Polynorbornene derived 8-hydroxyquinoline paper strips for ultrasensitive chemical nerve agent surrogate sensing†

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The detection of nerve agent simulants is achieved by the photoinduced electron transfer (PET) mechanism. A "turn-on" fluorescence response upon phosphorylation at 8-hydroxyquinoline of norbornene-based triazolyl functionalized 8-hydroxyquinoline (NCHQ) followed by intramolecular rearrangement provides very intense green emission. The detection limit of polymer (PNCHQ) coated paper strips is 25 ppb with instantaneous response.

Chemical warfare agents are produced not only to kill people in war, but also to terrorize people even in peace.[1a] Among the nerve gas agent family, sarin is the most dangerous and frequently used gas for the attack.[1b] It is well known that nerve gases act as scavengers of acetylcholinesterase, inhibiting its reactivity in the nervous system, which leads to several neurological disorders and even death.[2] Existing techniques, such as gas chromatography-mass spectrometry,[3] surface acoustic wave (SAW) devices,[4] molecular imprinting,[5] flame photometric detectors[6] *etc.*, are facing operational complexity, high cost and require a long detection time. So there is always a need for a portable and facile sensing system. Nerve agent simulants, such as diethyl chlorophosphate (DCP), diisopropyl fluorophosphate (DFP), diphenyl chlorophosphate (DPCP), are explored in the literature as they are less toxic.[7] Swager *et al.* developed a unique sensor system that cyclises in the presence of nerve gases and produces fluorescence response.[8] Based upon photoinduced electron transfer (PET), Rebek *et al.* have demonstrated another facile technique to detect nerve gases.[9] There are also reports on using supernucleophiles for nerve gas sensing by Anslyn *et al.*[10] Even various lanthanide complexes were explored as fluorometric sensor systems for nerve agent surrogates.[11] But most of the existing methods of sensing are either in very high polar solvents like DMF and DMSO or they require alkaline conditions.[12] According to Centres for Disease Control and Prevention (CDC), the concentration of sarin that is immediately dangerous to life is found to be 0.1 mg m^{-3}
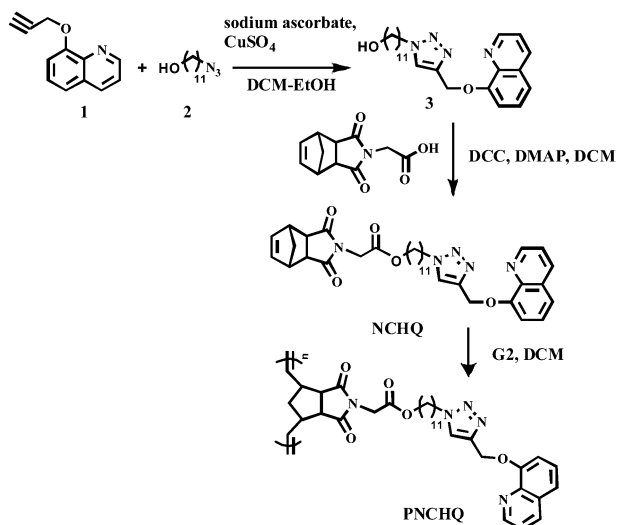
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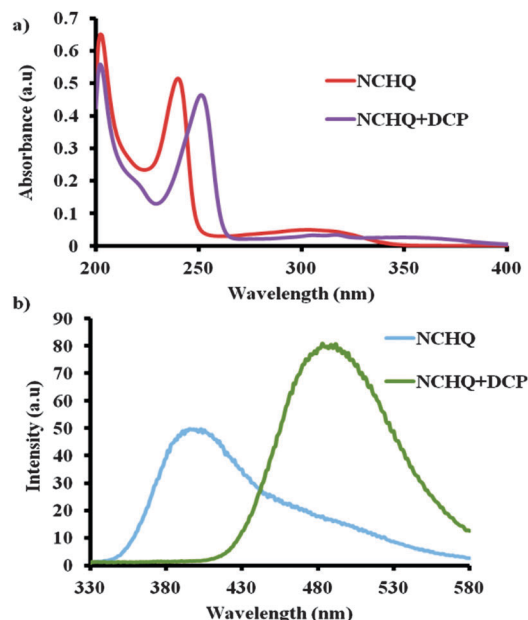
† Electronic supplementary information (ESI) available: Detailed synthesis, characterization, and selected UV and fluorescence data. See DOI: 10.1039/c4cc03361b

