Fluorescent sensing of anions using a bis-quinoxaline amidothiourea based supramolecular cleft; an example of an anion induced deprotonation event

Rebecca M. Duke, Thorfinnur Gunnlaugsson

PII: S0040-4039(10)01386-9
DOI: 10.1016/j.tetlet.2010.07.168
Reference: TETL 38206

To appear in: *Tetrahedron Letters*

Received Date: 8 May 2010
Revised Date: 16 July 2010
Accepted Date: 30 July 2010

Please cite this article as: Duke, R.M., Gunnlaugsson, T., Fluorescent sensing of anions using a bis-quinoxaline amidothiourea based supramolecular cleft; an example of an anion induced deprotonation event, *Tetrahedron Letters* (2010), doi: 10.1016/j.tetlet.2010.07.168

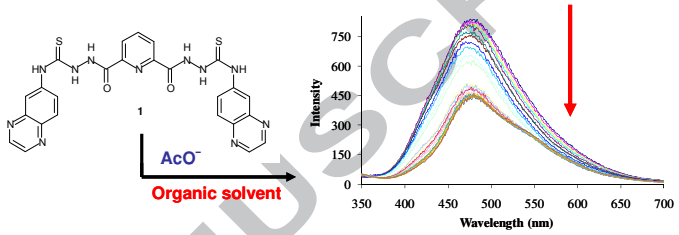
Graphical Abstract

To create your abstract, type over the instructions in the template box below.
Fonts or abstract dimensions should not be changed or altered.

Fluorescent sensing of anions using a bis-quinoxaline amido-thiourea based supramolecular cleft; an example of an anion induced deprotonation event

Leave this area blank for abstract info.

Rebecca M. Duke, Thorfinnur Gunnlaugsson



Pergamon

TETRAHEDRON
LETTERS

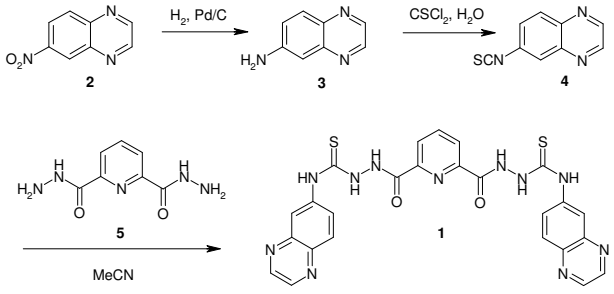
Fluorescent sensing of anions using a bis-quinoxaline amidothiourea based supramolecular cleft; an example of an anion induced deprotonation event

Rebecca M. Duke, Thorfinnur Gunnlaugsson*

School of Chemistry, Centre for Synthesis and Chemical Biology, Trinity College Dublin, Dublin 2, Ireland.

Abstract— The quinoxaline **1**, possessing a 2,6-pyridyl-based amidothiourea moiety, with the view of forming a pre-organised molecular cleft, was developed as a fluorescent anion sensor. The sensing ability of **1** was evaluated in organic solution where both the ground and the excited state of **1** was affected upon recognition of anions such as acetate [as tetrabutylammonium salt (TBAAc) solution] at the amiodothiourea moieties in MeCN. The fluorescence of **1**, with λ_{max} at 477 nm, was, on all occasions quenched, upon anion recognition. Using TBAOH, we also show that the same anion induced changes occurred; demonstrating that for this particular sensor, the anion sensing takes place via a deprotonation mechanism. This anion-induced deprotonation event was further investigated by carrying out ^{1}H NMR titrations on **1**, using both AcO^- and OH^- in DMSO-d_6.

The recognition and sensing of anions using colorimetric or fluorescent/phosphorescent-based sensors has become an active area of research within the field of supramolecular chemistry.[1-4] The use of such anion targeting/binding molecules in medicinal chemistry and biotechnology has also emereged.[5] Such sensors are often based on the use of hydrogen bonding ureas and thioureas,[6] amide,[7] indoles,[8] carbamates,[9] pyrroles and calixpyrroles,[10] and imidazolium-based receptors.[11] The use of a combination of more than one of these recognition moieties also been investigated and shown to give rise to increased anion binding affinity through synergetic action.[12-14] The use of amidourea or amidothiourea receptors has also been used in anion recognition chemistry, particularly by Jiang *et al*.,[15] Gale *et al*.,[16] ourselves[17] and Yang *et al*.,[18] in which such hydrogen bonding donors for use in colorimetric anion sensing were employed. To achieve this, the amidourea and the amidothiourea moieties are usually conjugated onto simple aryl groups, which themselves often possess one or more electron-withdrawing substituents, and usually the anion recognition is *via* a hydrogen bonding interaction when investigated in organic solvents. This gives rise to the formation of internal charge transfer (ICT) based systems, which usually give rise to significant changes in the absorption spectra upon anion sensing, often with striking colour changes that are visible to the naked eye. In addition, this design usually enables the use of fluorescence emission spectroscopy for monitoring the anion recognition event as the ICT excited state of such systems is often not highly emissive.[19] With this in mind, we set out to develop a novel amido-thiourea-based anion sensor which would give rise both to changes in the ground and in the excited states upon anion recognition. Our target **1**, possesses a central pyridyl-dicarboxamide moiety, where each side is conjugated to a quinoxaline fluorophore *via* a thiourea moiety. To the best of our knowledge, this is the first example of such a design, as well as the first time that this fluorophore has been employed in fluorescence anion



