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# Fluorometric, water-based sensors for the detection of nerve gas G mimics DMMP, DCP and DCNP†

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**Water-based $Zn^{II}$ bisterpyridine systems were used as fluorometric sensors for the detection of the nerve gas G mimics DMMP, DCP and DCNP. Analyte concentrations in the range of $10^{-7}$ to $10^{-6}$ M are detectable in solution. The utilization of a test stripe additionally allows the detection of organophosphonates from the gas phase.**

Although the research in the detection of chemical warfare agents was intensified, in particular after the gas attack on the Tokyo subway in 1995, there is still a need for new and improved systems for the detection of "nerve gases". These highly toxic compounds can inhibit acetylcholinesterase (AChE), a critical central-nervous enzyme.[1–4] Different detection methods have been investigated, which are generally based on emission (*i.e.* lanthanide emission[5–8] or fluorescence of organic dyes[9–13]), enzymes,[14,15] interferometry,[16] surface acoustic waves,[17,18] electrochemistry,[19] mass spectrometry,[20,21] chromogenic[22–24] and calorimetric methods.[25] However, for any practical use the detection system has to be portable, fast, easy to use, selective and sensitive. Metallopolymers represent a versatile class of materials featuring these properties.[26]

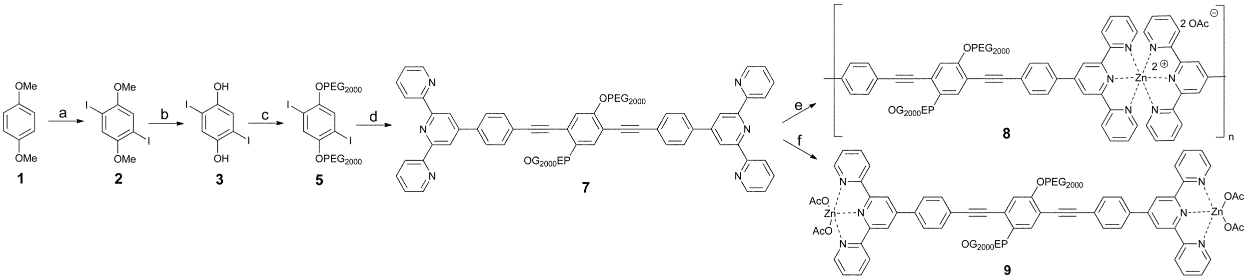
The herein presented $Zn^{II}$ bisterpyridine systems (**8**, **9**) reflect excellent examples of materials for such systems. Due to the PEG side chains, the polymers are water-soluble and the charged character of the zinc–terpyridine complex enables straightforward anion detection.[27]

The water-solubility of the bisterpyridine **7** was achieved *via* PEG sidechains. Initially, the 2,5-diiodo-hydroquinone core **3** was synthesized by applying optimized reaction conditions.[28] The PEG chains were introduced to the core (**3**) *via* Williamson ether synthesis with a tosylate-functionalized $mPEG_{2000}$ **4**. Subsequent Sonogashira reaction, with two equivalents of 4′-(4-ethynylphenyl)-2,2′:6′,2″-terpyridine (**6**), resulted in the PEG-functionalized bisterpyridine **7** (Scheme 1).

The homogeneity of this bisterpyridine was proven by its monomodal distributions in size exclusion chromatography (SEC) and MALDI-TOF mass spectrometry. The PDI values of **7**, calculated by SEC (1.04) and MALDI-TOF MS (1.01) are still very low. In the MALDI-TOF MS the shift to higher $m/z$ values is clearly visible (Fig. 1, right). The mass difference directly correlates with the mass difference of **5** and **7**, as expected.

As shown in Scheme 1, the addition of one equivalent of $Zn(OAc)_2$ to the PEG-functionalized bisterpyridine **7** resulted in the formation of the linear zinc coordination polymer **8**, whereas the addition of two equivalents of $Zn^{II}$ ions yielded the corresponding dinuclear complex **9**.[29] Performing a $^1H$ NMR titration experiment one can clearly follow the complexation reaction (Fig. S1, ESI†). The formation of **9** was moreover proven by MALDI-TOF MS (Fig. 1, right). Due to the PEG chains both the ligand **7** and the corresponding metal complexes (**8**, **9**) revealed excellent solubility in common organic solvents and water.

Absorption and emission spectra in water and dichloromethane are shown in the ESI† (Fig. S2). Upon complexation the absorption maximum is red-shifted (Table 1). Apparently, the hydrophobic conjugated core tends to form aggregates in



a) $I_2$, MeOH, rf, 3 h; b) $BBr_3$, $CH_2Cl_2$, -78 °C to rt, 14 h; c) **4**, $K_2CO_3$, acetone, rf, 48 h; d) **6**, THF, $Pd(PPh_3)_4$, CuI, 30 °C, 24 h; e) $Zn(OAc)_2$, NMP, 100 °C, 2 h; f) $Zn(OAc)_2$, MeOH, rt, 2 h

