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Simple naphthalimide based anion sensors: deprotonation induced colour changes and CO_2 fixation

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Abstract—The 4-amino-1,8-naphthalimide based chemosensors **2**, **4** and **6** show striking green-to-purple colour changes due to the deprotonation of the 4-amino moiety on interaction with strongly basic anions such as F^-: these colour changes reverse gradually with time due to the fixation of atmospheric CO_2 (as HCO_3^-) yielding 1:1 adducts as demonstrated by X-ray crystallography.

Currently, there is great interest within the field of supramolecular chemistry in the development of recognition units for the sensing of molecules and ions.[1] Whilst numerous luminescent and colorimetric sensors/chemosensors have been developed for cations,[1] less attention has been paid to the development of such sensors for anions.[2] Nevertheless, some excellent examples of compounds capable of anion recognition and sensing have been reported.[2,3] However, these approaches have often involved the synthesis of structurally complicated hosts.[4]

Our interest in this field has lead us to develop several luminescent chemosensors for biologically important anions using both cationic and charge neutral receptors.[5] To this end, we recently synthesised and evaluated combined thiourea/naphthalimide based anion sensors such as **1** (Fig. 1). Sensor **1**, was designed as a Photoinduced Electron Transfer (PET) chemosensor for anions such as acetate and fluoride, where the fluorescence emission of **1**, which occurs in the green, was quenched upon adding either of these ions (~1 equiv.) due to enhanced PET from the thiourea receptor to the excited state of the fluorophore.[6] We also observed a significant green-to-purple colour change in the presence of high concentrations of F^- (>2.5 equiv.). We suspected that F^- might be sufficiently basic such that it could deprotonate the NH and lead to the observed long wavelength colour change. Recently, Gale et al. have reported similar phenomena where deprotonation of pyrrole 2,5-diamide anion sensors by F^- induced a blue colour change.[7] Other colorimetric sensors displaying similar effects have been reported by Sessler et al. who used 'off-the-shelf' reagents possessing aniline-like NH_2 donors such as 1,2-diaminoanthroquinone as 'naked-eye' colorimetric sensors for anions.[8] In order to fully elucidate the process leading to the colour change that we observed for **1**, and potentially exploit this mechanism in the development of chemo-sensors, we designed the 4-amino-1,8-naphthalimide derivatives **2**, **4** and **6** (Fig. 1). These are structurally simple naphthalimide systems that are easily synthesised and possess acidic protons that can

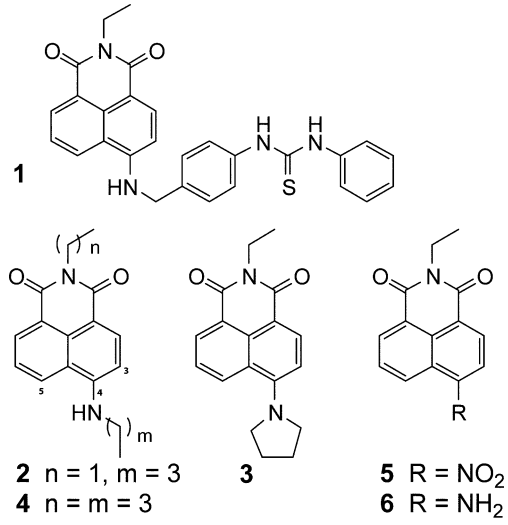

Figure 1. Structure of **1** and the simple naphthalimides **2**–**6**.

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participate in hydrogen bonding or be deprotonated by basic anions, giving rise to the above mentioned green-to-purple colour change. In this letter we discuss the results of this work and the unexpected ability of **2** and **4**, in the presence of F^- to fix atmospheric CO_2.

