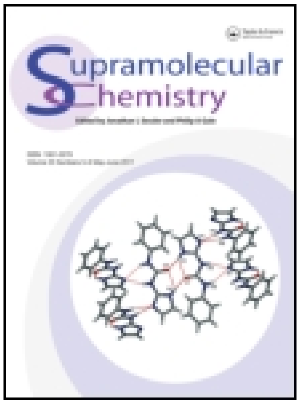

Supramolecular Chemistry
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/gsch20

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To cite this article: Eric S. Silver, Brett M. Rambo, Christopher W. Bielawski & Jonathan L. Sessler (2012): Poly(methyl methacrylate) copolymers containing dipyrrolylquinoxaline receptors for the colorimetric detection of halide anion salts, Supramolecular Chemistry, 24:2, 101-105

To link to this article: http://dx.doi.org/10.1080/10610278.2011.628392

Supramolecular Chemistry
Vol. 24, No. 2, February 2012, 101–105

Poly(methyl methacrylate) copolymers containing dipyrrolylquinoxaline receptors for the colorimetric detection of halide anion salts

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(*Received 2 July 2011; final version received 23 September 2011*)

Described herein is the synthesis of a dipyrrolylquinoxaline (DPQ) monomeric species containing methacrylamide functionality, and its subsequent copolymerisation with methyl methacrylate (MMA). The resulting copolymers were drop casted onto glass substrates, and the resulting thin films displayed distinct colorimetric change upon exposure to hydrofluoric acid (HF) vapour. Furthermore, glass substrates coated with the DPQ–MMA copolymer could be used as 'dip sticks' to test for trace acid in solution, turning from yellow to red upon immersion in an aqueous solution of HF. Analysis by UV–vis spectroscopic titration allowed the association constant (K_a) for interaction with fluoride (as the tetrabutylammonium salt) to be calculated as $6.16 \times 10^5\,M^{-1}$ in CH_2Cl_2. Polymer coatings of this type could find applications in the colorimetric detection of HF vapour, a common hazard associated with industrial processes, such as aluminium smelting.

Keywords: anion binding; sensor; fluoride; receptor immobilisation; polymers

Introduction

The role of anions in the natural world is becoming increasingly well understood, and as the importance of these negatively charged species becomes better appreciated, the need for systems capable of recognising, sensing and transporting anions has dramatically increased (*1*). Two species that stand out among the wide range of biologically relevant anions are fluoride and phosphate. The fluoride anion is being explored extensively as a treatment for osteoporosis (*2*, *3*), and also for its role in preventing dental caries (*4*). Separately, phosphate is known to play a critical role in energy storage and signal transduction (*5*), as well as being recognised as an essential structural element in teeth and bones (*6*). However, in some situations exposure (or overexposure) to these anionic species can have hazardous effects on both the environment and the human body. Excess fluoride anion, commonly caused by exposure to fluoride dust/fumes or present in some drinking waters, can lead to a medical condition known as fluorosis which generally manifests itself in terms of increased bone density (*7*). Phosphate, on the other hand, is a key pollutant whose role in the eutrophication of waterways is well established (*8*). Also, elevated levels of serum phosphate, a disease state known as hyperphosphatemia, can result in calcification of tissues and is a substantial problem in patients suffering from end-stage renal disease (*9*). The dual functionality of fluoride and phosphate has led to an increased interest in finding methods that will allow for their facile recognition and detection (*10*, *11*).

Recently, the Sessler group has reported a series of dipyrrolylquinoxaline (DPQ)-based receptors that display distinct colorimetric responses in the presence of selected anions. These receptors contain at least two pyrrolic NH groups that act as hydrogen bond donors and a built-in quinoxaline ring that acts as a colorimetric reporter (cf. Scheme 1) (*12*). The first member of this series, namely 2,3-dipyrrol-2′-yl-quinoxaline (DPQ), allowed for the detection of fluoride anions [e.g. the corresponding tetrabutylammonium (TBA) salts] in organic media via both fluorescence emission and naked-eye detection. It was also found that a 6-nitro-DPQ derivative (**1**) binds fluoride with a relatively high affinity ($K_a = 1.18 \times 10^5\,M^{-1}$ in CH_2Cl_2) and thus displays selectivity over phosphate ($K_a = 80\,M^{-1}$ in CH_2Cl_2), which displayed a weak response, and most other common anions (no appreciable binding or detectable optical response). These findings make DPQs attractive for incorporation into functional sensors. A key step towards the realisation of this goal is the incorporation of DPQ recognition and indicator elements into easy-to-manipulate polymeric materials.

