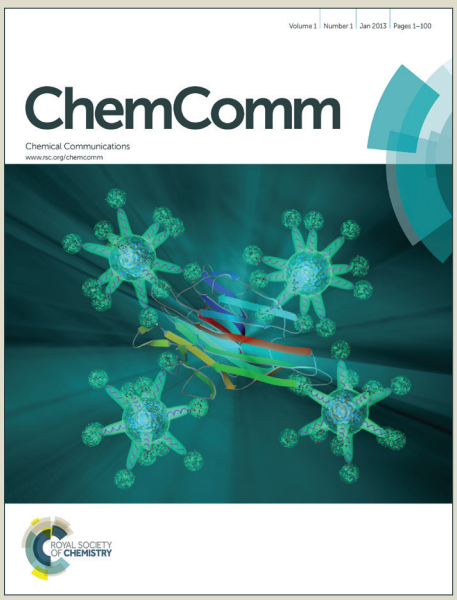
ChemComm

Accepted Manuscript



ROYAL SOCIETY OF CHEMISTRY

www.rsc.org/chemcomm

Cite this: DOI: 10.1039/c0xx00000x

www.rsc.org/xxxxxx

ARTICLE TYPE

Polynorbornene Derived 8-Hydroxyquinoline Paper Strips for Ultrasensitive Chemical Nerve Agent Surrogate Sensing

Santu Sarkar and Raja Shunmugam*

Received (in XXX, XXX) Xth XXXXXXXXX 20XX, Accepted Xth XXXXXXXXX 20XX

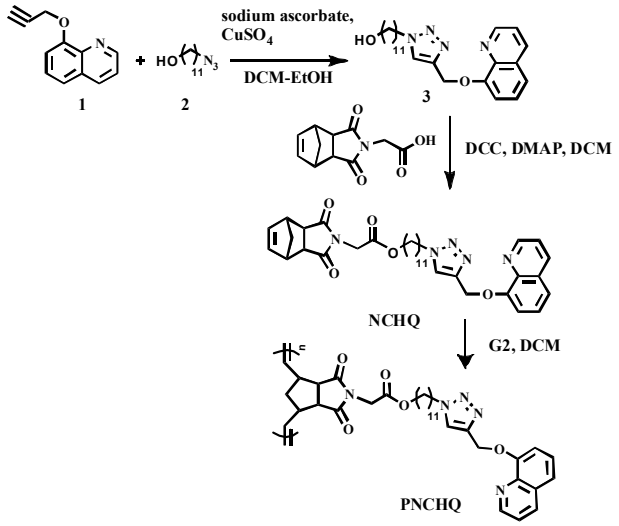
DOI: 10.1039/b000000x

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.[1a] Among the nerve gas agent family, Sarin is the most dangerous and frequently used for the attack.[1b] It is well known that nerve gases act as a scavenger for acetylcholinesterese, inhibiting its reactivity in the nervous system, which leads to several neurological disorder 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 complexiblity, high cost and long detection time. So there is always a need of a portable and facile sensing system. Nerve agents simulants, such as, diethyl chlorophosphate (DCP), diisopropyl fluorophospahte (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 presence of nerve gases and produce 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 of 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 solvent like DMF, 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 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[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 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 alkyne 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 ^{1}H NMR spectroscopy (Fig. S3). ESI-Mass and ^{13}C 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 ^{1}H, ^{13}C NMR and mass spectroscopy techniques (Fig.S5, S7 & S9). Ring opening metathesis polymerization (ROMP) using Grubbs'



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

second generation catalyst was employed to polymerize **NCHQ** due to its functional group tolerance.[15] 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,