Compounds **1**–**4** and **6** are based on the 4-amino-1,8-naphthalimide structure. Such compounds are highly coloured, as well as being fluorescent, emitting typically with $\lambda_{max} \sim 550$ nm in CH_2Cl_2, as they possess large excited state dipole moments due to their internal charge transfer (ICT) excited state nature.[9] The synthesis of these compounds is straightforward and high yielding. The synthesis of **2** and **3** was achieved in two steps by first reacting one equivalent of *n*-ethylamine in refluxing toluene with 4-bromo-1,8-naphthalic anhydride, which after aqueous work-up gave the imide in ca. 80% yield as an off-white powder.[6] This was followed by nucleophilic aromatic substitution using neat *n*-butylamine or pyrrolidine to give **2** and **3**, as yellow–orange coloured powders in 74 and 86% yield, respectively. The di-*n*-butyl derivative **4** was made in a single step by refluxing the naphthalic anhydride in neat *n*-butylamine followed by aqueous workup.[6] For the 4-amino derivative **6**, 4-nitro-1,8-naphthalic anhydride and ethylamine were used to make **5**, and subsequent reduction of the nitro group using 10% Pd/C and ammonium formate in MeOH afforded **6** in 78% overall yield. All new compounds were satisfactorily analysed using conventional methods. We were able to grow crystals of **2** suitable for X-ray crystal analysis, which confirmed the structure[10] (Fig. 2). We note that adjacent molecules participate in π···π, C–H···π, and weak hydrogen bond interactions, the strongest of these being between the proton of the 4-amino moiety and the imide oxygen of an adjacent molecule.

As discussed above, we predicted that the ICT state of **2** and **4** might be modulated by strongly basic anions such as F^- through strong hydrogen bonding to, or deprotonation of, the electron donating amino moiety. We first investigated these possibilities by observing the changes in the UV–vis spectrum of DMSO solutions of **2** upon addition of AcO^-, $H_2PO_4^-$, Cl^-, Br^-, F^- (as their $(C_4H_9)_4N^+$ salts). Compound **2** has a strong absorption band centred at 446 nm ($\log \varepsilon = 4.23$ M^{-1} cm^{-1}) due to its ICT character and a second band at 287 nm (n→π*) (Fig. 3). Upon addition of the above anions, only F^- gave rise to changes in these absorption bands (Fig. 3). Upon titration of **2** with F^- the absorptions at 446 and

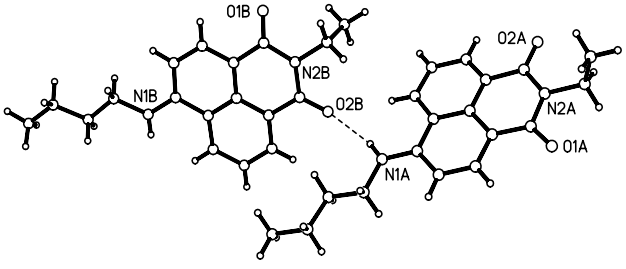

Figure 2. Crystal and molecular structure of **2** showing H-bond interaction between adjacent molecules.

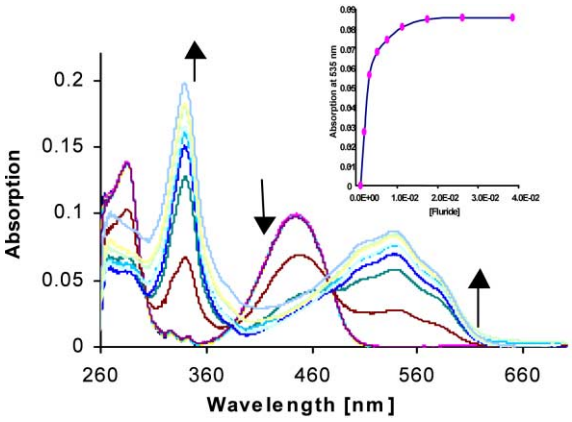

Figure 3. The changes in the (corrected) UV–vis spectra of **2** upon addition of F^- in DMSO. [2] = 5.8 μM. The intensities of the bands at 446 and 287 nm are reduced upon deprotonation of the 4-amino moiety of **2** with the formation of two new bands at 535 and 341 nm, respectively. *Insert*: The changes in the 535 nm band as a function of F^-.