In seminal work in the field, Anzenbacher and coworkers demonstrated the generation of chromogenic conductive polymers containing DPQ recognition moieties

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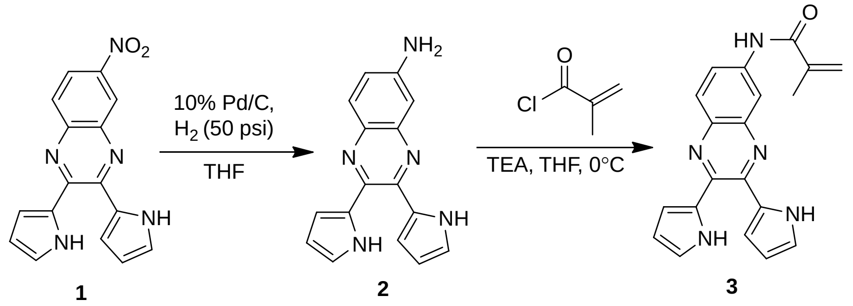
ISSN 1061-0278 print/ISSN 1029-0478 online

http://dx.doi.org/10.1080/10610278.2011.628392
http://www.tandfonline.com



Scheme 1. Synthesis of a methacrylamide-functionalised DPQ monomer.

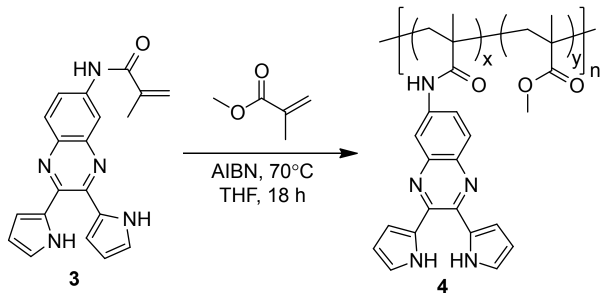
for the sensing of aqueous phosphate-related anions (*13*). In a more recent study, Sun and co-workers utilised DPQ-containing conjugated polymers to develop chromogenic and fluorescent chemosensors for inorganic anions (*14*). In both of these cases, the DPQ moiety was directly incorporated into the backbone of a conjugated polymer. While attractive, such approaches can give rise to materials with solubility characteristics that are difficult to control. We thus felt that an alternative strategy, involving the creation of polymeric materials containing DPQ subunits as pendants off the main polymeric backbone, would be worth exploring.

To date there are limited examples of polymeric systems containing supramolecular receptors as pendant side chains (*15*). This is particularly true in the area of sensing. Recently, our group has described several examples of polymeric materials containing supramolecular receptors appended to the polymeric backbone and showed that these systems have utility in the area of separations. In particular, we detailed the synthesis of several poly(methyl methacrylate)s (PMMAs) containing pendant calix[4]pyrroles and showed that these systems are capable of extracting TBA chloride and fluoride from aqueous media (*16*). This theme was further elaborated on by incorporating pendant crown ether subunits into the polymer; this allowed for the concurrent complexation of both halide and potassium ions (*17*). In a separate report, it was demonstrated that the selectivity of crown-strapped calixarenes could be dramatically improved when appended to PMMA backbones (*18*). However, none of these systems contains a ‘built-in’ recognition unit capable of signalling the presence of an ionic substrate via an optical response. Herein, we report the covalent attachment of DPQ to a PMMA backbone, a strategy that allows for facile solution processing. We also show that thin films of the resulting polymeric species (prepared from drop casting) give rise to an easy-to-visualise colorimetric response when exposed to either the fluoride or phosphate anions (as their TBA salts in CH_2Cl_2). Finally, we show how glass substrates coated with a thin film of the DPQ–MMA copolymer may be used to detect hydrofluoric acid (HF) vapours. This work thus marks a step forward in the rapid detection of what are potentially hazardous materials.

Results and discussion

The methacrylamide containing DPQ monomer (**3**) was prepared in two steps from 6-nitro-DPQ (see reference (*12*) for details on the synthesis of 6-nitro-DPQ; Scheme 1). First, 6-nitro-DPQ (**1**) was reduced to the corresponding amine using 10% Pd/C under an atmosphere of hydrogen gas at 50 psi to afford 6-amino-DPQ (i.e. **2**) in 97% isolated yield. Next, amine **2** was condensed with methacryloyl chloride in dry tetrahydrofuran (THF) under basic conditions (triethylamine) to produce the DPQ–methacrylamide monomer (**3**) in 53% yield.

With **3** in hand, efforts turned towards the incorporation of this monomer into a polymer backbone. For this, we chose free radical polymerisation due to its synthetic ease and high degree of versatility (*19*). The target poly(DPQ-co-MMA) copolymer (i.e. **4**) was synthesised as follows: an oven-dried Schlenk flask was charged with **3**, methyl methacrylate (MMA) and azobisisobutyronitrile in a 1:10:0.01 ratio, respectively, and dissolved in dry THF. The reaction vessel was then heated to 70°C for 18 h (Scheme 2). Precipitation into cold methanol and filtration then produced a yellow solid, copolymer **4**. This material proved to be soluble in a variety of organic solvents and



Scheme 2. Synthesis of the random copolymer (**4**) of DPQ based monomer and MMA.