Scheme 1. Synthesis of the quinoxaline fluorescent anion sensor **1**.

* Corresponding author. Tel.: + 353 1 896 3459; fax: + 353 1 671 2826; e-mail: gunnlaut@tcd.ie.

sensing.[20]

The synthesis of sensor **1** (Scheme 1) was achieved from 6-quinoxaline isothiocyanate (**4**), which is not commercially available, and was synthesized in three steps.[21,22] First, 4-nitrobenzene-1,2-diamine and glyoxal (40%) were heated at reflux in EtOH for three hours, after which the resulting precipitate was isolated by filtration and recrystallised from isopropanol, giving **2** as light brown needles in 70% yield. The nitro group was then reduced using 10% Pd/C with H_2 in MeOH. The crude product was treated with base and extracted with ethyl acetate to give **3** as an orange solid in 73% yield. Compound **3** was then reacted with 1.5 equivalents of thiophosgene ($CSCl_2$) in H_2O for two hours and the resulting orange precipitate was collected by suction filtration and dried in air.[21] The isothiocyanate **4**, was then immediately added to a suspension of **5** in MeCN. The synthesis of **5** has been previously reported[17,19] and involved formation of a diethyl ester from commercially available 2,6-pyridine dicarboxylic acid, which was then treated with hydrazine monohydrate in methanol at room temperature. This resulted in almost immediate precipitation of a white solid, which was filtered and dried in air to give the hydrazide **5**, in 65% yield. A suspension of **4** and **5** was refluxed overnight and the resulting solid isolated by suction filtration, followed by further work-up by refluxing a suspension of **1** in EtOH overnight, followed by hot filtration. This gave sensor **1** as an orange solid in 81% yield.[23]

The ^{1}H NMR spectrum of **1** (400 MHz, DMSO-d_6) is shown in Figure 1. Similar to that seen in our previous work, compound **1** was shown to exist, at room temperature, as a mixture of two (a major and a minor) rotamers in solution (assigned using VT NMR). Moreover, only two N-H signals were observed for **1** in which both of the thiourea protons resonated at 10.32 ppm, and the amide proton appeared further downfield, at 11.38 ppm. The ^{13}C NMR spectrum of **1** also displayed the expected number of resonances while the ES-MS analysis of **1** gave *m/z* = 570.1254 for the $[M+H]^+$ ion. The IR spectrum showed medium broad vibrations at *ca.* 2900 and 3100 cm^{-1}, due to N-H stretches, and strong sharp bands at *ca.* 1700, 1550 and 1450 cm^{-1}, which were assigned to the carbonyl groups, as well as N-H bending.

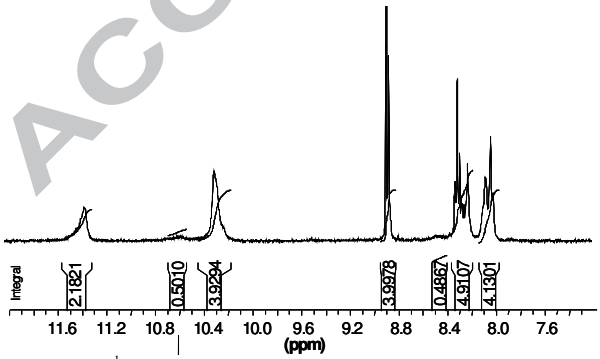


Figure 1. The ^{1}H NMR (400 MHz, DMSO-d_6) spectrum of **1**, showing the aromatic and amido and thiourea protons, and the presence of two, major and minor, rotamers in solution.

