthracene unit as the reporting group to a Cu^{2+} chelating 2,2′-dpa moiety as the binding site. Differences in the linking modes in **1−3** greatly affect the sensing behaviour. **1** and **2** show good affinities towards Cu^{2+} with easy formation of non-fluorescent **1-Cu^{2+}** and **2-Cu^{2+}** ensembles. Interestingly, the fluorescence can be fully recovered by the subsequent addition of CN$^-$, with the CN$^-$ detection limits of 3×10^{-7} and 2×10^{-7} M. These values lie well below the safe CN$^-$ limit of 1.9 μM in drinking water set by WHO. In contrast, **3-Cu^{2+}** shows much lower sensitivity due to the difference in the linking mode. These results indicate that the linkage of 2, 2′-dpa to a fluorophore through a carbon atom is promising for the design of strongly emissive compounds, whose Cu^{2+} ensembles can be used as fluorescence turn-on CN$^-$ probes. It is noteworthy that the CN$^-$ probes of **1-Cu^{2+}** and **2-Cu^{2+}** have the advantage of being effective in water-containing solvents over a wide pH range,[4i,6c] in addition to their high sensitivity,[5a,b,f−i,6b−d] high selectivity, good reversibility, and rapid response.[3c,5d,j,6c] It can be concluded that the suitable linkage of an effective chromophore to a chelating moiety followed by coordination with Cu^{2+} affords an ensemble, which can be developed as a promising prototype of "turn-on" fluorescent CN$^-$ probes. These results provide further insight into the design of relevant CN$^-$ probes.

Notes and references

1 (a) B. Vennesland, E. E. Comm, C. J. Knownles, J. Westly and F. Wissing, *Cyanide in Biology*, Academic Press, London, 1981; (b) R. Koenig, *Science*, 2000, **287**, 1737–1738.

2 (a) H. Hachiya, S. Ito, Y. Fushinuki, T. Masadome, Y. Asano and T. Imato, *Talanta*, 1999, **48**, 997–1004; (b) S. I. Baskin and T. G. Brewer, in *Medical Aspects of Chemical and Biological Warfare*, ed. F. Sidell, E. T. Takafuji and D. R. Franz, TMM publications, Washington, 1997.

3 (a) Z. Xu, X. Chen, H. N. Kim and J. Yoon, *Chem. Soc. Rev.*, 2010, **39**, 127–137; (b) H. Miyaji and J. L. Sessler, *Angew. Chem.,*

Int. Ed., 2001, **40**, 154–157; (c) Y. L. Liu, K. L. Ai, X. L. Cheng, L. H. Huo and L. H. Lu, *Adv. Funct. Mater.*, 2010, **20**, 951–956.

4 (a) M. Wenzel, J. R. Hiscock and P. A. Gale, *Chem. Soc. Rev.*, 2012, **41**, 480–520; (b) P. A. Gale, *Chem. Soc. Rev.*, 2010, **39**, 3746–3771; (c) E. Galbraith and T. D. James, *Chem. Soc. Rev.*, 2010, **39**, 3831–3842; (d) A. P. de Silva, G. D. McClean and T. S. Moody, *Encycl. Supramol. Chem.*, 2004, 572–578; (e) L. Fabbrizzi, M. Licchelli, F. Mancin, M. Pizzeghello, G. Rabaioli, A. Taglietti, P. Tecilla and U. Tonellato, *Chem.–Eur. J.*, 2002, **8**, 94–101; (f) J. S. Kim and D. T. Quang, *Chem. Rev.*, 2007, **107**, 3780–3799; (g) R. Martínez-Máñez and F. Sancenón, *Chem. Rev.*, 2003, **103**, 4419–4476; (h) H. Wang, L. Xue, Y. Qian and H. Jiang, *Org. Lett.*, 2010, **12**, 292–295; (i) Z. Liu, C. Zhang, W. He, Z. Yang, X. Gao and Z. Guo, *Chem. Commun.*, 2010, **46**, 6138–6140; (j) H. Zheng, M. Yan, X. Fan, D. Sun, S. Yang, L. Yang, J. Li and Y. Jiang, *Chem. Commun.*, 2012, **48**, 2243–2245; (k) X. Peng, Z. Yang, J. Wang, J. Fan, Y. He, F. Song, B. Wang, S. Sun, J. Qu, J. Qi and M. Yan, *J. Am. Chem. Soc.*, 2011, **133**, 6626–6635; (l) D. Buccella, J. A. Horowitz and S. J. Lippard, *J. Am. Chem. Soc.*, 2011, **133**, 4101–4114; (m) K. Hanaoka, Y. Muramatsu, Y. Urano, T. Terai and T. Nagano, *Chem.–Eur. J.*, 2010, **16**, 568–572.

