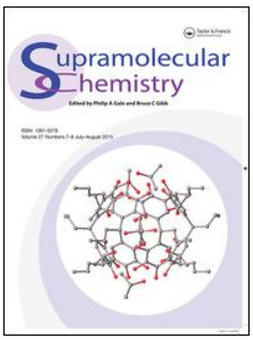

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S. Byrne & K. M. Mullen

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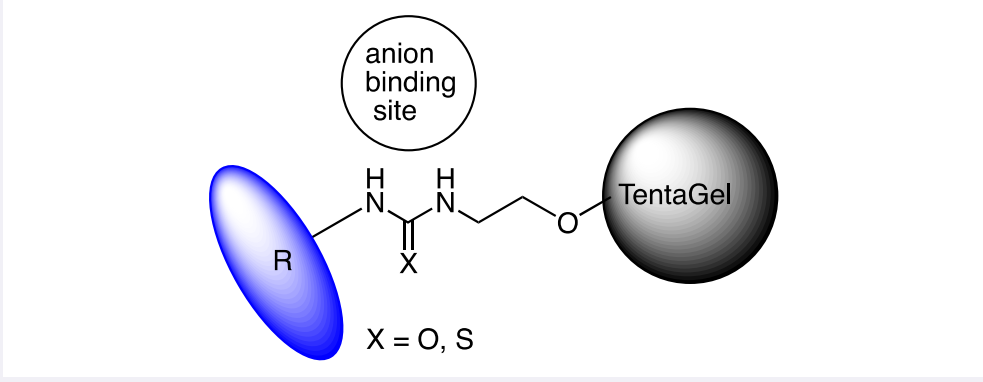
Urea and thiourea based anion receptors in solution and on polymer supports

S. Byrne and K. M. Mullen

School of Chemistry, Physics and Mechanical Engineering, Queensland University of Technology, Brisbane, Australia

ABSTRACT

Herein we report the development of a new series of surface bound anion sensors exploiting the urea or thiourea motif capable of binding anions through hydrogen bonding interactions. The use of high resolution magic angle spinning ^{1}H NMR allows the direct comparison of the anion binding properties of these receptors in solution versus those tethered to polymer resins. Some intramolecular hydrogen bonding and solvent effects were observed at the solution:surface interface however in general the anion binding properties of the polymer bound urea and thiourea receptors were maintained.



The development of a new series of surface bound anion sensors exploiting the urea or thiourea motif capable of binding anions is reported. The use of high resolution magic angle spinning ^{1}H NMR allows the direct comparison of the anion binding properties of these receptors in solution versus those tethered to polymer resins.

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Anion receptors; supramolecular chemistry; HR MAS NMR; hydrogen bonding

Introduction

Research into the development of molecular receptors that accurately and selectively detect the presence of negatively charged species, or anions, has grown rapidly. This is largely due to the essential role such negatively charged species have on a range of environmentally, chemically and biologically important processes becoming more apparent (*1*). The overall objective of this work is the development of a new range of functionalised surfaces capable of sensing anions in a step towards the development of functional anion sensing devices.

The design of anion receptors is challenging owing in part to their relatively low charge density (as compared to their isoelectronic cation counterparts), their pH dependence and large free energies of solvation, which need to be overcome when binding anions in competitive solvent environments (*2*). Supramolecular chemists have successfully designed and synthesised numerous acyclic, macrocyclic and interlocked anion receptors capable of binding anions by taking advantage of the coorperative effect of multiple ion–ion, ion–dipole, hydrogen bonding, or π-anion intermolecular interactions (*1f, 3*). Initial work was dominated by the use of electrostatic interactions to bind anions to a variety of charged receptors incorporating ammonium (*4*), imidizolium (*5*), guanidinium (*6*), thiouronium (*7*) and more recently triazolium (*8*) motifs. However given the ease of synthesis and handling of neutral receptors, and when strategically positioned within receptors, modern examples of neutral systems have been found to bind anions with the same strength and selectivity as many charged systems (*9*).

CONTACT K. M. Mullen kathleen.mullen@qut.edu.au
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Since the first reports of anion binding to urea derivatives were made by Wilcox et al. in 1992 (*10*), substantial research into the anion binding properties of (thio)urea derivatives has been done by Gunnlaugsson (*11*), Gale (*12*), Fabbrizzi (*13*) and many others (*14*). The urea motif which consists of two parallel NH groups either side of a carbonyl in a planar topology, is particularly effective in binding trigonal planar anions such as carboxylates or oxoanions (*15*). The synthetic ease at which they can be incorporated into more complex structures is evident in their use for a range of applications not only in anion sensing but also in transmembrane transportation of anions (*16*), as well as in the formation of self-assembled cages (*17*).

Whilst there has been much work in the development of molecular receptors capable of sensing molecular guests including anions in solution, it can be argued that in order for these systems to be integrated into functional sensory devices, they need to be incorporated into solid materials or deposited onto solid surfaces. To date there have been very few reported examples of anion receptors or sensors on surfaces (*18*). This has been attributed not just to challenging surface attachment chemistry but also to characterisation difficulties which can limit the detailed analysis that is otherwise possible with solution analogues. TentaGel polymer resins are particularly useful surfaces for this work given the number of differently functionalised TentaGel resins that are commercially available, and perhaps more importantly the fact that they can be easily characterised using ^{1}H High Resolution Magic Angle Spinning (HR MAS) NMR (*19*). This ability to directly compare the binding of anions on surfaces with solution analogues is vital as previous studies have established that the kinetic and thermodynamic factors that underpin molecular interactions in supramolecular systems are not always directly translated from solution, to the solution:surface interface (*19f, 20*).