The absorption spectrum of **1** exhibited a λ_{max} at 338 nm, assigned to the quinoxaline fluorophore and a shoulder at 260 nm, which we assigned to both the quinoxaline and the pyridyl unit, in 1% DMSO/MeCN solution. Excitation at 338 and 260 nm, respectively, led to long wavelength emissions, centered at 464 and 477 nm, for these two excitation wavelengths, respectively. The ability of **1** to detect various anions was next investigated in this solvent media, monitored using both absorption and fluorescence spectroscopy. Upon titration with AcO^-, an increase was observed in the absorption across the spectrum; accompanied by a bathochromic shift to *ca.* 490 nm, for the long wavelength λ_{max}, Figure 2. These changes were also accompanied with the formation of a single isosbestic point at 255 nm. As shown in the inset to Figure 2, a plateau was reached at two equivalents of AcO^-, indicating that each of

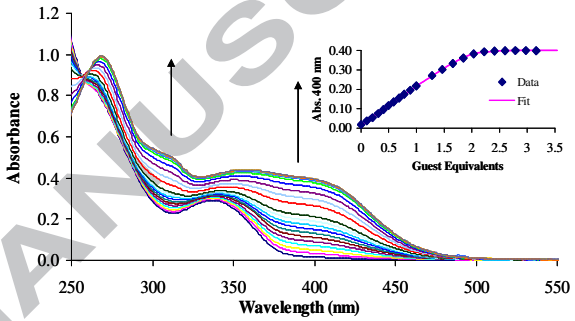


Figure 2 The changes in the absorption spectra of **1** in 1% DMSO in MeCN [2 × 10^{-5} M] upon addition of AcO^- (0 → 3.5 equivalents). Inset, the changes at 400 nm with a 1:2 (host:guest) fit.

the amidothiourea moieties was interacting with the anions, in an overall 1:2 (host:guest) stoichiometry. The changes in the presence of AcO^- were best fitted to a three-component binding model using the non-linear regression analysis programme SPECFIT, the fit being shown as a solid line in the inset in Figure 2. From this fit, we determined two binding constants for the 1:1 and the 1:2 (host:guest) interaction. However, these were the same with $\log K_{1:1}$ = $\log K_{1:2}$ = 6.4 (±0.1). This clearly indicates that both amidothiourea moieties are functioning independently, and from the species distribution diagram, shown in Figure 3, it is clear that both the 1:1 and the 1:2 host:guest

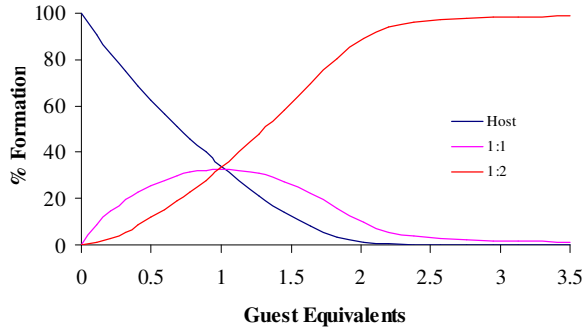


Figure 3. Species distribution diagram of **1** [2×10^{-5} M] upon titration with AcO^- (0 → 3.5 equivalents) in 1% DMSO in MeCN.

stoichiometries are formed simultaneously, and at one equivalent of the anion, a mixture of both the 1:1 and 1:2 host:guest complexes is formed in almost equal amount.

The changes in the fluorescence emission were also monitored during the course of the above anion titration. Excitation at 338 and 262 nm led to the formation of broad emission bands centred at 464 and 477 nm, respectively; where the emission at 477 nm was of a higher relative intensity. Figure 4 shows that the fluorescence emission at 464 nm was quenched by ca. 62% after the addition of two equivalents of AcO^-; with a concomitant bathochromic

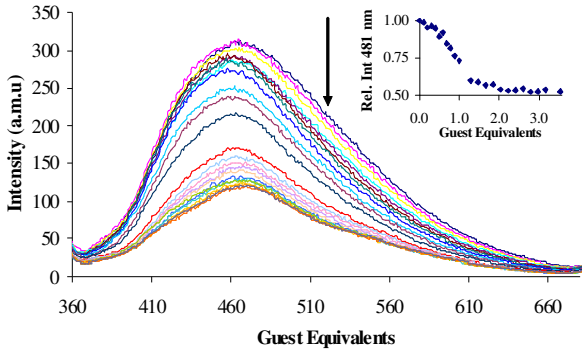


Figure 4. The changes in the emission spectra (λ_{ex} = 338 nm) of **1** [2×10^{-5} M] upon addition of AcO^- (0 → 3.5 equivalents) in 1% DMSO in MeCN. Insert, the relative changes in intensity at 481 nm.