(1.7 ppm vapour). So there is always a need for a very sensitive system which can be used as an 'in-field' detector.

Though many existing nerve agent sensors have been reported in the literature, polymer based sensors for 'in-field' application have not been explored so far. Here we report a polymer based "turn-on" fluorometric sensing approach using a norbornene derived 8-hydroxyquinoline motif. 8-Hydroxyquinoline (8-HQ) acts as a weak fluorophore[13] due to excited state intramolecular proton transfer (ESIPT) from oxygen to nitrogen.[14] When 8-HQ is attached to the norbornene functionality by click chemistry, a triazole functionality is generated. Photoinduced electron transfer (PET) from the triazole nitrogen to 8-HQ is the reason for the non-emissive nature of **NCHQ**. As the non-bonding electrons are involved in phosphorylation, it is obvious that they are not available for the PET process. Due to this a turn-on response is achieved. The sensing response of **NCHQ** and its polymer, **PNCHQ**, to the simulant of a nerve agent surrogate is highly sensitive and selective. To the best of our knowledge, this is the first report on a polymeric sensor that has instantaneous 'turn-on' response and a ppb level detection limit upon exposure to the nerve agent simulants.

First of all, 8-HQ was functionalized with alkyne to generate compound **1** (Scheme 1). 11-Bromoundecanol was converted to 11-azidoundecanol (**2**). Cu(ɪ) catalyzed 1,3 dipolar cycloaddition of **1** and **2** yielded compound **3** and it was confirmed through the characteristic proton signal at 7.7 ppm by ^{1}H NMR spectroscopy (Fig. S3, ESI†). ESI-mass and ^{13}C NMR further confirmed the formation of a pure product (Fig. S4 and S8, ESI†). Finally, norbornene acid was coupled with **3** using the DCC coupling reagent to produce monomer **NCHQ**. It must be noted that the norbornene was attached to the 8-HQ moiety through a long alkyl chain to avoid solubility issues. The successful formation of **NCHQ** was confirmed by ^{1}H, ^{13}C NMR and mass spectroscopic techniques (Fig. S5, S7 and S9, ESI†). Ring opening metathesis polymerization (ROMP) using Grubbs' second generation catalyst was employed to polymerize **NCHQ** due to its functional group tolerance.[15] Formation of a polymer (**PNCHQ**) was confirmed by the absence of the norbornene double bond peak at 6.1 ppm and the appearance of a new peak at 5.5–5.6 ppm (Fig. S6, ESI†). The molecular weight

Scheme 1 Schematic representation of synthesis of **NCHQ** and **PNCHQ**.

Fig. 1 (a) UV-vis absorption spectra and (b) emission spectra of 3.33 μM **NCHQ** before and after the addition of DCP in methanol.

and PDI of the polymer were obtained by GPC analysis. The detailed synthesis procedure with characterisation is given in the ESI.†

After the successful synthesis of **NCHQ** and **PNCHQ**, their ability to detect nerve agent surrogates was explored. First, the response of **NCHQ** in methanol against the nerve agent surrogate, DCP, was monitored through UV and fluorescence spectroscopy. **NCHQ** (3.33 μM) showed three absorption maximum bands at 202, 240 and 310 nm in UV spectra. Upon addition of DCP solution, the absorbance bands at 240 nm and 310 nm were observed to undergo a red shift towards 250 nm and 340 nm, respectively (Fig. 1a).