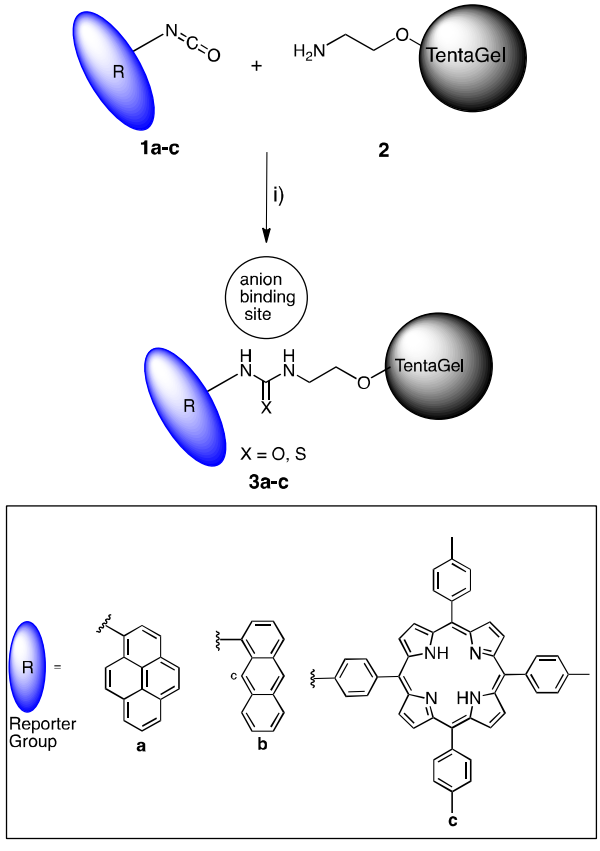
The work outlined here describes the development of a range of urea and thiourea based anion sensors both in solution and attached to polymer TentaGel resins (see Scheme 1). The initial synthetic strategy incorporates anthracene, pyrene or porphyrin sensing motifs to translate the anion binding at the urea receptor into an optical response. TentaGel-NH_2 resins were chosen as the solid support, and in a concerted synthetic effort the urea bond forming reaction is also used for the surface attachment. Full characterisation of the resulting functionalised resins was performed using ^{1}H HR MAS NMR.

Results and discussion

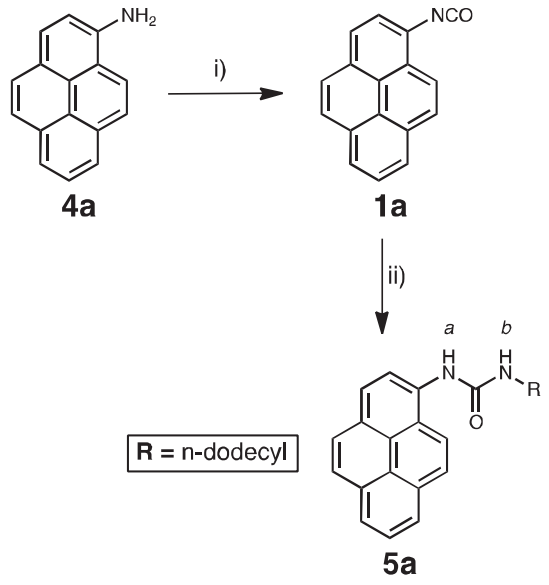
Synthesis and anion binding properties of solution based urea anion receptors

The synthesis of a series of solution based model anion sensors was initially undertaken so that future comparisons between the binding properties of urea based anion receptors in solution versus those attached to polymer resins could be made (see Scheme 2, Scheme S1 and Scheme S2). While 1-aminopyrene **4a** and 1-aminoanthracene **4b** were commercially available, the porphyrin amine **4c** was prepared by adapting Lindsey's salt/BF_3 co-catalytic porphyrin reaction procedures (*21*). Each of these amines was then reacted with triphosgene to produce the corresponding isocyanates **1a–c**, which due to their high reactivity, were filtered and used immediately in the next step without further purification. The unpurified isocyanate products were then reacted with n-dodecylamine to produce the pyrene, anthracene and porphyrin urea receptors **5a–c** in reasonable yields.

After synthesising a range of soluble urea functionalised fluorophores, the potential of these compounds as anion receptors was investigated. Initially the binding of chloride to the pyrene urea receptor **5a** in $CDCl_3$ was examined by ^{1}H NMR titration experiments. As shown in Figure 1, upon addition of one equivalent of TBA Cl to the pyrene urea **5a** a significant downfield shift of both urea protons a and b (Δδ 1.21 and 1.33 ppm, respectively) was observed, indicative of anion binding. Further titration experiments were then carried out with other anions (Br^-, I^-, AcO^-,



Scheme 1. (Colour online) Synthesis of the target surface attached urea receptors **3a–c**. Reagents and conditions: (i) CH_2Cl_2, rt, 7 days.



Scheme 2. Synthesis of the pyrene urea receptor **5a**. Reagents and conditions: (i) triphosgene, Et_3N, toluene, 80 °C, 5 h; (ii) n-dodecylamine, CH_2Cl_2, rt, 48 h.

$H_2PO_4^-$) and the respective 1:1 binding constants were calculated using WinEQNMR (see Figure S1 and Table 1). Similar downfield shifts in the urea protons were observed during anion binding titrations with the porphyrin receptor **5c** in $CDCl_3$ indicative of anion binding (see Figure S2 and Table 1).