shift of *ca*. 5 nm. It is worth pointing out that only minor quenching was observed after the addition of one equivalent of the anion. Analysis of these changes gave rise to similar binding constants as seen above indicating a strong affinity of **1** for AcO^-. In a similar manner, the fluorescence emission at 477 nm was quenched by 48%, after the addition of *ca.* one equivalent of AcO^-. The emission spectrum also exhibited a change in the shape of its emission band, with the appearance of a slight shoulder around 545 nm. In agreement with that observed in the absorption titrations, a plateau was reached for both excitations upon addition of two equivalents of anion, however, and as shown in the inset to Figure 4, most of the changes occurred from addition of 0→1 equivalents of AcO^-. These results clearly demonstrate that anion sensing information can be obtained from both the ground and the excited state properties of **1**.

Having established that both the absorption and the emission spectra of **1** were affected by AcO^-, we next carried out a ^{1}H NMR anion titration of **1**. The results from the ^{1}H NMR (400 MHz) titrations of **1** with AcO^- in DMSO-d_6 are shown in Figure 5A; the titrations were also carried out in 1% DMSO-d_6:MeCN-d_3 solution. On both occasions, the results were the same; upon binding of AcO^- to **1**, an initial broadening was observed for the resonances assigned to both the N-H and the aromatic protons. However, to our surprise, no measurable up- or downfield shift was observed for the N-H protons, as is commonly seen for such hydrogen bonding donors upon binding to anions. From Figure 5A it is clear that this behaviour exists

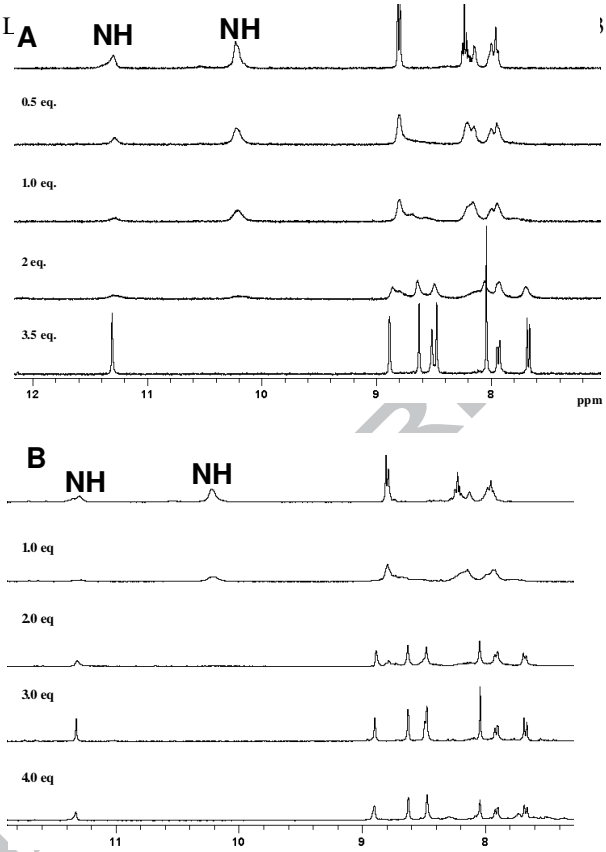


Figure 5. A) ^{1}H NMR (400 MHz, DMSO-d_6) titration of **1** [1×10^{-3} M] with AcO^- upon addition of 0, 1, 2 and 3 equivalents of the anion. **B)** ^{1}H NMR (400 MHz, DMSO-d_6) titration of **1** [3×10^{-3} M] with TBAOH upon the addition of 0, 1, 2, 3 and 4 equivalents of the anion.

up to the addition of two equivalents of the anion. However, after the addition of further equivalents of the anion, the NMR spectra become significantly affected; all the aromatic resonances are quite sharp, and the N-H proton assigned to the amide part is still visible. The results from these titrations, suggest that the thiourea N-H protons are deprotonated over the course of the titration.[24] Consequently, we repeated the titration using OH^-, with the view of confirming if indeed such a deprotonation did occur for **1**. The results from these anion titrations are shown in Figure 5B and demonstrate great similarity to that observed for the titration with AcO^-, *i.e.* initial broadening for both the N-H and the aromatic protons, followed by sharpening of the amido N-H and the aromatic protons after the addition of two equivalents of OH^-. Moreover, the final spectrum observed for both AcO^- and OH^-, seems to indicate the formation of the same species in solution. From these results it can deduced that both anions are functioning here as a base, giving rise to the deprotonation upon interaction with **1**.

