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Nerve agent simulant detection by using chromogenic triaryl methane cation probes

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ABSTRACT

Two triaryl methane cations have been used as probes for colorimetric detection of nerve agent simulants. Buffered mixed aqueous solutions of **1** and **2** showed bathochromic shifts in the presence of DCNP (diethylcyanophosphonate) and DCP (diethylchlorophosphate). The colour modulation can be observed to the naked eye. Appropriate mechanisms for the recognition event are proposed.

1. Introduction

Many nerve agents are highly toxic phosphoric acid esters, and are structurally related to the organophosphates family. These compounds have rapid, severe effects on human and animal health when used in gas, aerosol or liquid. The effects of nerve agents are mainly due to their ability to inhibit the action of acetylcholinesterase, a critical central nervous system enzyme.[1] Nerve agents are considered to be among the most dangerous chemical warfare agents (CWAs).[2] In addition, their easy production, their extreme toxicity and their possible use in terrorist attacks, emphasise the need to detect these odourless and colourless chemicals via the development of reliable and accurate methods.[3,4] Current protocols for monitoring nerve agents are based on the use of biosensors,[5,6] ion mobility spectroscopy (IMS),[7] electrochemistry,[8,9] microcantilevers,[10,11] photonic crystals,[12,13] optical-fibre arrays,[14] etc. As an alternative to these, the development of easy-to-use fluorogenic and chromogenic probes has proved useful for signalling these derivatives in different media and has kindled interest in recent years.[4,15–19] Moreover, colorimetric sensing is particularly attractive as it requires low-cost, widely used instrumentation, and also offers the possibility of detecting these target analytes 'to the naked eye'.

We have recently shown an interest in developing chemical probes capable of signalling the presence of nerve agent simulants following different sensing paradigms.[20,21] Moreover, given the high toxicity of nerve agents Sarin, Soman and Tabun, the related compounds DCP and DCNP have been typically used as models for the design of indicators and sensing systems as they have a similar reactivity, but lack severe toxicity (Fig. 1).

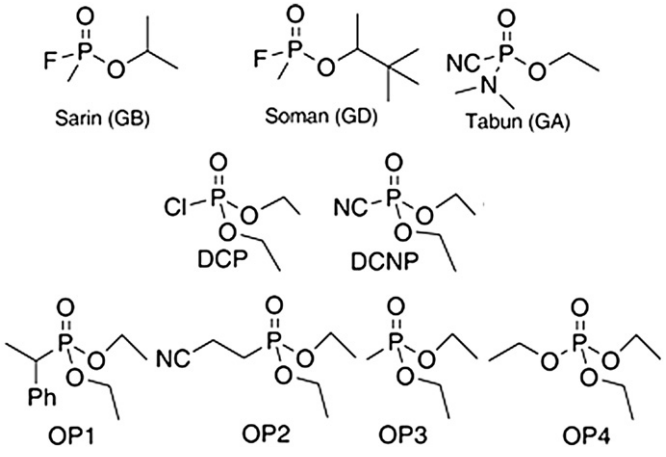

Fig. 1. Nerve agents and simulants.

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To design the probes, we followed the well-established paradigm that relies on the use of dyes containing suitable reactive sites which, upon reaction with target guests, result in a colorimetric event. The use of specific reactions to generate the observable changes ensures the selectivity of chemodosimeters. In addition, the adequate selection of the dyes gives rise to probes that shows high sensitivity. Probably, the most common chemical reaction involving nerve agents takes place directly at the phosphorus atom; in fact, the P–X bond is easily broken by nucleophiles such as water or hydroxyl ions. Given the versatility of this approach, we designed chromogenic probes **1** and **2** (see Fig. 2), whose structures contain nucleophilic moieties (able to react with nerve agents) connecting triaryl methane cations dyes.

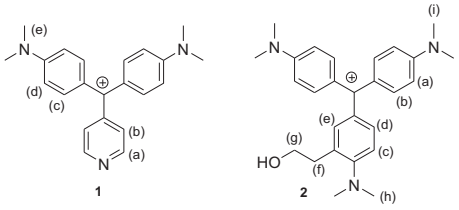
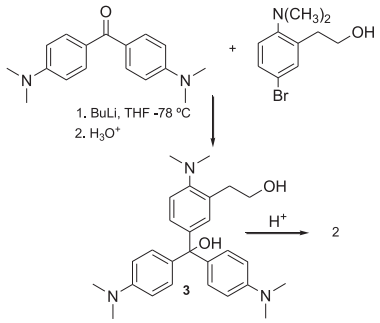


Fig. 2. Chromogenic triaryl methane cations.