Interestingly, a red shift of 90 nm was observed upon addition of DCP to **NCHQ** (3.33 μM) solution by fluorescence spectroscopy. Initially **NCHQ** emission peak was observed at 398 nm upon excitation at 300 nm. In the presence of DCP, a new emission band at 488 nm was found upon excitation at 300 nm (Fig. 1b). A ratiometric emission spectrum was obtained upon gradual addition of DCP to **NCHQ**, where emission intensity at 398 nm decreased while emission intensity at 488 nm gradually increased (Fig. S10, ESI†). An isoemissive point was found at 450 nm. The lowest detection limit was found to be 25 ppb of DCP in methanol (Fig. S11, ESI†). Quantum yield of **NCHQ** was calculated to be 0.053 taking quinine sulphate as a standard. After the addition of DCP to **NCHQ**, a huge increase in quantum yield (0.146) was observed. This supported the strong 'turn-on' emission response upon addition of DCP to **NCHQ**. The response of **NCHQ** was also studied under a handheld UV-lamp to demonstrate naked eye detection. **NCHQ** in methanol was colourless but instantaneous green emission was observed upon addition of DCP under UV light. Selectivity of **NCHQ** towards DCP was confirmed when no change in emission was observed with addition of other phosphate reagents (Fig. S12, ESI†). Response of **NCHQ** against HCl solution was tested and compared with the response against DCP. The emission response of HCl was found to be very less compared to DCP (Fig. S14, ESI†). The ability of the sensor molecule **NCHQ** to detect other organophosphate nerve agent surrogates was also tested. Diphenyl chlorophosphate (DPCP) was added to the solution of **NCHQ** in

methanol and the emission spectrum was recorded by exciting at 300 nm. The same spectral shift of 90 nm with enhancement in the intensity was observed as with DCP (Fig. S15, ESI†). This control experiment prompted us to propose the phosphorylation mechanism for the sensing event (Scheme 2).

To explore the unusual red shift, the mechanism of the phosphorylation reaction between **NCHQ** and DCP was investigated. ^{1}H NMR spectra were recorded for **NCHQ** and **NCHQ** with DCP in CDCl$_3$. It was found that **NCHQ** aromatic protons, responsible for 8-HQ, shifted to the downfield region upon addition of DCP (Fig. S13, ESI†). 8-HQ protons in **NCHQ** appeared at δ 8.9, 8.2, 7.5, 7.4 and 7.3 ppm. Upon addition of DCP, a shift in all the peaks (at δ 9.3, 8.9, 8.0, 7.9 and 7.8 ppm) was observed as shown in Fig. 2. Also the characteristic proton signal at 7.7 ppm for the triazole double bond was absent after DCP addition. The shift in the signals was attributed to the nucleophilic attack of 8-HQ nitrogen to the
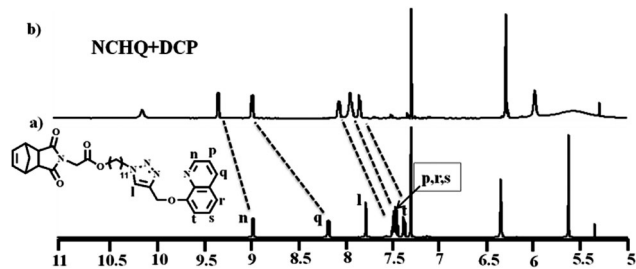

Scheme 2 A schematic proposal for the intramolecular rearrangement.

Fig. 2 Peak shifting in ^{1}H NMR spectra of **NCHQ** (a) before and (b) after the addition of DCP.