**Scheme 1** Schematic representation of the synthesis of metallopolymer **8** and dinuclear complex **9**.

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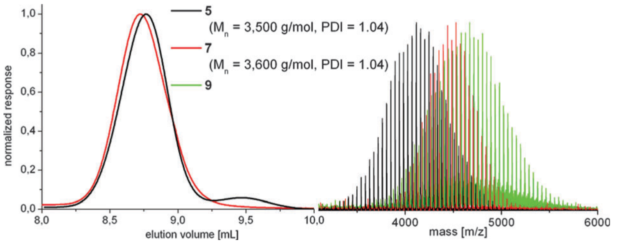

**Fig. 1** Left: SEC traces of **5** and **7**. Right: MALDI-TOF MS spectra of **5**, **7** and **9**.

**Table 1** Selected photophysical data of **7–9**

| | $\lambda_{max}$[a]/nm | | $\lambda_{Pl}$[b]/nm | | $\Phi$[c] | |
|---|---|---|---|---|---|---|
| | Water | $CH_2Cl_2$ | Water | $CH_2Cl_2$ | Water | $CH_2Cl_2$ |
| **7** | 377 | 379 | 524 | 429 | 0.17 | 0.79 |
| **8** | 383 | 393 | 590 | 439 | 0.03 | 0.78 |
| **9** | 393 | 406 | 570 | 521 | 0.01 | 0.69 |

[a] Longest wavelength absorption maximum. [b] Excited at the longest wavelength absorption maximum. [c] Absolute quantum yield.

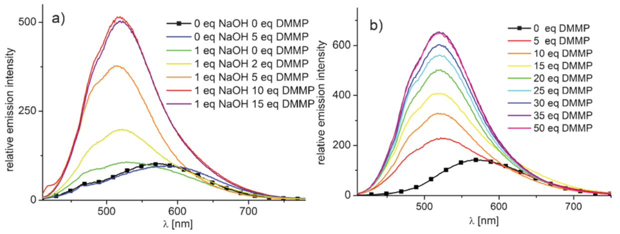

**Fig. 3** Emission spectra of (a) **8** and (b) **9** (water, $c = 5.8 \times 10^{-7}$ M, $\lambda_{ex} = 400$ nm) upon addition of DMMP (water, $c = 0.116$ mM).

aqueous solution *via* π–π interactions, which explains the bathochromically shifted emission and the lowered quantum yield, in particular in polymer **8**, compared to dichloromethane. This assumption was proven by DLS and TEM measurements. Complex **9** revealed, due to the two attached terpyridine zinc(II) complexes, a lower solubility in dichloromethane and, for that reason, red-shifted emission ($\lambda_{PL}$ = 521 nm) compared to **7** ($\lambda_{PL}$ = 429 nm) and **8** ($\lambda_{PL}$ = 439 nm).

As shown already in a screening of 15 different common anions, the $Zn^{II}$ bisterpyridine metallopolymer **8** features a high affinity to phosphate and cyanide ions in aqueous solution.[27] The phosphate coordinates as competitive binder with high binding constants to the $Zn^{II}$ ion, resulting in a recovery of the ligand emission. This behavior is visualized by an increased emission intensity and a shift of the emission wavelength.[27]

Among chemical warfare reagents, nerve gasses such as Sarin, Tabun or Soman belong probably to the most dangerous, since they can be lethal in minutes when inhaled[3] or absorbed through the skin (Fig. 2).[2,30] As mimics for Sarin and Tabun we utilized DMMP, DCP and DCNP, which are commonly used as analytes for organophosphonate sensing.[24,31,32]

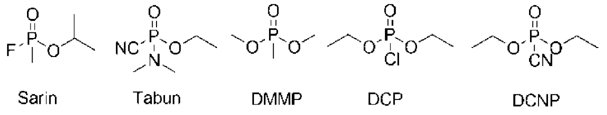

**Fig. 2** Schematic representation of the chemical structure of Sarin, Tabun, DMMP, DCP and DCNP.

The titration experiments were performed as follows: to a solution of **8** or **9** in water ($c = 5.8 \times 10^{-7}$ M) an aqueous analyte solution ($c$ = 0.116 mM) was added and the corresponding emission spectra ($\lambda_{ex}$ = 400 nm) were measured. Apparently, organophosphonates are not capable of coordinating to $Zn^{II}$ ions bound in a bisterpyridine complex, since reactive Lewis acid sites are missing.[32] The addition of 5 equivalents ($c = 2.9 \times 10^{-6}$ M) of DMMP did not result in an obvious optical response (Fig. 3a, blue). However, after addition of 1 equivalent of sodium hydroxide, the $Zn^{II}$–terpyridine polymer partially depolymerized, enabling a DMMP attack (Fig. S3 and S4, ESI†).[32] Subsequent addition of 10 equivalents DMMP ($c = 5.8 \times 10^{-6}$ M) leads to a 5-fold increased emission intensity at 522 nm, as shown in Fig. 3a. Since the measurements were performed significantly above the detection limit, concentrations of $10^{-7}$ M are detectable (Fig. S5a, ESI†), representing a significant improvement in comparison to published systems ($10^{-3}$ to $10^{-4}$ M).[5,23,30]

