This is an Accepted Manuscript, which has been through the Royal Society of Chemistry peer review process and has been accepted for publication.

Accepted Manuscripts are published online shortly after acceptance, before technical editing, formatting and proof reading. Using this free service, authors can make their results available to the community, in citable form, before we publish the edited article. We will replace this Accepted Manuscript with the edited and formatted Advance Article as soon as it is available.

You can find more information about Accepted Manuscripts in the Information for Authors.

Please note that technical editing may introduce minor changes to the text and/or graphics, which may alter content. The journal’s standard Terms & Conditions and the Ethical guidelines still apply. In no event shall the Royal Society of Chemistry be held responsible for any errors or omissions in this Accepted Manuscript or any consequences arising from the use of any information it contains.
Polynorbornene Derived 8-Hydroxyquinoline Paper Strips for Ultrasensitive Chemical Nerve Agent Surrogate Sensing

Santu Sarkar and Raja Shunmugam*

The detection of nerve agent stimulants is achieved by the photoinduced electron transfer (PET) mechanism. A “turn-on” fluorescent response upon phosphorylation at 8-hydroxyquinoline of norbornene based triazolyl functionalized 8-hydroxyquinoline (NCHQ), followed by intramolecular rearrangement provides very intense green emission. The polymer (PNCHQ) coated paper strips’ detection limit 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. Among the nerve gas agent family, Sarin is the most dangerous and frequently used for the attack. It is well known that nerve gases act as a scavenger for acetylcholinesterase, inhibiting its reactivity in the nervous system, which leads to several neurological disorder and even death. Existing techniques, such as gas chromatography-mass spectrometry, surface acoustic wave (SAW) devices, molecular imprinting, flame photometric detectors etc., are facing operational complexity, high cost and long detection time. There is always a need of a portable and facile sensing system. Nerve agents simulants, such as, diethyl chlorophosphate (DCP), diisopropyl fluorophosphatate (DFP), diphenyl chlorophosphate (DPCP) are explored in the literature as gas chromatography-mass spectrometry, photoinduced electron transfer (PET), Rebek et al. have demonstrated another facile technique to detect nerve gases. Swager et al developed a unique sensor system that cyclises in presence of nerve gases and produce fluorescence response. Based upon Photoinduced Electron Transfer (PET), Rebe et al. have demonstrated another facile technique to detect nerve gases. There are also reports of using supernucleophiles for nerve gas sensing by Anslyn et al. Even various lanthanide complexes were explored as fluorometric sensor systems for nerve agent surrogates. But most of the existing methods of sensing are either in very high polar solvent like DMF, DMSO or they require alkaline conditions.

According to Centres for Disease Control and Prevention (CDC), the concentration of sarin that is immediately dangerous to life is to be 0.1 mg m⁻³ (1.7 ppm vapour). So there is always need for a very sensitive system which can be used as ‘in-field’ detector. Though many existing nerve agent sensors are reported in the literature, polymer based sensors for ‘in-field’ application are not explored so far. Here we report a polymer based “turn-on” fluorometric sensing approach with norbornene derived 8-hydroxyquinoline motif. 8-hydroxyquinoline (8-HQ) acts as a weak fluorophore due to excited state intramolecular proton transfer (ESIPT) from oxygen to nitrogen. When 8-HQ is attached to the norbornene functionality by click chemistry, a triazole functionality is generated. Photoinduced electron transfer (PET) from the triazol nitrogen to 8-HQ is the reason for non emissive nature of NCHQ. As the non-bonding electrons are involved in phosphorylation, it is obvious that they are not available for PET process. Due to this a turn-on response is achieved. The sensing response of NCHQ and its polymer, PNCHQ, to the stimulant of nerve agent surrogate is highly sensitive and selective. To the best of our knowledge, this is the first report on polymeric sensor that has instantaneous ‘turn-on’ response and ppb level detection limit upon exposure to the nerve agent stimulants.

First of all, 8-HQ was functionalized with alkyn¹ to generate compound 1. 11-bromoundecanol was converted to 11-azidoundecanol (2). Cu(I) catalyzed 1,3 dipolar cycloaddition of 1 & 2 yielded compound 3 and it was confirmed through the characteristic proton signal at 7.7 ppm in ¹H NMR spectroscopy (Fig. S3). ESI-Mass and ¹³C NMR further confirmed formation of pure product (Fig. S4 & S8). Finally, norbornene acid was coupled with 3 using DCC coupling reagent to produce monomer NCHQ. It must be noted that the norbornene was attached to 8-HQ moiety through a long alkyl chain to avoid solubility issues. The successful formation of NCHQ was confirmed by ¹H, ¹³C NMR and mass spectroscopy techniques (Fig.S5, S7 & S9). Ring opening metathesis polymerization (ROMP) using Grubbs¹¹ yielded polymer (PNCHQ) with high molecular weight (85000). The polymer coated paper strips were able to detect 8-HQ in few minutes with high sensitivity and selectivity.