Figure 1. Solutions of copolymer **4** in CH_2Cl_2 (left) and after exposure to TBAF (right).

was characterised by ^1H NMR spectroscopy. Such analyses allowed for quantification of the monomer ratio as 10:1, MMA to DPQ–methacrylamide. The weight average molecular weight (M_w) was determined to be 29.7 kDa with a polydispersity index of 2.83 by size exclusion chromatography using well-defined polystyrene standards.

Once copolymer **4** was synthesised and characterised as described above, our efforts turned to understanding the binding properties and subsequent response of this material to anionic species, specifically the fluoride and dihydrogen phosphate anions. Initial evidence of anion binding was found when 5 mL of a 50 μM solution of **4** in CH_2Cl_2 was exposed to 10 mg of tetrabutylammonium fluoride (TBAF) resulting in a marked naked-eye detectable colour change from yellow to red (cf. Figure 1).

Table 1. Association constants for the interaction of selected anions with 6-nitro-DPQ (**1**) compared to copolymer **4**, normalized with respect to the DPQ repeat unit, as determined from UV–vis spectroscopic titrations.

	6-Nitro-DPQ[12]	Copolymer **4**
F^-	118,000 M^{-1}	616,000 M^{-1}
$H_2PO_4^-$	80 M^{-1}	56,600 M^{-1}
Cl^-	65 M^{-1}	N/A

Notes: The actual association constants were derived by fitting the changes in absorption at 410 nm to a quadratic equation for 1:1 binding. The values given for copolymer **4** are the average of two to three trials.

In an effort to quantify this binding event, UV–vis spectroscopic titrations were used to determine the association constant (K_a) of copolymer **4** for TBAF in CH_2Cl_2. The resulting study showed that copolymer **4** bound fluoride in the form of its TBA^+ salt in a 1:1 binding mode (based on the DPQ repeat unit) with a relatively high binding affinity ($K_a = 6.16 \times 10^5$; cf. Figure 2).[1] This stands in marked contrast to what was seen in the case of dihydrogen phosphate and chloride anions, species that were found not to bind effectively when studied as their TBA^+ salts in dichloromethane under identical conditions (cf. Table 1). On the basis of these analyses, the affinity, albeit not the selectivity, of copolymer **4** for the fluoride anion was found to be improved over the nitro-containing DPQ species (**1**) from which it is formally derived. However, the major rationale for attaching the DPQ sensing unit to the backbone of PMMA was to allow for facile solution processing and the subsequent deposition of this material onto a variety of substrates. Studies designed to probe these features are described below.

Thin films of polymer **4** on glass slides were produced by both drop-cast and spin-cast methods. The resulting materials were tested for their ability to detect HF in solution, as a 'dip stick', as well as in the vapour form

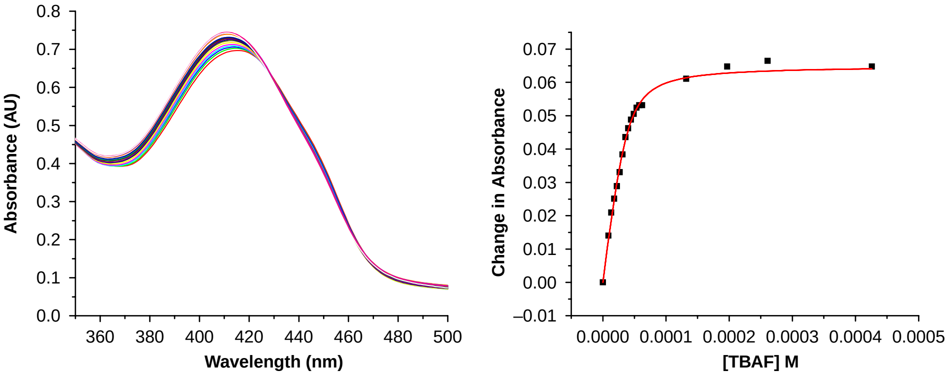


Figure 2. UV–vis spectroscopic titration of copolymer **4** with TBAF in dichloromethane. The spectra on the left show the changes in absorption as a function of concentration, whereas the plot on the right shows the binding isotherm (solid points) and best fit derived from the change in absorption at 410 nm vs. concentration of TBAF.