With this in mind, we carried out an absorption titration of **1** using TBAOH, under identical conditions to those described above. The results observed in the UV-Vis absorption spectra of **1** are shown in Figure 6, and again demonstrate that the deprotonation event has a significant effect upon the overall absorption spectra, which is at the end-point, very similar to that observed for the titration of **1**

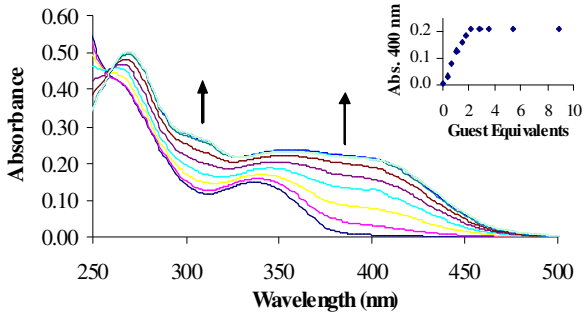


Figure 6. The changes in the absorption spectrum of **1** [1×10^{-5} M] upon titration with OH^- (0 → 9 equivalents) in 1% DMSO in MeCN. Insert, the changes at 360 nm against numbers of equivalents.

with AcO^-, Figure 2. By plotting the changes occurring at 400 nm, as a function of anion equivalent, it was also clear that these changes occur within the addition of two equivalents, as demonstrated by the inset to Figure 6. These results support our hypothesis that in the case of **1**, the anion recognition is most likely caused *via* a deprotonation event. This is in contrast with many other reports, both from our own research group[17] and others,[15,18] where hydrogen bonding interactions usually dominate such anion recognition events in amidourea-based systems. Hence, these results seem to demonstrate that great care has to be paid to the nature of the anion, which can also function as a base.[24,] This is particularly important when examining such recognition in organic solvents such as DMSO and MeCN, as the anion can give rise to deprotonation of the receptor, with concomitant changes in the absorption and the emission spectra of the sensor.[25]

In summary, we have developed **1** as a fluorescent sensor for anions. We have demonstrated that the anion sensing occurs most likely via deprotonation of the amidothiourea receptor adjacent to the quinoxaline fluorophore, which causes significant changes in the absorption spectra, which is red shifted, and in the emission spectra which is quenched significantly upon interaction of **1** with anions such as AcO^- and OH^-. We are currently exploring the sensing ability of other structurally related sensors, possessing both water-soluble functional groups and other types of chromophores/fluorophores, in greater detail, with the aim of establishing criteria for the effect of such structures and media on the sensing mechanism of such pyridyl-amiodothiourea cleft-like systems.

Acknowledgements

We thank TCD (College award to RMD), Science Foundation Ireland for SFI RFP 2008 grant, and HEA-PRTLI Cycle 3 and Cycle 4 (CSCB) for financial support. We thank Robert B. P. Elmes for his help with the initial synthesis of compound **3**, Dr. John E. O'Brien for assisting with NMR measurements and Dr. Emma B. Veale for helpful discussions.