287 nm were substantially reduced with the formation of new bands at ca. 535 and 341 nm and concomitant formation of three isosbestic points at ca. 480, 380 and 300 nm. Although these isosbestic points were very clear at lower concentrations, at higher concentrations some broadening was observed (possibly due to aggregation). We propose that these spectral changes are due to the deprotonation of the amino moiety by F^- rather than hydrogen bonding. This would suggest that two species were formed, namely the negatively charged naphthalimide ($Naph^-$) and HF. This causes a significant increase in the charge density on the amino nitrogen with associated enhancement in the push–pull character of the ICT transition, bathochromically shifting the absorption. As demonstrated above, the absorption at 446 nm for **2** was almost '*switched off*' upon gradual addition of F^-, and the 535 nm absorption was '*switched on*'. The F^- recognition by **2** was also evident in its fluorescence emission ($\lambda_{max} = 535$ nm), which was considerably quenched upon F^- addition. Moreover, upon excitation at 535 nm a new broad fluorescence emission was observed between 580 and 800 nm, which gradually increased in intensity as a function of $[F^-]$.

When these measurements were repeated using **3**, which lacks the acidic proton, no such spectroscopic changes were observed, whereas **4** and **6** displayed similar behaviour as that observed for **2**. These results clearly indicate that **2**, **4** and **6** have potential as colorimetric sensors for F^-, caused by the deprotonation of the 4-amino moiety of these compounds giving rise to large colour changes at long wavelength as in the case of F^-. Similar phenomena were observed in other organic solvents such as THF and CH_2Cl_2. In contrast, however, only a minor shift was observed in the naphthalimide ICT band in water.[9]

The above recognition process was highly visible to the naked eye with a colour change from yellow/green-to-red/purple upon addition of F^- (Fig. 4). Similar results

Figure 4. Colour change observed upon the addition of F^- to a DMSO solution of **2**. Left: **2**; Right: **2**+F^-.

were obtained when strong bases such as TBAOH, NaH, and LDA were specifically employed. In contrast, no colour changes were observed upon addition of NEt_3 or DMAP. This further confirms our suspicion that deprotonation of the amino moiety and not hydrogen bonding to it is responsible for the pronounced colour changes.

To investigate this deprotonation process further we also monitored the changes in the ^1H NMR spectra of DMSO-d_6 solutions of **2** upon addition AcO^-, $H_2PO_4^-$, Cl^-, Br^-, F^- (as their $(C_4H_9)_4N^+$ salts) for F^-. Of these anions only F^- gave rise to spectral changes, as seen in Figure 5. The ^1H NMR of **2** (Fig. 5) shows the aromatic region and a resonance at 7.76 ppm for the 4-amino proton. Upon addition of the anion, substantial changes occur. The shift of the resonance assigned

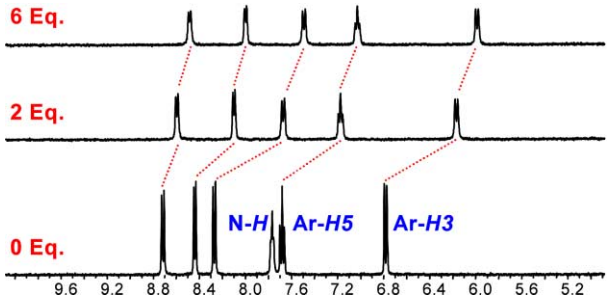

Figure 5. Stack plot of ^1H NMR spectra (in DMSO-d_6) of **2** and after addition of various quantities of TBA·F.