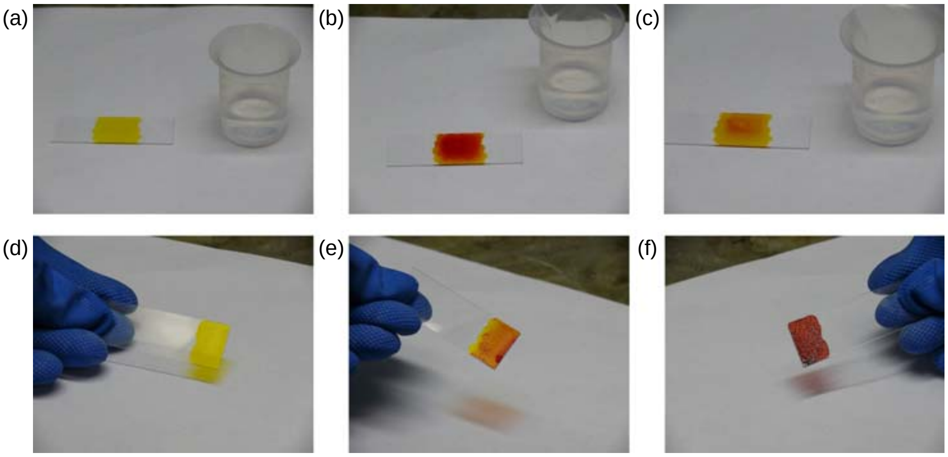


Figure 3. Photographs showing (a) a glass slide coated with copolymer **4**, (b) exposure of the slide to HF vapours and (c) reversibility of the response seen after allowing the slide to stand for 2 min under ambient conditions. Photographs showing (d) a glass slide coated with copolymer **4**, (e) after dipping the slide into 6% w/w HF solution and (f) after dipping the slide into 49% w/w HF solution.

(cf. Figure 3). To our delight, we were able to demonstrate a distinct naked-eye detectable colorimetric change in our polymers upon exposure to vapours of 12.5% HF solutions by weight. Upon exposure, the initially bright yellow thin films shifted to a distinct red colour. Furthermore, it was found that this colour change was readily reversible upon exposure to vapours of concentrated ammonium hydroxide, or slowly over time under ambient conditions. Analogously, performing a ‘dip-stick’ test by submerging the end of the slide covered with the thin film. Into an aqueous solution of HF produced an even stronger response, with the 49% w/w solution eliciting a yellow to purple change. Lowering the concentration to 6% w/w still produced a yellow-to-red naked-eye detectable response on the order of seconds.[2] Although it is appreciated that these tests are qualitative in nature, it is nevertheless to be noted that they provide a clear indication that the systems of this report are useful in the area of HF sensing. They also provide some indication of the limits of detection accessible with this new polymeric material.

As noted above, incorporating the DPQ receptor unit into a PMMA backbone produced a slight increase in binding affinity for fluoride, as well as phosphate, relative to the starting nitro-DPQ. While further experiments will be needed to solidify any conclusion, we tentatively rationalise this on the basis of multivalency. In particular, we propose that the observed enhancement in affinity may be due to the multiple DPQ subunits present within the polymer backbone which may help stabilise a bound fluoride anion. Regardless of the binding interaction, the incorporation of DPQ into a polymeric material may ultimately enable the facile production of thin films capable of rapidly detecting acidic vapours.

Conclusions

In summary, we have designed and synthesised a novel poly(DPQ-co-MMA) copolymer containing DPQ sensing moieties. This copolymer system proved capable of producing a naked-eye detectable signal when exposed to the fluoride ions in organic media. It also displays a higher sensitivity (as inferred from the relevant affinity constants) than the nitro-DPQ precursor from which it is derived. Unlike the latter precursor, the copolymer of this study (**4**) can easily be cast as a thin film on glass slides. The resulting slides proved capable of detecting HF vapours, as inferred from preliminary testing experiments. The versatile immobilisation approach described here is attractive because it may represent a general strategy for incorporating sensing elements into polymeric supports thereby providing improved functional materials useful in, e.g. the sensing of hazardous materials, including HF as described herein.

Acknowledgements

This work was supported by the NIH (grant GM 58907 to J.L.S.) and the Robert A. Welch Foundation (grants no. F-1018 and F-1621 to J.L.S. and C.W.B, respectively).

Notes

1. The ratio of DPQ receptor to MMA was determined to be 1:10. Therefore, the K_a was determined by considering the molecular weight of the host to be the combined molecular weight of the DPQ functionalised subunit plus 10 MMA subunits. The effective concentration of the host solution in dichloromethane used for the UV–vis titrations and associated calculations was then determined using this combined molecular weight. The binding data were then fit as one fluoride ion binding to one effective (or combined) DPQ receptor unit.

2. Similar behaviour was observed with other concentrated acids, such as trifluoroacetic acid and concentrated hydrochloric acid vapours, though to a lesser extent than HF.

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