Notes and References

1. Gunnlaugsson, T.; Glynn, M.; Tocci (née Hussey), G. M.; Kruger, P. E.; Pfeffer, F. M. *Coord. Chem. Rev*. **2006**, *250*, 3094.
2. Cametti, M.; Rissanen. K. *Chem. Commun*. **2009**, 2809. Gale, P. A., Garcia-Garrido, S. E.; Garric, J. *Chem. Soc. Rev*. **2008**, *37*, 151; Padros P. Quesada, R. *Supramol. Chem*. **2008**, *20*, 201; Sessler, J. L.; Gale, P. A.; Cho, W. S., *Anion Receptor Chemistry*; Royal Society of Chemistry: Cambridge, UK, **2006**; Gunnlaugsson, T.; Ali H.D.P.; Glynn, M.; Kruger, P.E.; Hussey G. M. Pfeffer F. M.; dos Santos, C. M. G.; Tierney, J.; *J. Fluoresc*. **2005**, *15*, 287; Gale, P. A., *Acc. Chem. Res*. **2006**, *39*, 465; Steed, J. W. *Chem. Commun*. **2006**, 2637.
3 Swinburne, A. N.; Paterson, M. J.; Beeby, A..; Steed, J. W. *Chem. Eur. J*. **2010**, *16*, 2714; Bose, P.; Ghosh, P. *Chem. Commun.* **2010**, *46*, 2962; Kondo, S. I.; Kobayashi, Y.; Unno, M. *Tetrahedron Lett*. **2010**, *51*, 2512; Ghosh, K.; Saha, I.; Masanta, G.; Wang, E. B.; Parish C. A. *Tetrahedron Lett*. **2010**, *51*, 343; Ghosh, K.; Masanta, G.; Chattopadhyay, A. P. *Eur. J. Org. Chem*. **2009**, *26*, 4515; Lowe A. J.; Pfeffer, F. M. *Org. Biomol. Chem.* **2009**, *7*, 4233; Ali, H. D. P.; Quinn, S. J.; McCabe, T.; Kruger, P. E.; Gunnlaugsson, T. *New J. Chem*. **2009**, *33*, 793; Ali, H. D. P.; Kruger, P. E. Gunnlaugsson, T. *New. J. Chem*. **2008**, *32*, 1153; Lowe, A. J. Dyson, G. A. Pfeffer, F. M. *Eur. J. Org. Chem*. **2008**, 1559. Lowe, A. J.; Pfeffer, F. M. *Chem. Commun.* **2008**, 1871; dos Santos, C. M. G.; McCabe, T.; Gunnlaugsson, T. *Tetrahedron Lett.* **2007**, *48*, 3135; Harte, A. J., Jensen, P., Plush, S. E., Kruger, P. E., Gunnlaugsson, T. *Inorg. Chem.* **2006**, *45*, 9465.
4 Swinburne, A. N.; Paterson, M. J.; Beeby, A.; Steed, J. W. *Org. Biomol. Chem.* **2010**, *8*, 1010; Farinha, A. S. F.; Tome, A. C.; Cavaleiro, J. A. S.; *Tetrahedron Lett*. **2010**, *51*, 2184. Dorazco-Gonzalez, A.; Hopfl, H.; Medrano, F.; Yatsimirsky, A. K., *J. Org. Chem*. **2010**, *75*, 2259; Minami, T.; Kubo, Y. *Chem. Asian J*. **2010**, *5*, 605. Evans, L.S.; Gale, P.A.; Light, M.E.; Quesada, R. *Chem. Commun*. **2006**, 965; Jun, E. J.; Swamy, K. M. K.; Bang, H.; Kim, S. J., Yoon, J. Y. *Tetrahedron Lett*. **2006**, *47*, 3103; Evans, L. S.; Gale, P. A.; Light, M. E.; Quesada, R. *New. J. Chem.* **2006**, *30*, 1019; Wu, F. Y.; Li, Z.; Guo, L.; Wang, X.; Lin, M. H.; Zhao, Y. F.; Jiang, Y. B., *Org. Biomol. Chem*. **2006**, *4*, 624; Ghosh, K.; Adhikari, S. *Tetrahedron Lett*. **2006**, *47*, 8165; Pfeffer, F. M.; Gunnlaugsson, T.; Jensen, P.; Kruger, P.E., *Org. Lett*. **2005**, *7*, 5375; Gunnlaugsson T.; Bichell, B.; Nolan, C. *Tetrahedron* **2004**, *60*, 5799
5 Henderson, C. L.; Li, J.; Nation, R. L.; Velkov, T. Pfeffer, F. M. *Chem. Commun*. **2010**, *46*, 3197. Gale, P. A.; Tong, C. C.; Haynes, C. J. E.; Adeosun, O.; Gross, D. E.; Karnas, E.; Sedenberg, E. M.; Quesada, R.; Sessler, J. L. *J. Am. Chem. Soc.* **2010**, *132*, 3240. Judd, L. W.; Davis, A. P. *Chem. Commun*. **2010**, *46*, 2227; Davis, J. T.; Gale, P. A.; Okunola, O. A.; Prados, P.; Iglesias-Sanchez, J. C.; Torroba, T.; Quesada, R. *Nature Chem*. **2009**, *1*, 138; Davis, A. P.; Sheppard, D. N.; Smith, B. D. *Chem. Soc. Rev*. **2007**, *36*, 348; McNally, B. A.; Koulov, A. V.; Smith, B. D.; Joos, J.-B.; Davis, A. P. *Chem. Commun*. **2005**, 1087.
6. Veale, E. B.; Tocci, G. M.; Pfeffer, F. M.; Kruger, P. E.; Gunnlaugsson, T. *Org. Biomol. Chem.* **2009**, *7*, 3447; Veale, E. B.; Gunnlaugsson, *J. Org. Chem*. **2008**, *73*, 8073; Duke, R. M.; Gunnlaugsson, T. *Tetrahedron Lett.* **2007**, *48*, 8043; Lowe, A. J.; Dyson, G. A.; Pfeffer, F. M. *Org. Biomol. Chem*. **2007**, *5*, 1343; Pfeffer, F. M.; Kruger, P. E.; Gunnlaugsson T. *Org. Biomol. Chem*. **2007**, *5*, 1894; Bonizzoni. M.; Fabbrizzi, L.; Taglietti, A.; Tiengo, E. *Eur. J. Org. Chem.* **2006**, 3567; Esteban-Gomez, D.; Fabbrizzi, L.; Liechelli, M. *J. Org. Chem.* **2005**, *70*, 5717; Pfeffer, F. M.; Seter, M.; Lewcenko, N.; Barnett, N. W. *Tetrahedron Lett*. **2006**, *47*, 5251; Gunnlaugsson, T.; Kruger, P.E.; Jensen, P.; Tierney, J. Ali H.D.P.; Hussey G. M. *J. Org. Chem.* **2005**, *70,* 10875; Pfeffer F. M.; Buschgens, A. M.; Barnett, N. W.; Gunnlaugsson, T.; Kruger, P. E., *Tetrahedron Lett.* **2005**, *46*, 6579; Gunnlaugsson T.; Davis, A. P.; Glynn, M. *Chem. Commun*. **2001**, 2556.
7 Bondy, C. R.; Loeb, S. J. *Coord. Chem. Rev*. **2003**, *240*, 77.
8 Makuc, D.; Lenarcic, M.; Bates, G. W.; Gale, P. A.; Plavec, J. *Org. Biomol. Chem*. **2009**, *7*, 3507; Bates, G. W.; Triyanti, Light, M. E.; Albrecht, M.; Gale, P. A. *J. Org. Chem*. **2007**, *72*, 8921; Pfeffer, F. M.; Lim K. F.; Sedgwick, K. J. *Org. Biomol. Chem*. **2007**, *5*, 1795.
9 Edwards, P. R.; Hiscock, J. R.; Gale, P. A.; Light, M. E. *Org. Biomol. Chem*. **2010**, *8*, 100; Edwards, P. R.; Hiscock, J. R.; Gale, P. A.