However, much stronger anion binding was observed when the titrations were repeated in acetone-d_6 (*22*). Interestingly, prior to any anion addition, the chemical shifts of the urea protons a and b were found to have a significant downfield shift in acetone-d_6 when compared to the same spectrum in $CDCl_3$, presumably due to hydrogen bonding interactions between the urea moiety and the solvent acetone. The addition of TBA Cl to a solution of anthracene urea **5b** in acetone-d_6 resulted in significant downfield shifts of both urea protons a and b (Δδ 1.76 and 2.17 ppm, respectively), indicative of anion binding (Figure 2). Similar downfield shifts were observed upon the addition of other anions (Br^-, I^-, AcO^-) to both the porphyrin and anthracene receptors and the resulting anion binding affinities calculated using WinEQNMR can be seen in Table 1.

Two important observations were noted. Firstly the calculated association constants are significantly higher in acetone-d_6 as compared to $CDCl_3$. This is perhaps unsurprising given the competition between the neutral receptor and the ion-pairing of the tetrabutylammonium cation in non-polar solvents. Secondly, the binding of chloride anions to the porphyrin and anthracene receptors was stronger than for acetate anions. Significant shifts of the neighbouring anthracene proton c were observed upon additions of chloride and acetate (Δδ 1.454 and 1.047 ppm, respectively) indicative of complimentary C–H binding, however these shifts were not as pronounced with the addition of acetate, suggesting that secondary halide -π interactions are also contributing to this deviation from typical anion binding trends.

Fluorescence studies were then carried out to determine sensing potential of receptors **5a–c**. Unfortunately photodegradation problems were encountered for the pyrene and anthracene receptors **5a** and **5b**, as evidenced by a linear decrease in fluorescence emission as a function of the number of scans (see Figure S3). Whilst the photostability of the porphyrin urea receptor **5c** was higher, addition of anions did not result in significant changes in the fluorescence spectrum.

Synthesis and anion binding properties of solution based thiourea anion receptors

In an effort to improve the strength of anion binding from that observed for the urea receptors **5a–c** an analogous series of thiourea receptors were then prepared. Given the lower pKa of thioureas compared to ureas, e.g. 18.7 for diphenylurea and 13.4 for diphenylthiourea (*23*), stonger anion binding is expected. The synthesis of thioureas is similar to that for ureas, with the difference being the preparation of an isothiocyanate instead of the isocyanate.

Initial work used the thiophosgene derivative, bis(1-benzotriazolyl)methanethione **6** (*24*) to prepare the target isothiocyanates **7a–c**. Reaction of 1-(trimethylsilyl)benzotriazole and thiophosgene in CH_2Cl_2 produced bis(1-benzotriazolyl)methanethione in 90% yield. This thiophosgene derivative was then reacted with amine derivatives **4a–c** to give the desired isothiocyanates **7a–c** in high yields (75–98%). Unlike the corresponding isocyanates these were stable enough to be purified by column chromatography. These isothiocyanates **7a–c** were then reacted with dodecylamine to give the desired thiourea receptors **8a–c** (Scheme 3).

With the thiourea compounds prepared, the anion binding properties of this series were investigated using ^{1}H NMR titration experiments following the same protocols used for the urea compounds. No significant binding of anions to the pyrene urea receptor **8a** was observed in $CDCl_3$ (see Figure S4). Unfortunately solubility issues prevented the anion binding properties of this thiourea receptor to be examined in different solvents. Anion binding studies were then carried out for the anthracene **8b** and porphyrin thiourea receptors **8c** in acetone-d_6 as the equivalent urea receptors discussed above showed higher anion binding in this solvent. Upon addition of one equivalent of TBA Cl to the anthracene thiourea **8b** significant downfield shifts of the thiourea protons a and b were observed (Δδ1.53 and 1.96 ppm, respectively) along with

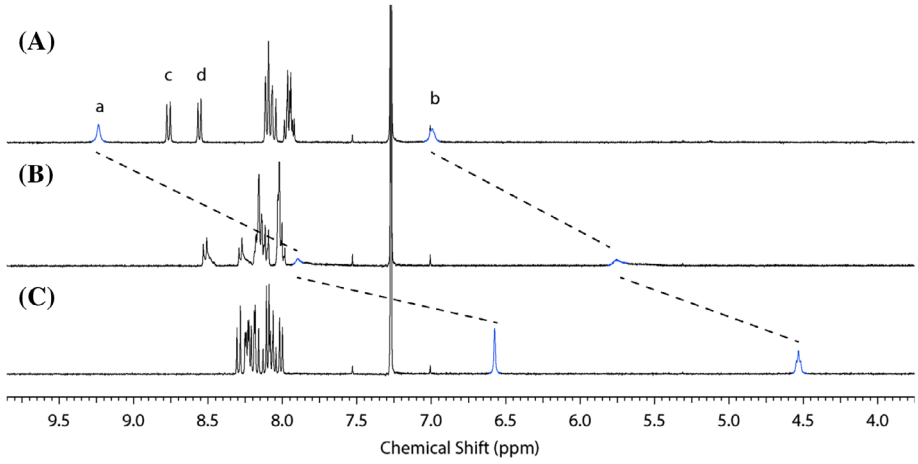


Figure 1. (Colour online) ^{1}H NMR spectrum in $CDCl_3$ of: (A) pyrene dodecyl urea **5a** with 5 equivalents of TBA Cl; (B) pyrene dodecyl urea **5a** with 1 equivalent of TBA Cl; (C) pyrene dodecyl urea **5a.**