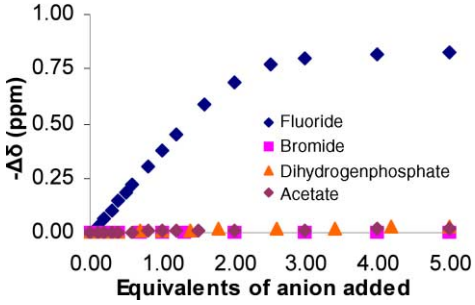

Figure 6. Changes in the chemical shift of proton three within **2** upon addition of various anions in DMSO-d_6.

to the proton at position three (see Fig. 1) of the naphthalimide ring was monitored as the N–H signal became significantly broadened after the addition of only small quantities of F^- and completely disappeared after the addition of 0.5 equiv. We noted that for the saturation to occur in the ^1H NMR signals, approximately 2 equiv. of F^- were needed (see Fig. 6), which might suggest the formation of bifluride (HF_2^-) as a new signal was observed as a triplet at ca. 16 ppm.[14] Even though we have been unable to prove this unambiguously, it is possible that full deprotonation of the 4-amino group occurs only after 2 equiv. of the anion have been added; hence the first equivalent forms a strong hydrogen bond to the amino hydrogen, and only after the second equivalent of F^- has been added is the proton removed. We are currently investigating this further.

During the course of the titration experiments we observed that upon leaving the purple coloured solutions of **2**+F^- open to the air for several hours, the colour change reversed, i.e. the green colour was returned. We originally surmised this to be due to the absorption of water by the solution. To investigate this further we attempted to grow crystals from **2**+F^- solution (or the deprotonated form of **2** after addition of F^-) under a dry atmosphere. Whilst a crystalline form of **2**+F^- was obtained, the crystals were unsuitable for a single crystal diffraction study. Nevertheless, exposure of the mother liquor to air for even the briefest time induced the formation of yellow/orange crystals. Fortunately, these were suitable for a single-crystal X-ray diffraction experiment. The structural determination showed that these crystals are not the deprotonated form of **2**, but in fact the TBA salt of the 1:1 adduct formed between **2** and HCO_3^-, the HCO_3^- having arisen following atmospheric CO_2 fixation (Fig. 7). Each molecule of **2** is strongly hydrogen bonded via its amino proton to O3 of HCO_3^-. The HCO_3^- ion is also involved in a self-complimentary hydrogen bonded association with its nearest neighbour. In contrast with the structure of **2**, the naphthalimide moieties in TBA[**2**·HCO_3] do not participate in π-stacking interactions with each other but interact through alkyl C–H···π contacts with the TBA cations, whose alkyl chains separate the aromatic units. Whilst the fixation of CO_2 (as carbamate) by aliphatic amines is well known,[11] the formation of bicarbonate with amines is less so, with the structural characterisation of these

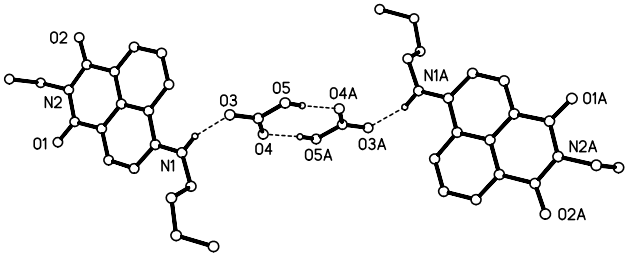

Figure 7. The structure of the 1:1 adduct formed between **2** and HCO_3^- showing H-bonded pairs (*t*-butylammonium cations omitted for clarity).

species remaining especially rare.[12] It has been noted previously by other researchers that melts of partially hydrated tetra-alkylammonium salts of relatively basic anions such as F^-, readily and reversibly absorb CO_2, giving bicarbonate and bifluoride (HF_2^-) within the melt.[13] This process requires water to be present, which is itself strongly hydrogen bonded to the anion, F^-, such that its basicity is enhanced making it more able to react with CO_2. However, when solution of **2** in the presence of TBAOH was allowed to interact with air in the same manner as above, the green colour also reappeared. It is thus possible that this hydroxide solution is also able to fix CO_2 and perhaps the deprotonated amine (not F^-) plays the key role in the CO_2 fixation process. We are currently investigating these features in greater detail.