Tetrahedron Lett. **2009**, *50*, 4922; Chang, K. J.; Moon, D.; Lah, M. S.; Jeong, K. S. *Angew. Chem., Int. Ed*. **2005**, 46, 7926.

10 Anzenbacher, P.; Nishiyabu, R.; Palacios, M. A. *Coord. Chem. Rev*. **2006**, *250*, 2929; Sessler, J. L.; Camiolo, S.; Gale, P. A. *Chem. Rev*. **2003**, *240*, 17.

11 Xu, Z.; Kim, S. K.; Yoon, *J. Chem. Soc. Rev*. **2010**, *39*, 1457.

12 dos Santos, C. M. G.; Gunnlaugsson, T. *Dalton Trans*. **2009**, 4712.

13 dos Santos, C. M. G.; McCabe, T.; Watson, G. W.; Kruger, P. E.; Gunnlaugsson, T. *J. Org. Chem*. **2008**, *73*, 9235.

14 Kang, J.; Lee, Y. J.; Lee, S. K.; Lee, J. H.; Park, J. J.; Kim, Y.; Kim, S.-J.; Kim, C. *Supramol. Chem*. **2010**, *22*, 267.

15 Jiang, Q. Q.; Darhkijav, B.; Liu, H.; Wang, F.; Li, Z.; Jiang, Y. B. *Chem, Asian J*. **2010**, *5*, 543; Liu, W. X.; Yang, R.; Li, A. F.; Li, Z.; Gao, Y. F.; Luo. X. X.; Ruan, Y. B.; Jiang, Y. B. *Org. Biomol. Chem*. **2009**, *7*, 4021; Yang, R.; Liu, W.-X.; Shen, H.; Huang, H.-H.; Jiang, Y.-B. *J. Phys. Chem. B*, **2008**, *112*, 5105; Liu, W.-X.; Jiang, Y.-B. *Org. Biomol. Chem.* **2007**, *5*, 1771

16 Bates, G. W.; Gale P. A. Light, M. E. *Chem. Commun*. **2007**, 2121.

17 Duke, R. M.; O'Brien, J. E.; McCabe T.; Gunnlaugsson, T. *Org. Biomol. Chem.* **2008**, *6*, 4089; Quinlan E.; Matthews S. E.; Gunnlaugsson, T. *J. Org. Chem.* **2007**, *72*, 7497; Quinlan, E.; Matthews, S. E.; Gunnlaugsson T. *Tetrahedron Lett*. **2006**, *47*, 9333.