5 (a) D. S. Kim, Y. M. Chung, M. Jun and K. H. Ahn, *J. Org. Chem.*, 2009, **74**, 4849–4854; (b) Y. Shiraishi, S. Sumiya and T. Hirai, *Chem. Commun.*, 2011, **47**, 4953–4955; (c) H. J. Kim, K. C. Ko, J. H. Lee, J. Y. Lee and J. S. Kim, *Chem. Commun.*, 2011, **47**, 2886–2888; (d) H. S. Jung, J. H. Han, Z. H. Kim, C. Kang and J. S. Kim, *Org. Lett.*, 2011, **13**, 5056–5059; (e) H. Yu, Q. Zhao, Z. Jiang, J. Qin and Z. Li, *Sens. Actuators, B*, 2010, **148**, 110–116; (f) L. Peng, M. Wang, G. Zhang, D. Zhang and D. Zhu, *Org. Lett.*, 2009, **11**, 1943–1946; (g) H. Niu, X. Jiang, J. He and J. Cheng, *Tetrahedron Lett.*, 2009, **50**, 6668–6671; (h) D. G. Cho, J. H. Kim and J. L. Sessler, *J. Am. Chem. Soc.*, 2008, **130**, 12163–12167; (i) Y. Kim, H. S. Huh, M. H. Lee, I. L. Lenov, H. Zhao and F. P. Gabbaï, *Chem.–Eur. J.*, 2011, **17**, 2057–2062; (j) L. B. Zang, D. Y. Wei, S. C. Wang and S. M. Jiang, *Tetrahedron*, 2012, **68**, 636–641.

6 (a) V. Amendola and L. Fabbrizzi, *Chem. Commun.*, 2009, 513–531; (b) X. Chen, S. Nam, G. Kim, N. Song, Y. Jeong, I. Shin, S. Kim, J. Kim, S. Park and J. Yoon, *Chem. Commun.*, 2010, **46**, 8953–8955; (c) L. Shang, L. Zhang and S. Dong, *Analyst*, 2009, **134**, 107–113; (d) Y. Liu, X. Lv, Y. Zhao, J. Liu, Y. Sun, P. Wang and W. Guo, *J. Mater. Chem.*, 2012, **22**, 1747–1750; (e) X. Lou, D. Ou, Q. Li and Z. Li, *Chem. Commun.*, 2012, **48**, 8462–8477; (f) X. Lou, Y. Zhang, S. Li, D. Ou, Z. Wan, J. Qin and Z. Li, *Polym. Chem.*, 2012, **3**, 1446–1452; (g) C. R. Maldonado, A. Touceda-Varela, A. C. Jones and J. C. Mareque-Rivas, *Chem. Commun.*, 2011, **47**, 11700–11702; (h) H. Gee, C. Lee, Y. Jeong and W. Jang, *Chem. Commun.*, 2011, **47**, 11963–11965.

7 (a) X. M. Huang, Z. Q. Guo, W. H. Zhu, Y. S. Xie and H. Tian, *Chem. Commun.*, 2008, 5143–5145; (b) Z. A. Li, X. D. Lou, H. B. Yu, Z. Li and J. G. Qin, *Macromolecules*, 2008, **41**, 7433–7439; (c) A. Touceda-Varela, E. I. Stevenson, J. A. Galve-Gasion, D. T. F. Dryden and J. C. Mareque-Rivas, *Chem. Commun.*, 2008, 1998–2000.

8 (a) Y. Ding, Y. Xie, X. Li, J. Hill and W. Zhu, *Chem. Commun.*, 2011, **47**, 5431–5433; (b) Y. Ding, W. Zhu and Y. Xie, *Org. Biomol. Chem.*, 2012, **10**, 4201–4207; (c) Q. Wang, Y. Xie, Y. Ding, X. Li and W. Zhu, *Chem. Commun.*, 2010, **46**, 3669–3671; (d) Y. Xie, T. Morimoto and H. Furuta, *Angew. Chem., Int. Ed.*, 2006, **45**, 6907–6910.

9 (a) Y. Q. Weng, F. Yue, Y. R. Zhong and B. H. Ye, *Inorg. Chem.*, 2007, **46**, 7749–7755; (b) Y. Q. Weng, Y. L. Teng, F. Yue, Y. R. Zhong and B. H. Ye, *Inorg. Chem. Commun.*, 2007, **10**, 443–446.

10 (a) C. A. Parker and W. Rees, *Analyst*, 1960, **85**, 587–600; (b) D. F. Eaton, *Pure Appl. Chem.*, 1988, **60**, 1107–1114; (c) A. T. Williams, S. A. Winfield and J. N. Miller, *Analyst*, 1983, **108**, 1067–1071.

11 (a) A. F. Li, H. He, Y. B. Ruan, Z. C. Wen, J. S. Zhao, Q. J. Jiang and Y. B. Jiang, *Org. Biomol. Chem.*, 2009, **7**, 193–200; (b) H. S. Jung, M. Park, D. Y. Han, E. Kim, C. Lee, S. Ham and J. S. Kim, *Org. Lett.*, 2009, **11**, 3378–3381.

12 M. Shortreed, R. Kopelman, M. Kuhn and B. Hoyland, *Anal. Chem.*, 1996, **68**, 1414–1418.

13 *Guidelines for Drinking-Water Quality*, World Health Organization, Geneva, 1996.