In summary, we have confirmed that deprotonation is responsible for the colour change observed upon F^- titration of **2** (and therefore **1**) and demonstrated that simple highly coloured ICT chromophores have potential as naked eye sensors for F^- in DMSO. We are currently examining the naphthalimide frameworks with an eye to improving these simple colorimetric sensors and assessing as to whether they might perform as reporters of CO_2.[11]

Experimental

4-*N*-Butyl *N*′-ethyl-1,8-naphthalimide 2
Yield 132 mg (74%). Mp 172.6–173.8°C. Anal. calcd for $C_{18}H_{20}N_2O_2$: C, 72.95; H, 6.80; N, 9.45%. Found: C, 72.83; H, 7.17; N, 9.43%; δ_H (400 MHz, DMSO-d_6): 0.95 (3H, t, $J=7.6$, CH_3); 1.18 (3H, t, $J=7.0$, CH_3); 1.41–1.46 (2H, m, CH_2); 1.67–1.71 (2H, m, CH_2); 3.37 (2H, q, $J=6.9$, CH_2); 4.05 (2H, q, $J=7.0$, CH_2); 6.78 (1H, d, $J=8.0$, H3 Naphth); 7.68 (1H, t, $J=8.5$, H6 Naphth); 7.76 (1H, brs, NH); 8.27 (1H, d, $J=8.5$, H2 Naphth); 8.44 (1H, d, $J=7.6$, HNaphth); 8.71 (1H, d, $J=8.5$, HNaphth); δ_C (400 MHz, [D_6]Acetone): 12.99, 13.42, 19.90, 30.61, 34.73, 42.98, 103.86, 109.91, 119.70, 122.84, 124.21, 125.20, 129.34, 130.58, 133.97, 148.92, 163.52, 164.06.

4-*N*-Pyrolidinyl *N*′-ethyl 1,8 naphthalimide 3
Yield 78 mg (86%). Mp 157.7–159.2°C. Anal. calcd for $C_{18}H_{18}N_2O_2{\cdot}0.1\ H_2O$: C, 72.97; H, 6.12; N, 9.51%. Found: C, 72.80; H, 6.12; N, 9.49%; δ_H (400 MHz, $CDCl_3$): 1.34 (3H, t, $J=7.0$, CH_3); 2.10–2.14 (4H, m, 2×CH_2 pyrolidine); 3.79–3.82 (4H, m, 2×CH_2 pyrolidine); 4.26 (2H, q, $J=7.0$, CH_2); 6.83 (1H, d, $J=8.5$, H3 Naphth); 7.55 (1H, t, $J=7.8$, H6 Naphth); 8.44 (1H, d, $J=8.5$, H2 Naphth); 8.59-8.61 (2H, m, H5, H7 Naphth); δ_C (400 MHz, $CDCl_3$): 13.36, 26.04, 35.10, 53.11, 108.03, 110.41, 122.17, 122.21, 122.56, 130.51, 131.40, 132.87, 152.16, 163.47.

4-Nitro-*N*′-ethyl-1,8-naphthalimide 5
Yield 510 mg (93%). Mp 187.6–188.9°C. Anal. calcd for $C_{14}H_{10}N_2O_4$: C, 62.22; H, 3.73; N, 10.37%; Found: C, 62.18; H, 3.68; N, 10.15%; δ_H (400 MHz, $CDCl_3$) 1.37 (3H, t, $J=7.0$, CH_3), 4.28 (2H, q, $J=7.0$, CH_2), 8.01 (1H, dd, $J=7.6$ and 8.8, Ar-H), 8.43 (1H, d, $J=8.0$, Ar-H), 8.72 (1H, d, $J=8.0$, Ar-H), 8.76 (1H, d, $J=7.5$, Ar-H), 8.86 (1H, d, $J=8.5$, Ar-H); δ_C (100 MHz, $CDCl_3$) 13.2, 36.0, 123.1, 123.7, 123.9, 127.0, 129.1, 129.3, 129.7, 129.9, 132.4, 149.5, 162.3, 163.1; m/z (ESMS): 293 $(M+Na)^+$.