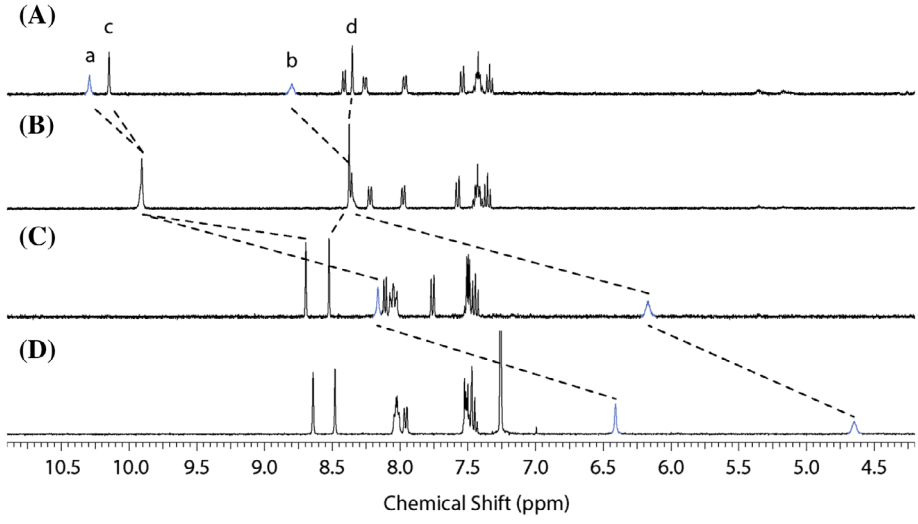
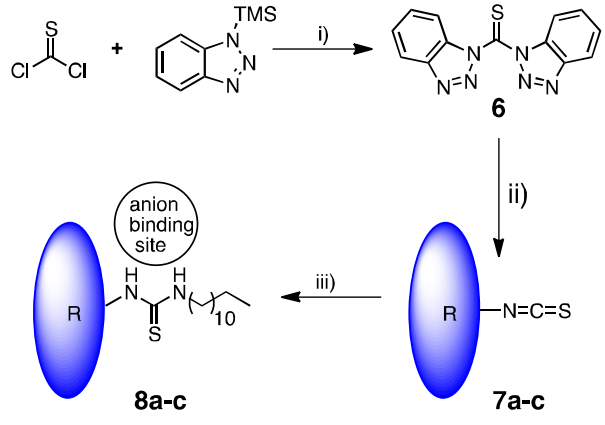


Figure 2. (Colour online) ^{1}H NMR spectrum in acetone-d_6 of: (A) anthracene dodecyl urea **5b** with 5 equivalents of TBA Cl; (B) anthracene dodecyl urea **5b** with 1 equivalent of TBA Cl; (C) anthracene dodecyl urea **5b**; (D) anthracene dodecyl urea **5b** in $CDCl_3$.

Table 1. Calculated association constants (K_a M^{-1}) for the binding of various anions to urea receptors **5a–c** at 293 K.

Anion	Pyrene **5a** ($CDCl_3$)	Porphyrin **5c** ($CDCl_3$)	Anthracene **5b** (acetone-d_6)	Porphyrin **5c** (acetone-d_6)
Chloride	450	810	12,000	9300
Bromide	160	370	1090	1600
Iodide	50	170	67	140
Acetate	790	1150	2440	6600
Dihydrogen phosphate	550	590	–	–

smaller shifts of the neighbouring protons on the anthracene group (see Figure 3). Similar downfield shifts were observed upon addition of a variety of anions (Br^-, I^-, AcO^-) for both the anthracene and porphyrin thiourea receptors **8b** and **8c** and the resulting anion binding affinities and



Scheme 3. (Colour online) Synthesis of the target thiourea anion receptors **8a–c**. Reagents and conditions: (i) CH_2Cl_2, rt, 2 h; (ii) CH_2Cl_2, rt, 12 h; (iii) CH_2Cl_2, rt, 16 h.

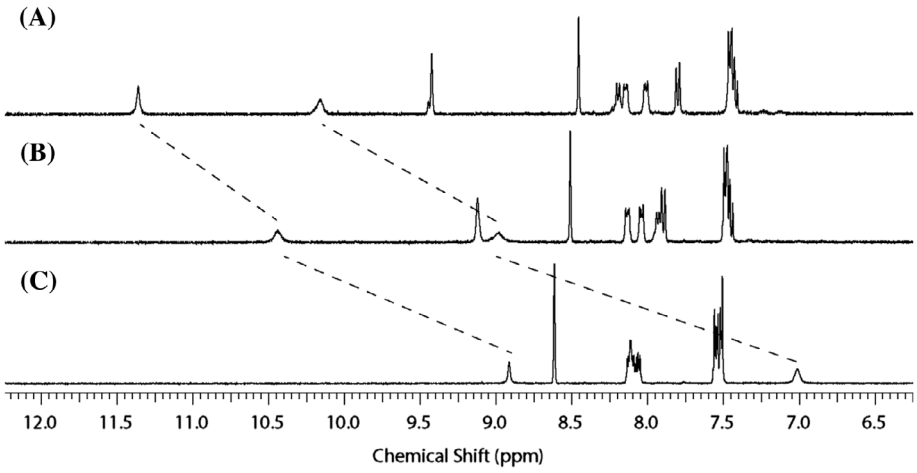


Figure 3. ^{1}H NMR spectrum in Acetone-d_6 of: (A) anthracene thiourea **8b** with 5 equivalents of TBA Cl; (B) anthracene thiourea **8b** with 1 equivalent of TBA Cl; (C) anthracene thiourea **8b**.