Scheme 1. Schematic representation of synthesis of NCHQ and PNCHQ.
second generation catalyst was employed to polymerize NCHQ due to its functional group tolerance. Formation of polymer (PNCHQ) was confirmed by the absence of norbornene double bond peak at 6.1 ppm and appearance of new peak at 5.5-5.6 ppm (Fig. S6). Molecular weight and PDI of the polymer was obtained by GPC analysis. Detailed synthesis procedure with characterisation has been given in supporting information.

After the successful synthesis of NCHQ and PNCHQ, their detecting ability of nerve agent surrogate was explored. First, response of NCHQ in methanol against nerve agent surrogate, change in emission was observed with addition of other phosphate reagents (Fig. S12). Response of NCHQ against HCl solution was tested and compared with the response against DCP. The emission response of HCl was found very less compared to DCP (Fig. S14). Detection of the sensor molecule NCHQ towards other organophosphate nerve agent surrogate was also tested. Diphenyl chlorophosphate (DPCP) was added to the solution of NCHQ in methanol and emission spectrum was recorded by exciting at 300 nm. Same spectral shift of 90 nm with enhancement in the intensity was observed as with DCP (Fig. S15). This control experiment prompted us to propose the phosphorylation mechanism for the sensing event.

To explore the unusual red shift, the mechanism of the phosphorylation reaction between NCHQ and DCP was investigated. NMR spectra were taken for NCHQ and NCHQ with DCP in CDCl₃. It was found that NCHQ aromatic protons, responsible for 8-HQ, shifted to downfield region upon addition of DCP (Fig. S13). 8-HQ protons in NCHQ appeared at δ 8.9, 8.2, 7.5, 7.4 and 7.3 ppm. Upon addition of DCP, shift in all the peaks (at δ 9.3, 8.9, 8.0, 7.9, 7.8 ppm) was observed as shown in Figure 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 due to the nucleophilic attack of 8-HQ nitrogen to the electrophilic centre of the organophosphate. First, it was assumed as 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, it was expected to observe a peak of the complex in the mass spectrum. Surprisingly, it was still showing the intense 600 peak which prompted us to explore the other possible mechanisms. To confirm the formation of new molecule, TLC analysis was performed.
performed. Interestingly, a fluorescent spot with higher polarity was observed. Based on mass and TLC analysis, we proposed that two molecules with same mass but different polarity could be possible only when there was an intramolecular rearrangement.

This prompted us to hypothesise that the double bond of triazol was involved in the cyclisation process to form NCHQ-I. Our proposed structure with mechanism has been 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 emission spectra tosyl chloride is inducing same 90 nm red shift, as DCP and DPCP, when added to NCHQ solution (Fig. S16). As expected, MALDI analysis of NCHQ-TsCl and NCHQ-DPCP produced the characteristic mass peak at 600.53, due to formation of NCHQ-I through our proposed intramolecular rearrangement (Fig. S17 & S18). \(^1\)H NMR spectral shift of NCHQ-TsCl was found to be same as NCHQ-DCP (Fig. S19).

After demonstrating the sensing ability of NCHQ successfully, detection ability of its polymer, PNCHQ, was explored through fluorescence spectroscopy (Fig. S21). Reactivity of PNCHQ towards DCP was monitored through \(^1\)H NMR analysis and corresponding downfield shift in the peak positions were observed (Fig. S20). Paper strips were made from solutions of PNCHQ (0.5 mg/ml). 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 at a distance up from the bottom level. Under the UV light, the PNCHQ coated paper strip was colourless. Interestingly, when few drops of DCP was added into the glass chamber, an immediate ‘turn-on’ response was observed (video attached). Even it was seen that holding the strip over the DCP solution also produced colour change of the strip as shown in Figure 3. The responsive nature of PNCHQ coated strip towards DCP in presence of other chlorinated compounds and water vapours was observed to remain undisturbed (Fig. S22 & S23). These experiments demonstrated the ultra sensitivity of our new polymeric nerve agent sensor.

Conclusions

In conclusion, we have demonstrated the ultrasensitive detection of 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 concentration as low as 25 ppb, hence can be utilized for in-field application.

Notes and references

Polymer Research Centre, Department of Chemical Sciences, Indian Institute of Science Education and Research Kolkata (IISER-K), India. E-mail: sruja@iiserkol.ac.in

† Electronic Supplementary Information (ESI) available: [Detailed synthesis, characterization, and selected UV & fluorescence data are reported.] See DOI: 10.1039/b000000x/

TOC Content:

Polynorbornene Derived 8-hydroxyquinoline Paper Strips for Ultrasensitive Chemical Nerve Agent Surrogate Sensing
Santu Sarkar and Raja Shunmugam*
Polymer Research Centre, Department of Chemical Sciences, Indian Institute of Science Education and Research Kolkata (IISER K), India.