Triaryl methane cations dyes present the advantage of being more stable when they are compared with the triarylcarbinol compounds previously used in our laboratory. In fact, triarylcarbinol derivatives can be dehydrated in a very small yield under many different conditions giving rise to colour changes in the sensor when solutions are kept for long times.

2. Results and discussion

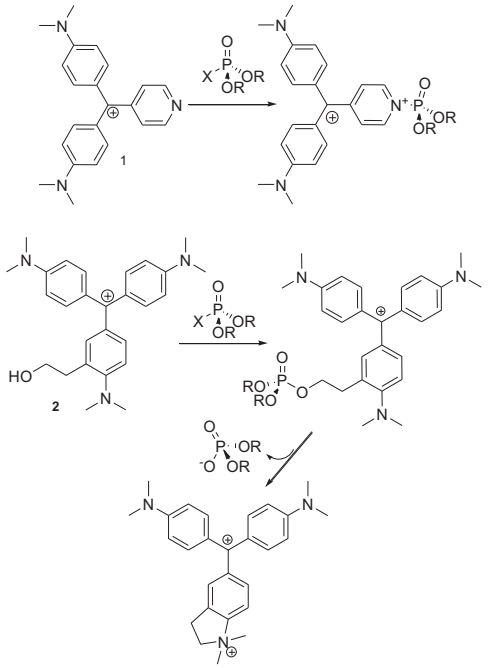
Compound **1** is the well-known 4-Pyridine Green cation and **2** is a modification of the Crystal Violet dye whose structure contains an additional 2-hydroxyethyl moiety. The former contains a pyridine group capable of undergoing phosphorylation reactions. The latter holds a 2-(2-(dimethylamino)phenyl)ethanol moiety (see Scheme 1), which is known to give reactions with phosphonate substrates to further undergo rapid intramolecular N-alkylation to yield a quaternary ammonium salt.[20–22] We expected, upon reaction with certain organophosphorous (OP) substrates, the transformation of pyridine **1** into the corresponding pyridinium salt. The stronger electron withdrawing character of the pyridinium salt would result in a modulation of the push–pull character on the dye and in a colour shift. Similarly the phosphorylation of the hydroxyl group in compound **2** that is followed by an intramolecular S_N2 reaction would transform the tertiary amine into a quaternary ammonium salt with similar changes that these described for compound **1**.



Scheme 1. Synthesis of chromoreagent **2**.

2.1. Detection studies

First, reactivity of **1** and **2** was tested with DCP and DCNP (see Scheme 2) in acetonitrile/water (25:75 v/v) buffered at pH 5.5 with MES (2-morpholinoethanesulfonic acid) 0.1 mol dm^{-3}. These conditions were chosen for two reasons: (i) to guarantee that the observed changes were due to the expected reaction and not to a mere acid–base process and (ii) to ensure the probe solubility.



Scheme 2. Reactivity of **1** and **2** with DCP and DCNP.

In this medium, compound **1** displays an intense absorption band at 635 nm, typical of triarylcations. Addition of either DCP or DCNP resulted in a bathochromic shift of 20 nm. This change in colour is consistent with the phosphorylation of the pyridine, and gives rise to a pyridinium salt showing a stronger electron withdrawing character (when compared with pyridine)[23,26] (see Fig. 2). In order to assess the proposed mechanism, ^{1}H NMR studies were carried out. Addition of DCNP to the CD_3CN solutions of chromoreagent **1** induced clear changes in the ^{1}H NMR spectrum. Thus, H_b underwent a downfield shift of $\Delta\delta$=0.13 ppm, whereas the variation of the H_a shifts was almost negligible. In the dimethylaniline ring, H_c and H_d were downfield shifted ($\Delta\delta$=0.03 ppm and $\Delta\delta$=0.02 ppm, respectively). The signals corresponding to the methyl groups underwent no chemical shift variation (Fig. 3). The changes observed were in agreement with the proposed formulation.

Compound **2** (1×10^{-5} mol dm^{-3} in acetonitrile/water (25:75) buffered at pH 5.5 using MES 0.1 mol dm^{-3}) showed an absorption band at 603 nm, which underwent a bathochromic shift at 627 nm, along with the appearance of a new band at 427 nm upon addition of DCNP or DCP (Fig. 2). This colour modulation from marine blue to turquoise (see Fig. 5) was consistent with the intramolecular cyclisation process in which the donor character of *N*,*N*-