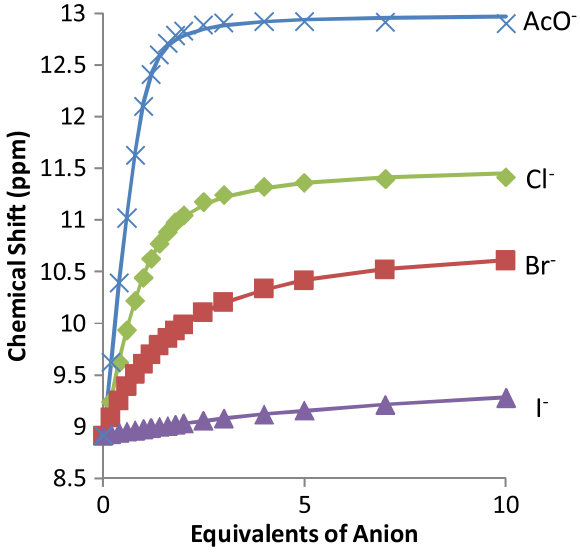


Figure 4. (Colour online) Change in the chemical shift of thiourea proton a upon addition of anions to a 2 mM solution of anthracene thiourea **8b** in acetone-d_6 at 293 K.
Notes: Symbols represent experimental data points; continuous lines represent calculated curves. All anions were added as their TBA salts.

Table 2. Calculated association constants (K_aM^{-1}) for the binding of various anions to thiourea receptors **8b** and **8c** in acetone-d_6 at 293 K.

Anion	Anthracene thiourea **8b**	Porphyrin thiourea **8c**
Chloride	1900	23,000
Bromide	430	2920
Iodide	31	160
Acetate	9200	38,700

Note: Errors < 25%.

associated errors were calculated using WinEQNMR (see Figure 4, and S5 and Table 2) (*25*). As expected a significant increase in the binding affinity of the thiourea receptors

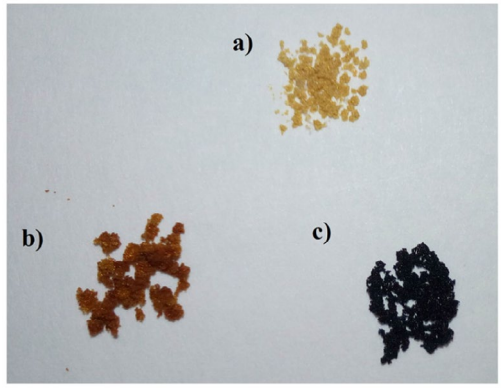
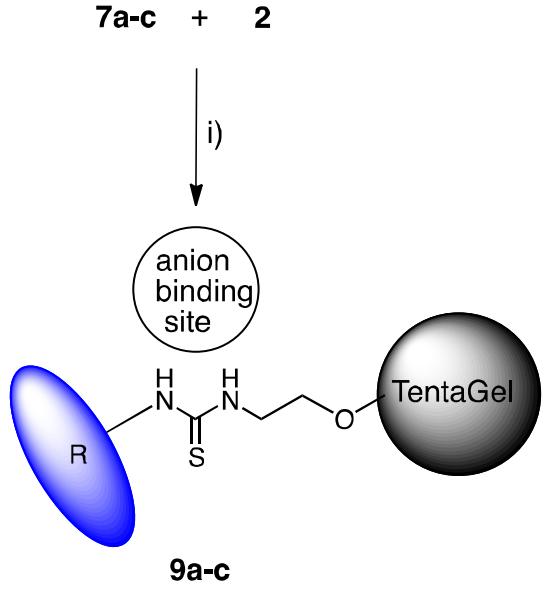


Figure 5. (Colour online) Qualitative evidence of bead functionalisation of (a) **3a**, (b) **3b**, and (c) **3c**.



Scheme 4. (Colour online) Preparation of surface attached thiourea anion receptors **9a–c**. Reagents and conditions: (i) CH_2Cl_2, rt, 7 d.

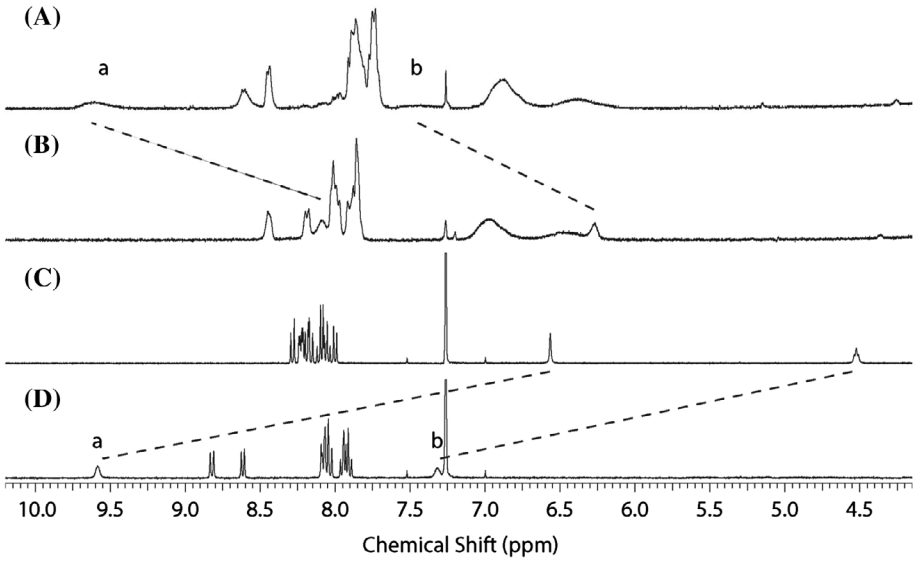


Figure 6. HR MAS ^{1}H NMR spectra in $CDCl_3$ of: (A) pyrene urea functionalised TentaGel resins **3a** plus TBA Cl, with 32 CPMG loops; (B) pyrene urea functionalised TentaGel resins **3a**. ^{1}H NMR spectra in $CDCl_3$ of: (C) pyrene urea **3a**; (D) pyrene urea **3a** plus 10 equivalents TBA Cl.