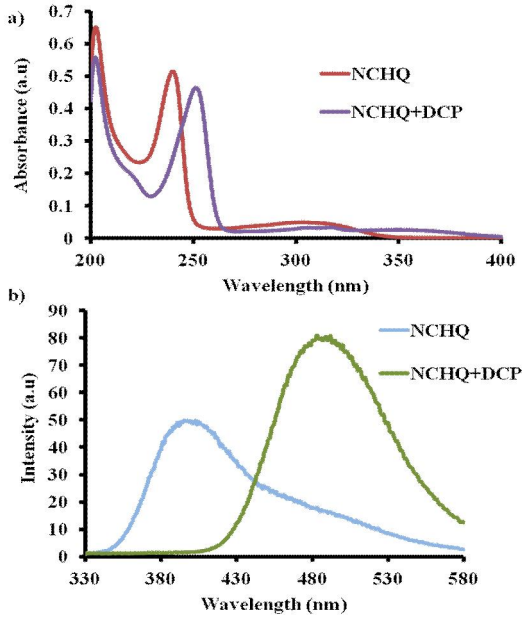


Figure 2. a) UV-Vis absorption spectra and b) emission spectra of 3.33 μM **NCHQ** before and after the addition of DCP in methanol.

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 spectroscopy. Upon addition of DCP solution, the absorbance at 240 nm and 310 nm bands were observed a red shift towards 250 nm and 340 nm respectively (Figure 1a).

Interestingly, a red shift of 90 nm was observed upon addition of DCP to **NCHQ** (3.33 μM) solution in fluorescence spectroscopy. Initially **NCHQ** emission was observed at 398 nm upon excitation at 300 nm. In presence of DCP, a new emission at 488 nm was found with excitation at 300 nm (Figure 1b). A ratiometric emission spectrum was obtained with gradual addition of DCP to **NCHQ**, where emission intensity at 398 nm decreased while emission intensity at 488 nm gradually increased (Fig. S10). An isoemissive point was found at 450 nm. The lowest detection limit was found to be 25 ppb of DCP in methanol (Fig. S11). Quantum yield of **NCHQ** was calculated as 0.053 taking quinine sulphate as 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 while adding DCP to **NCHQ**. The response of **NCHQ** was also studied under 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

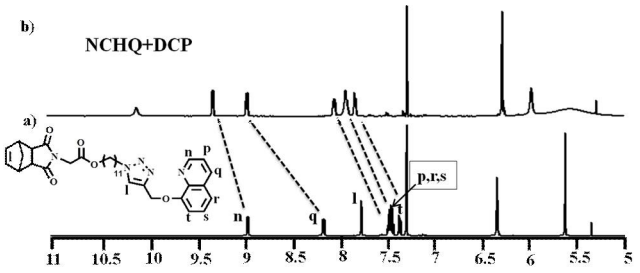
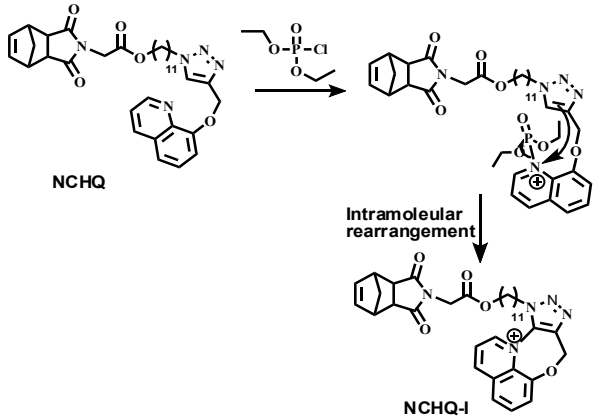


Figure 1. Peak shifting in ^{1}H NMR spectra of **NCHQ** a) before and b) after the addition of DCP.

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 $CDCl_3$. 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



Scheme 1. A schematic proposal for the intramolecular rearrangement.

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. 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

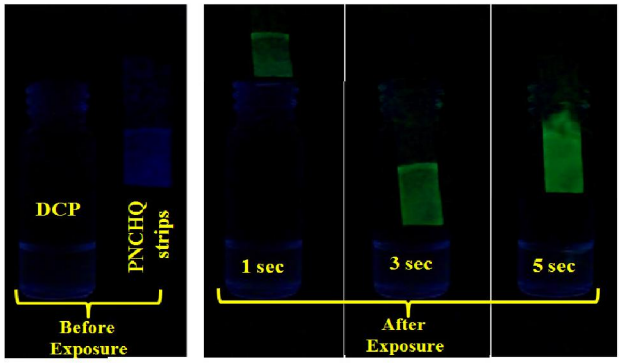


Figure 3. Demonstration of vapour phase sensing of DCP using **PNCHQ** coated paper strip under UV lamp.

with **PNCHQ** solution and dried. The strip was kept hanging from the inside wall of a glass chamber so that it remained 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: sraja@iiserkol.ac.