Fig. 3 Demonstration of vapour phase sensing of DCP using a **PNCHQ** coated paper strip under a UV lamp.

electrophilic centre of the organophosphate. First, it was assumed to be a **NCHQ**–DCP complex. But the ESI-MS experiment did not support the proposal. Pure **NCHQ** displayed a mass peak at 600. Upon addition of DCP to **NCHQ**, a peak of the complex was expected to occur in the mass spectrum. Surprisingly, it still showed an intense 600 peak which prompted us to explore the other possible mechanisms. To confirm the formation of new molecules, TLC analysis was performed. Interestingly, a fluorescent spot with higher polarity was observed. Based on mass and TLC analyses, we proposed that two molecules with the same mass but different polarities could be possible only when there was an intramolecular rearrangement. This prompted us to hypothesise that the double bond of triazole was involved in the cyclisation process to form **NCHQ-I**. Our proposed structure along with the mechanism are given in Scheme 2.

To further confirm the formation of **NCHQ-I**, **NCHQ** was reacted with the well-known alkylating agent tosyl chloride and changes were monitored through fluorescence, mass and NMR spectroscopy. It was observed that in the emission spectra tosyl chloride induces the same 90 nm red shift, as DCP and DPCP, when added to **NCHQ** solution (Fig. S16, ESI†). As expected, ESI-MS analysis of **NCHQ**-TsCl and **NCHQ**-DPCP produced the characteristic mass peak at 600.53, due to the formation of **NCHQ-I** through our proposed intramolecular rearrangement (Fig. S17 and S18, ESI†). The ^{1}H NMR spectral shift of **NCHQ**-TsCl was found to be the same as **NCHQ**-DCP (Fig. S19, ESI†).

After demonstrating the sensing ability of **NCHQ** successfully, the detection ability of its polymer, **PNCHQ**, was explored through fluorescence spectroscopy (Fig. S21, ESI†). Reactivity of **PNCHQ** towards DCP was monitored through ^{1}H NMR analysis and the corresponding downfield shifts in the peak positions were observed (Fig. S20, ESI†). Paper strips were made from solutions of **PNCHQ** (0.5 mg ml^{-1}). A strip of Whatman filter paper was coated with **PNCHQ** solution and dried. The strip was kept hanging from the inside wall of a glass chamber so that it remained above the bottom level. Under the UV light, the **PNCHQ** coated paper strip was colourless. Interestingly, when a few drops of DCP were added into the glass chamber, an immediate 'turn-on' response was observed (video attached). It was even seen that holding the strip over the DCP solution also produced a colour change of the strip as shown in Fig. 3. The responsive nature of the **PNCHQ** coated strip towards DCP in the presence of other chlorinated compounds and water vapour was observed to remain undisturbed (Fig. S22 and S23, ESI†). These experiments demonstrated the ultrasensitivity of our new polymeric nerve agent sensor.
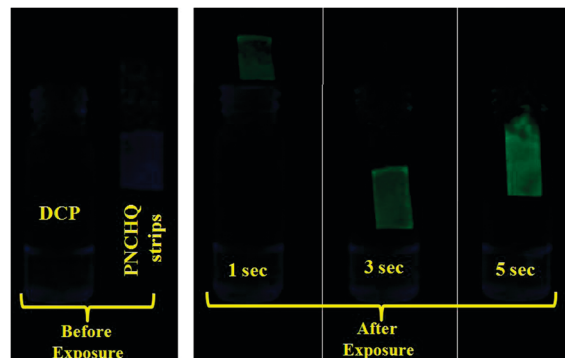
In conclusion, we have demonstrated the ultrasensitive detection of a nerve agent surrogate, DCP, using **NCHQ** and **PNCHQ** sensors. From NMR and mass analysis, an intramolecular rearrangement has been proposed for the unique 'turn-on' response. Paper strips of **PNCHQ** show an instantaneous response upon exposure to DCP. Most interestingly, the paper strips enable the possibility of vapour phase sensing of DCP at a concentration as low as 25 ppb, and hence can be utilized for in-field applications.

Notes and references

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