Table 3. Change in chemical shift of urea NH proton a of the surface and solution anion receptors upon addition of an excess (10 equivalents for solution, at least 10 equivalents for surface) of various anions.

	Pyrene **3a** ($CDCl_3$)		Anthracene **3b** (Acetone-d_6)		Porphyrin **3c** (Acetone-d_6)	
	Solution	Surface	Solution	Surface	Solution	Surface
Chloride	3.02	1.53	2.15	1.97	2.70	2.41
Bromide	2.20	0.59	1.45	1.16	2.01	1.40
Iodide	1.18	0.13 *	0.47	0.33	0.88	0.27
Acetate	4.08	2.81	2.79	2.68	3.93	3.87

*Shift estimated due to broadening and overlapping pyrene resonance.

towards anions as compared to the urea receptors were observed.

Synthesis and anion binding properties of surface bound urea and thiourea anion receptors

Having established the anion binding properties of a range of solution based urea and thiourea receptors the attachment of these receptors to solid supports was investigated. We have previously demonstrated that ^{1}H HR MAS NMR is an invaluable technique in monitoring the anion binding properties of receptors attached to polymer resins (*26*). Furthermore we have recently shown that surface functionalization can be extended to resins with lower functional group loading (0.24 mmol/g) (*26a*). The commercial availability of such resins with a far greater diversity of end group functionalization (i.e. amines, carboxylic acids, thiols) than the higher loading resins opens up a wide range in the attachment chemistry that could be used in the development of future polymer bound anion receptors. It was proposed that commercially available TentaGel-NH_2 resins could be reacted with the previously prepared isocyanate compounds **1a–c** to produce the target surface attached urea anion receptors. In this design, synthetic efficiencies are achieved by using the surface attachment chemistry as the method to also introduce the urea anion binding receptor to the system.

To this end urea functionalised resins **3a–c** were obtained by reacting freshly prepared pyrene, anthracene or porphyrin isocyanate **1a–c** with TentaGel-NH_2 resins **2**. Whereas the amine functionalised beads are colourless, the pyrene, anthracene and porphyrin beads **3a–c** are yellow, orange and purple, respectively, indicating at least qualitatively successful formation of the surface bound urea receptors (see Figure 5). IR analysis of the urea functionalised resins **3a–c** showed the presence of additional absorption bands between 1625 and 1645 cm^{-1} attributed to the distinctive urea C = O stretch, C–N–H bend frequencies between 1560 and 1530 cm^{-1} as well as a more prominent NH signal at 3500 cm^{-1} when compared to the initial TentaGel-NH_2 resins (see Figure S6–S8) (*27*).

Thiourea functionalised TentaGel resins were prepared by reaction of the isothiocyanate functionalised reporter groups **7a–c** with the TentaGel-NH_2 resins **2** using the same protocols as were used for the urea resins **3a–c** (see Scheme 4). These resins exhibited the same changes in colouration as was seen for the urea resins and additional qualitative evidence was again provided by IR spectroscopy, with the appearance of a more prominent NH signal at 3500 cm^{-1}, unfortunately any contribution of the C = S absorptions was not visible due to overlap with the absorptions of the resin's polymer core (see Figure S9–S11).

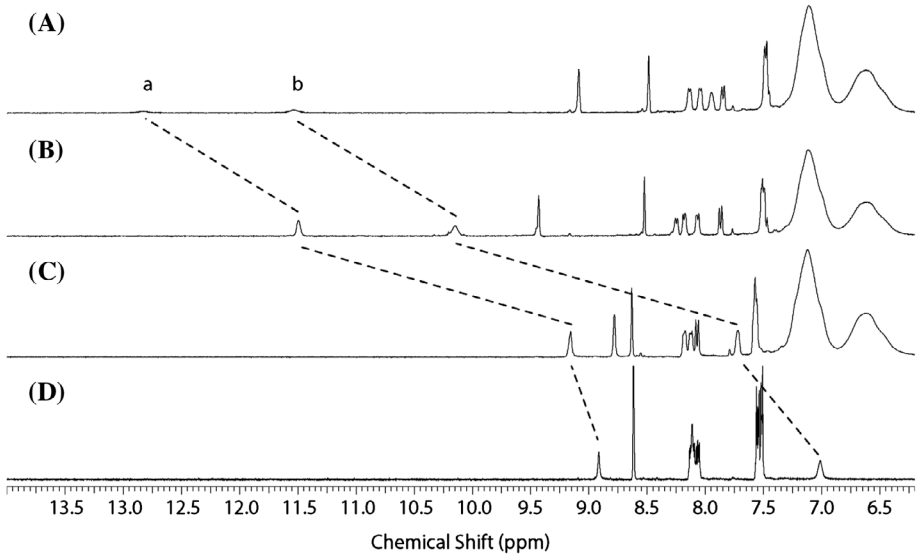


Figure 7. ^{1}H HR MAS NMR spectra in acetone-d_6, of: (A) anthracene thiourea functionalised TentaGel resins **9b** plus TBA acetate with 8 CPMG loops; (B) anthracene thiourea functionalised TentaGel resins **9b** plus TBACl with 8 CPMG loops; (C) anthracene thiourea functionalised TentaGel resins **9b** with 8 CPMG loops; (D) ^{1}H NMR spectrum in acetone-d_6 of anthracene thiourea **8b**.