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

1. (a) Y. C. Yang, J. A. Baker and J. R. Ward, *Chem. Rev.,* 1992, **92**, 1729; (b) A. T. Tu, *Toxin Rev.,* 2007, **26**, 231.
2. (a) C. H. Gunderson, C. R. Lehmann, F. R. Sidell and B. Jabbari, *Neurology.,* 1992, **42**, 946; (b) F. R. Sidell and J. Borak, *Ann. Emerg. Med.,* 1992, **21**, 865.
3. W. E. Steiner, S. J. Klopsch, W. A. English, B. H. Clowers and H. H. Hill, *Anal. Chem.,* 2005, **77**, 4792.
4. (a) Y. Yang, H.-F. Hi and T. Thundat, *J. Am. Chem. Soc.,* 2003, **125**, 1124; (b) C. Hartmann-Thompson, J. Hu, S. N. Kaganove, S. E. Keinath D. L. Keeley and P. R. Dvornic, *Chem. Mater.* **2004**, *16*, 5357.
5. A. L. Jenkins and M. O. Uy, *Anal. Commun.,* 1997, **34**, 221.
6. S. Kendler, A. Zaltsman and G. Frishman, *Instrum. Sci. Technol.,* 2003, **31**, 357.
7. (a) S. Royo, R. Martinez-Manez, F. Sancenon, A.M. Costero, M. Parra and S. Gil, *Chem. Commun.,* 2007, 4839; (b) L. Ordronneau, A. Carella, M. Pohanka and J.-P. Simonato, *Chem. Commun.,* 2013, **49**, 8946. (c) L. Feng, C. J. Musto, J. W. Kemling, S. H. Lim and K. S. Suslick, *Chem. Commun.,* 2010, **46**, 2037; (d) A. M. Costero, M. Parra, S. Gil, R. Gotor, R. Martı´nez-Man˜ez, F. Sanceno´n and S. Royo, *Eur. J. Org. Chem.,* 2012, 4937; (e) G. H. Dennison, M. R. Sambrook and M. R. Johnston, *Chem. Commun.* 2014, **50**, 195.
8. S.-W. Zhang and T. M. Swager, *J. Am. Chem. Soc.,* 2003, **125**, 3420.
9. T. J. Dale and J. Jr. Rebek, *J. Am. Chem. Soc.,* 2006, **128**, 4500.
10. (a) K. J. Wallace, J. Morey, V. M. Lynch and E. V. Anslyn, *New J. Chem.,* 2005, **29**, 1469; (b) K. J. Wallace, R. I. Fagbemi, F. J. Folmer-Andersen, J. Morey, V. M. Lynth and E. V. Anslyn, *Chem. Commun.,* 2006, 3886.
11. (a) R. Shunmugam and G. N. Tew, *Chem. Eur. J.,* 2008, **14**, 5409; (b) S. Sarkar, A. Mondal, A. K. Tiwari and R. Shunmugam, *Chem. Commun.,* 2012, **48**, 4223.
12. (a) S. Han, Z. Xue, Z. Wang and T. B. Wen, *Chem. Commun.,* 2010, **46**, 8413; (b) A. M. Costero, S. Gil, M. Parra, P. M. E. Mancini, R. Martinez-Manez, F. Sancenon and S. Royo, *Chem. Commun.,* 2008, 6002.
13. S. Sarkar and R. Shunmugam, *ACS Appl. Mater. Interfaces,* 2013, **5**, 7379.
14. E. Hao, T. Meng, M. Zhang, W. Pang, Y. Zhou and L. Jiao, *J. Phys. Chem. A.,* 2011, **115**, 8234.
15. (a) R. H. Grubbs, Handbook of Metathesis; Wiley-VCH: New York, 2003; Vol. 3; (b) S. Bhattacharya, S. Sarkar and R. Shunmugam, *J. Mater. Chem. A*, 2013, **1**, 8398; (c) S. Bhattacharya, V. N. Rao, S. Sarkar and R. Shunmugam, *Nanoscale*, 2012, **4**, 6962.

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.