18 Wei, L.-H.; He, Y.-B.; Wu, J.-L.; Meng, L.-Z.; Yang, X. *Supramol. Chem*. **2004**, *16*, 561.

19 Veale, E. B.; Frimannsson, D. O.; Lawler, M. Gunnlaugsson, T. *Org. Lett.* **2009**, *11*, 4040.

20 An example of a fluorophore-spacer-receptor based PET system has recently been developed incorporating an amidourea moiety: Liu, W. X.; Jiang, Y. B. *Biomol. Chem.* **2007**, *5*, 1771.

21 Vicker, N.; Xiandong, S.; Ganeshapillai, D.; Purohit, A.; Reed, M., John.; Potter, B.; Victor Llyod. *PCT. Int. Appl.* **2005**, WO2005042513 (A1)

22 Nasielski-Hinkens, R.; Benedek-Vamos, M.; Maetens, D. *J. Heterocyc. Chem.* **1980**, *17*, 873-875.

23 **1,6–Bis-[6-aminoquinoxaline(thioureidocarbomoyl)]-pyridine (1)** 6-Aminoquinoxaline (**3**) (0.200 g, 1.3 mmol) was stirred vigorously in water (5 mL). $CSCl_2$ (0.174 g, 1.5 mmol) was then added dropwise with stirring and the reaction mixture was stirred at room temperature for 2 h. The resulting orange solid was isolated by suction filtration and then added to a suspension of **5** (0.258 g, 1.3 mmol) in MeCN (30 mL). The reaction mixture was refluxed for 16 h and the solid was then isolated by suction filtration. Minor impurities were removed by refluxing a suspension of the solid in EtOH (20 mL) overnight. The compound was collected and dried by suction filtration, giving **1** as an orange solid (0.316 g, 81%). m.p. 214-216 °C; HRMS (ES^+): Calculated for $C_{23}H_{20}N_{11}O_2S_2$ $[M+H]^+$: 570.1243; found: 570.1254; δ_H (600 MHz, DMSO-d_6), 11.38 (2H, br s, $N\underline{H}_{amido}$), 10.32 (4H, br s, $N\underline{H}_{urea}$), 8.90 (2H, br d, J = 2.0 Hz, $C\underline{H}_{quin}$), 8.87 (2H, br d, J = 2.0 Hz, $C\underline{H}_{quin}$), 8.40-8.20 (5H, br m, $C\underline{H}_{py}$, $C\underline{H}_{quin}$), 8.04-8.02 (4H, br m, $C\underline{H}_{quin}$); δ_C (150 MHz, DMSO-d_6), 181.1 (C=S), 162.8 (C=O), 147.8 (q), 145.7 (CH), 144.8 (CH), 142.1 (q), 140.6 (q), 139.9 (CH), 139.6 (q), 129.1 (CH), 128.0 (CH), 125.0 (CH), 122.6 (CH); δ_N (60 MHz, DMSO-d_6), 129.4, 126.5, 124.0; IR υ_{max} (cm^{-1}) 3147, 2943, 1699, 1619, 1521, 1470, 1367, 1304, 1267, 1219, 1151, 1024, 999, 949, 889, 861, 831, 730, 650, 591, 545, 525.

24. Camiolo, S.; Gale, P.; Hursthouse, M. B.; Light, M. E. *Org. Biomol. Chem.*, **2003**, *1*, 741; Gunnlaugsson, T.; Kruger, P. E.; Lee, T. C.; Parkesh, R.; Pfeffer, F. M.; Hussey, G. M. *Tetrahedron Lett.* **2003**, *44*, 6575; Gunnlaugsson, T., Kruger, P. E., Jensen, P., Pfeffer, F. M.; Hussey, G. M. *Tetrahedron Lett*. **2003**, *44*, 8909; Amendola, V.; Esteban-Gomez, D.; Fabbrizzi L.; Liechelli, M. *Acc. Chem. Res*. **2006**, *44*, 8690.

25 Gale *et al.* have recently shown, using X-ray crystallography, that dihydrogen phosphate can also function as a base and deprotonate other dihydrogen phosphate molecules that are bound by hydrogen bonding receptors: Gale, P. A..; Hiscock, J. R.; Moore, S. J.; Caltagirone, C.; Hursthouse, M. B.; Light, M. E. *Chem. Asian, J*., **2010**, *5*, 555.