Table 4. Change in chemical shift of thiourea NH proton a of the surface and solution anion receptors upon addition of an excess (10 equivalents for solution, at least 10 equivalents for surface) of various anions.

	Anthracene thiourea (acetone-d_6)		Porphyrin thiourea (acetone-d_6)	
	Solution **8b**	Surface **9b**	Solution **8c**	Surface **9c**
Chloride	2.50	1.96	3.00	2.2
Bromide	1.69	1.16	2.28	1.4
Iodide	0.36	0.18	1.06	0.7
Acetate	4.00	3.57	4.26	3.3

Elemental analysis was used on both the urea and thiourea functionalised resins which determined the loading of the various receptors to be between 0.1 and 0.18 mmol/g which is between 35 and 65% of the loading quoted by the manufacturer (see Table S1).

^{1}H HR MAS NMR analysis provided more conclusive evidence for the successful surface attachment of the urea and thiourea receptors **3a–c** and **9a–c**. For the pyrene urea functionalised resins **3a**, distinctive peaks for the urea protons a and b can be seen at 8.18 and 6.37 ppm, respectively along with the various peaks associated with the pyrene protons between 8.55 and 7.96 ppm, indicative of successful bead functionalization (see Figure 6). However, when compared to the solution based pyrene urea receptor **5a** there is a noticeable difference in the chemical shift of the urea protons a and b, Δδ 1.53 and 1.77, respectively. This is thought to be primarily due to the close proximity of the polyethylene glycol chains of the resins leading to intramolecular hydrogen bonding between the urea N–H protons and the oxygen of the polyethylene glycol. As observed for the solution analogue **5a**, addition of anions to the pyrene urea functionalised resin **3a** resulted in significant downfield shifts in the urea N–H protons a and b with the greatest change seen with upon addition of acetate (see Figure 6 and Table 3). Similar downfield shifts in the urea protons a and b were observed during anion binding titrations with the surface bound anthracene and porphyrin urea receptors **3b** and **3c** with the largest change in chemical shift being observed upon addition of acetate (Δδ2.81 for **3a**, Δδ2.68 for **3b** and Δδ3.87 for **3c**; see Figure S12 and S13 and Table 3).

Although practical considerations prevent quantitative anion NMR titrations for the resins, the magnitude of these changes in chemical shift upon anion addition can be at least qualitatively compared to the solution analogues **5a–c**. In general good agreement between the change in chemical shift upon anion addition for the surface bound porphyrin and anthracene receptors as compared to the solution analogues was observed. For the pyrene functionalised beads **3a** however, the change in chemical shift upon addition of anions was lower than that observed for the solution analogue **5a**. This is not due to weakened anion interaction but rather is a result of the fact that when compared to the solution based pyrene urea receptor **5a** there is a noticeable difference seen in the chemical shift of the urea protons a and b for **3a** as discussed above. Overall these results show that attachment of urea based anion binding systems to TentaGel resins is possible with minimal impact on anion binding properties.

Similar results were also obtained for the thiourea functionalised resins **9a–c**, as shown in Figure 7, the ^{1}H NMR spectrum of the anthracene thiourea beads **9b** clearly shows two distinctive peaks for the thiourea NH protons a and b (*δ* 9.18 and 7.73 ppm, respectively) as well as the

various resonances of the anthracene moiety between δ 7.56 and 8.78 ppm, indicating successful bead functionalization. As observed for solution analogue **8b**, addition of TBA chloride to the anthracene thiourea beads **9b** in acetone-d_6 resulted in large downfield shifts for both of the thiourea NH protons a and b ($\Delta\delta$ 2.33 and 2.41, respectively, see Figure 7). Similar downfield shifts were observed upon addition of an excess of a variety of anions to the anthracene and porphyrin thiourea functionalised resins **9b–c** (see Table 4). Although practical considerations prevent a quantitative analysis of anion binding strength, the magnitude of the changes in chemical shift upon binding is similar to that observed for solution analogues (see Table 4) (*28*).

As shown in Table 4 the change in chemical shift upon addition of an excess of anions to the surface bound thiourea receptors **9b** and **9c** is slightly lower than the change observed upon addition of 10 equivalents to the solution analogues **8b** and **8c**. This difference can be attributed to surface effects, as the initial position of the thiourea NH proton a and b is also shifted downfield when compared to the solution analogues (for **8b** proton a $\Delta\delta$ 0.24 ppm and proton b $\Delta\delta$ 0.71 ppm).