Dissociation constants ($K_d$) were calculated using the fluorescence intensities at the beginning ($I_0$), the point-of-equivalence ($I_{end}$) and at a certain concentration of added analyte $[A]$ ($I_x$) and fitting to eqn (1) (Fig. S5, ESI†).[33–35]

$$I = (I_0 + I_{end}[A]/K_d)/(1 + [A]/K_d) \qquad (1)$$

Applying eqn (1), the dissociation constant was calculated to be $K_d = 3.2 \times 10^{-7}$. This value is in the same order of magnitude as the one obtained by addition of $Na_3PO_4$.[27]

In analogy to **8**, also **9** was applied as sensor material. Here the accessibility and Lewis acidity of the $Zn^{II}$ ion are much higher, since it is complexed only weakly by one terpyridine ligand. For that reason, DMMP attacks the $Zn^{II}$ already without addition of base and the system exhibits a 7-fold emission intensity (35 eq., Fig. 3b). Since for the detection of organophosphonates by **8** the addition of base appeared to be essential, an easy distinction between organophosphonates and inorganic phosphates is possible. Thus, only inorganic phosphates and cyanides can potentially interfere with each other.[27] To also distinguish between these two, the well-known reaction of cyanide ions with ammonium polysulfide and subsequent reaction with $Fe^{III}$ ions in acidic media leads to the characteristic red color of $Fe(SCN)_3$ (Fig. 4a III).

Moreover to study the detection of organophosphates with reactive phosphoryl halides, DCP was utilized. Addition of an aqueous DCP solution ($c = 0.116$ mM) to **9** ($c = 5.8 \times 10^{-7}$ M) led to an increased emission intensity (10 eq., 5 fold, Fig. S7a, ESI†). Most likely, initial DCP addition leads to hydrolysis

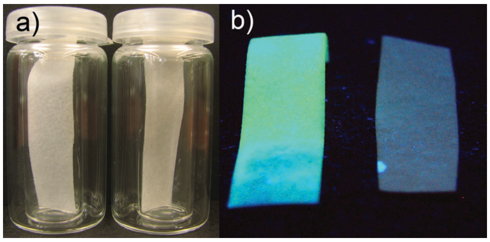

**Fig. 4** (a) Test stripes dipped into a $10^{-5}$ M solution of **8** and NaOH. One of both vials was exposed to DMMP atmosphere. (b) After 10 minutes the test stripes were irradiated ($\lambda_{ex}$ = 365 nm).

and consequently attack at the $Zn^{II}$ ion, resulting in increased emission intensity (Fig. S4 and S7, ESI†).[32,36] Subsequent addition of DCP leads, due to the phosphorylation of the *N*-atoms, to a decreased emission intensity (Fig. S4, ESI†).[24] Most probably, an internal charge transfer (ICT) from the electron-rich chromophore to the electron-accepting pyridinium moiety occurs, as indicated also by the red-shift in the UV-Vis absorption spectrum (Fig. S6, ESI†).[4,24,37] Performing an analogue experiment with **8**, the addition of 10 equivalents DCP caused already decreased emission intensity (Fig. S7b, ESI†). Since in **8** no weakly bound acetate ions are present, DCP directly phosphorylates the pyridine of a dissociated $Zn^{II}$ bisterpyridine complex. To prove this assumption, DCP was added to **7** and also here instantly the emission intensity decreased (Fig. S7c, ESI†). To exclude a potential *N*-protonation upon DCP hydrolysis, the reaction of **8** with DCP was accomplished again in a buffered solution at pH = 7.0. A similar observation could be found, underlining the robustness of the detection system (Fig. S7d, ESI†). The Tabun mimic DCNP exhibits similar detection behavior, as proven in the reaction with **8**. However, the cyanide ions formed upon DCNP hydrolysis complex the $Zn^{II}$ ions, accelerating the phosphorylation of the *N*-atoms (Fig. S8, ESI†).

Moreover, a straightforward protocol for the detection of organophosphonates in the gas phase was established. Two filter papers were dipped into a $10^{-5}$ M solution of **8** and NaOH. Both test stripes were placed into a small sample vial and these were transferred into a larger vial (Fig. 4b). Into one of these larger vials 5 μL of DMMP were added and the vials were closed. After 10 minutes, the test stripes were taken out and irradiated with UV light ($\lambda_{ex}$ = 365 nm). The dipstick exposed to the DMMP atmosphere showed significantly enhanced emission (Fig. 4c).

A π-conjugated PEG-functionalized water-soluble bisterpyridine was synthesized and characterized. The corresponding $Zn^{II}$ coordination polymer **8** and complex **9** were utilized as fluorometric sensor materials for nerve gas G mimics. Upon analyte addition ($c = 10^{-7}$ to $10^{-6}$ M) the emission intensity increased by a factor of 5 to 7. The different reactivity of **8** and **9** towards DMMP and DCP allows a clear distinction between both. To exclude a positive response caused by inorganic phosphates or cyanides we set up a test series to selectively determine them in aqueous solution. The use of a test stripe, dipped into a mixture of polymer **8** and NaOH, allows additionally the detection of organophosphonates from the gas phase.

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