4-Amino-*N*′-ethyl-1,8-naphthalimide 6
Yield 150 mg (84%). Mp 275.8–276.5°C. Anal. calcd for $C_{14}H_{12}N_2O_2$: C, 69.99; H, 5.03; N, 11.66%; Found: C, 69.78; H, 5.23; N, 11.37%; δ_H (400 MHz, DMSO-d_6) 1.18 (3H, t, $J=7.0$, CH_3), 4.05 (2H, q, $J=7.0$, CH_2CH_3), 6.85 (1H, d, $J=8.8$, Ar-H), 7.43 (2H, brs, NH_2), 7.66 (1H, dd, $J=7.6$ and 7.9, Ar-H), 8.20 (1H, d, $J=8.8$, Ar-H), 8.44 (1H, d, $J=7.0$, Ar-H), 8.61 (1H, d, $J=8.2$, Ar-H); δ_C (100 MHz, DMSO-d_6) 13.4, 34.3, 107.6, 108.2, 119.4, 121.8, 124.0, 129.3, 129.7, 131.0, 133.9, 152.7, 162.7, 163.6; m/z (ESMS): 241 $[M+H]^+$.

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References

1. (a) Rurack, K.; Resch-Genger, U. *Chem. Soc. Rev.* **2002**, 116–127; (b) Rurack, K. *Spectrochem. Acta A* **2001**, *57*, 2161–2195; (c) Gunnlaugsson, T.; Nieuwenhuyzen, M.; Richard, L.; Thoss, V. *J. Chem. Soc., Perkin Trans. 2* **2002**, 141–159; (d) Gunnlaugsson, T.; MacDónaill, D. A.; Parker, D. *J. Am. Chem. Soc.* **2001**, *123*, 12866–12876; (e) de Silva, A. P.; Fox, D. B.; Huxley, A. J.; Moody, T. S. *Coord. Chem. Rev.* **2000**, *205*, 41–57; (f) Gunnlaugsson, T. *Tetrahedron Lett.* **2001**, *42*, 8901–8905; (g) Gunnlaugsson, T.; MacDónaill, D. A.; Parker, D. *Chem. Commun.* **2000**, 93–95; (h) de Silva, A. P.; Gunaratne, H. Q. N.; Gunnlaugsson, T.; Huxley, A. J. M.; McCoy, C. P.; Rademacher, J. T.; Rice, T. E. *Chem. Rev.* **1997**, *97*, 1515–1566.
2. (a) Suksai, C.; Tuntulani, T. *Chem. Soc. Rev.* **2003**, *32*, 192–202; (b) Lee, D. H.; Lee, H. Y.; Hong, J.-I. *Tetrahedon Lett.* **2002**, *43*, 7273–7276; (c) Gale, P. A. *Coord. Chem. Rev.* **2001**, *213*, 79–128; (d) Gale, P. A. *Coord. Chem. Rev.* **2000**, *199*, 181–233; (e) Beer, P. D.; Gale, P. A. *Angew. Chem., Int. Ed.* **2001**, *40*, 486–516; (f) Beer, P. D. *Chem. Commun.* **1996**, 689–696; (g) Schmidtchen, F. P.; Berger, M. *Chem. Rev.* **1997**, *97*, 1609–1646; (h) Beer, P. D.; Smith, D. K. *Prog. Inorg. Chem.* **1997**, *46*, 1–96; (i) Atwood, J. L.; Holman, K. T.; Steed, J. W. *Chem. Commun.* **1996**, 1401–1407.
3. (a) Keegan, J.; Kruger, P. E.; Nieuwenhuyzen, M.; O'Brien, J.; Martin, N. M. *Chem. Commun.* **2002**, 2192–2193; (b) Liao, J. H.; Chen, C. T.; Fang, J. M. *Org. Lett.* **2002**, *4*, 561–564; (c) Fabbrizzi, L.; Licchelli, M.; Mancin, F.; Pizzeghello, M.; Rabaioli, G.; Taglietti, A.; Tecilla, P.; Tonellato, U. *Chem. Eur. J.* **2002**, *8*, 94–101; (d) Miyaji,