Conclusions

A series of solution based and surface attached urea and thiourea anion receptors incorporating a range of fluorescent reporter groups has been successfully prepared and their anion binding properties analysed. For the urea receptors **5a–c**, the strength of anion association was significantly higher in acetone-d_6 when compared to $CDCl_3$, with the highest association constants with these receptors being calculated upon the addition of chloride anions. Successful functionalization of TentaGel resins with urea anion receptors was achieved and ^{1}H HR MAS NMR analysis allowed the anion binding potential of these resins to be qualitatively assessed. In contrast to the solution analogues, some intramolecular and solvent effects for the surface attached urea receptors **3a–c** were observed. However in general the changes in chemical shift of the urea protons upon addition of anions was comparable to solution analogues indicating the anion binding properties of these receptors is maintained at the solution:surface interface. The 'reporting' of this anion binding through changes in fluorescence was not observed largely due to photodegredation issues. In an attempt to increase the strength of anion binding, a second series of thiourea functionalised resins and associated solution analogues were synthesised. This was successful with increased anion binding affinities calculated for the thiourea receptors **8b–c**, with the exception of halides for **8b**, however in this series acetate was found to have the higher binding affinity. Again ^{1}H HR MAS NMR analysis of the thiourea functionalised resins demonstrated similar anion binding trends as compared to solution analogues. Two challenges that will be the focus of future work are firstly, the development of better methodology to allow the strength of anion binding interactions on the surface to be quantified, and secondly, the better incorporation of reporter groups into the anion receptor framework to allow communication of the anion binding event through optical or electrochemical means.

Experimental

General remarks

Unless otherwise stated, reagents were purchased from commercial sources and used without further purification. All solvents were dried before use over type 3 Å or 4 Å molecular sieves according to standard procedures. Triethylamine was dried over KOH. Silica gel column chromatography was carried out using Merck silica gel 60 (grade 9835, 230–400 mesh). Analytical TLC was carried out on Merck silica gel F_{254} precoated aluminium sheets. Solution NMR spectra were recorded on a Bruker Avance or Varian INOVA 400 MHz spectrometer and referenced to the relevant solvent peak. TentaGel™ S–NH2 resins were purchased from Peptides International with a quoted loading of 0.27 mmolg^{-1} and a particle size of approximately 90 µm. HR MAS NMR Spectra were acquired on a Bruker Avance 400 spectrometer at room temperature using a Bruker HR MAS probe. Rotors containing a suspension of the beads in $CDCl_3$ or Acetone-d_6 were spun at 4 or 5 kHz. One-dimensional HR MAS spectra were obtained with 64 scans. Unless otherwise stated, the CPMG pulse sequence contained 0, 32 or 128 π-pulses with a repetition time of 30 ms. ESI high-resolution mass spectra were obtained using a QTOF LC mass spectrometer which utilised electrospray ionization. Melting points were measured on a variable-temperature apparatus by the capillary method and are uncorrected. IR spectra were obtained using a Thermo Nicolet Nexus 870 esp spectrometer at 4 cm^{-1} resolution using 64 scan averaging.

Synthetic procedures

For specific synthetic procedures please see the supporting information.

General procedure for the synthesis of urea receptors 5a–c

Amine **4a**, **4b** or **4c** (1 equiv.) and triphosgene (0.5 equiv) dissolved in dry, degassed toluene (50 mL) under argon. Triethylamine (0.1 mL) was then added and reaction heated to 70 °C and left to stir for five hours. The reaction mixture

was allowed to cool, filtered and the solvent removed. The crude isocyanate was then dissolved in dry CH_2Cl_2 under argon. Dodecylamine (1.5 equiv) was then added and reaction stirred for 48 h. The solvent was evaporated and the crude product purified by silica gel column to give the pure products in 36–82% yield.

General procedure for the synthesis of urea functionalised Tentagel resins 3a–c

To a flask containing TentaGel-NH_2 (100 mg, 0.27 mmol/g loading) suspended in dry CH_2Cl_2 (10 mL) was added freshly prepared isocyanate **1a**, **1b** or **1c** (2.7 mmol). The reaction mixture was then left under Argon for one week with occasional gentle stirring. The TentaGel resins were then filtered and the resulting beads were washed thoroughly with CH_2Cl_2 and hexane (5 × 5 mL sequentially), followed by acetone (5 mL), water (5 mL), acetone (5 mL) and CH_2Cl_2 (5 mL). The resulting beads were then allowed to air dry.

General procedure for the synthesis of isothiocyanates 7a–c

Amine **4a**, **4b** or **4c** (1 equiv.) was dissolved in dry, degassed CH_2Cl_2 (10 mL). Bis(1-benzotriazolyl)methanethione **6** (1 equiv.) added and reaction was stirred at room temperature for two days. After this time the solvent was evaporated and the crude product was purified by silica gel column to give the isothiocyanates in 75–98% yield.

General procedure for the synthesis of thioureas 8a–c

Freshly isolated isothiocyanate **7a**, **7b** or **7c** (1 equiv.) and dodecylamine (1.5 equiv.) were dissolved in dry CH_2Cl_2 (25 mL) and the resulting reaction mixture was stirred at room temperature overnight. After this time the solvent was removed in vacuo and the crude residue purified by silica gel column to give the pure product in 29–99% yield.

General procedure for the synthesis of thiourea functionalised Tentagel resins 9a–c

To a flask containing TentaGel-NH_2 (100 mg, 0.27 mmol/g loading) was added isothiocyanate **7a**, **7b** or **7c** dissolved in CH_2Cl_2 (10 mL). The reaction was left for one week with occasional gentle stirring. The TentaGel resins were then filtered from the reaction mixture and washed thoroughly with CH_2Cl_2 and hexane (5 × 5 mL sequentially), followed by acetone (5 mL), water (5 mL), acetone (5 mL) and CH_2Cl_2 (5 mL). The resulting beads were then allowed to air dry.

Disclosure statement

No potential conflict of interest was reported by the authors.

ORCID

K. M. Mullen http://orcid.org/0000-0003-4480-0985

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