H.; Anzenbacher, P., Jr.; Sessler, J. L.; Bleasdale, E. R.; Gale, P. A. *Chem. Commun.* **1999**, 1723–1724; (e) Cooper, C. R.; Spencer, N.; James, T. D. *Chem. Commun.* **1998**, 1365–1366; (f) Kubo, Y.; Tsukahara, M.; Ishihara, S.; Tokita, S. *Chem. Commun.* **2000**, 653–654; (g) Xie, H.; Yi, S.; Yang, X.; Wu, S. *New J. Chem.* **1999**, *23*, 1105–1108.

4. (a) Davis, A. P.; Lawless, L. J. *Chem. Commun.* **1999**, 9–10; (b) Davis, A. P.; Perry, J. J.; Williams, R. P. *J. Am. Chem. Soc.* **1997**, *119*, 1793–1794.
5. (a) Gunnlaugsson, T.; Harte, A. J.; Leonard, J. P.; Nieuwenhuyzen, M. *Chem. Commun.* **2002**, 2134–2135; (b) Gunnlaugsson, T.; Davis, A. P.; O'Brien, J. E.; Glynn, M. *Org. Lett.* **2002**, *4*, 2449–2452; (c) Gunnlaugsson, T.; Davis, A. P.; Glynn, M. *Chem. Commun.* **2001**, 2556–2557; (d) Kruger, P. E.; Mackie, P. R.; Nieuwenhuyzen, M. *J. Chem. Soc., Perkin Trans. 2* **2001**, 1079–1083.
6. Gunnlaugsson, T.; Kruger, P. E.; Lee, T. C.; Parkesh, R.; Pfeffer, F. M.; Hussey, G. M. *Tetrahedron Lett.* **2003**, *43*, 6575–6578.
7. Camiolo, S.; Gale, P.; Hursthouse, M. B.; Light, M. E. *Org. Biomol. Chem.* **2003**, *1*, 741–744.
8. Miyaji, H.; Sessler, J. L. *Angew. Chem., Int. Ed.* **2001**, *40*, 154–157.
9. (a) de Silva, A. P.; Rice, A. *Chem. Commun.* **1999**, 163–164; (b) de Silva, A. P.; Gunaratne, H. Q. N.; Gunnlaugsson, T. *Tetrahedron Lett.* **1998**, *39*, 5077–5080; (c) de Silva, A. P.; Gunaratne, H. Q. N.; Habib-Jiwan, J. L.; McCoy, C. P.; Rice, T. E.; Soumillion, J. P. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1728–1731.
10. SMART and SAINT-NT, Bruker-AXS, Madison, WI, 1998; G. M. Sheldrick, SHELXTL Version 5.1, Bruker-AXS, Madison, WI, 1998. Crystallographic data for the structures in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication numbers CCDC: Compound **2** (Fig. 2): 204241; Compound **2** and HCO_3 adduct (Fig. 7): 204242. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44(0)-1223-336033 or e-mail: deposit@ccdc.cam.ac.uk].
11. Hampe, E. M.; Rudkevich, D. M. *Chem. Commun.* **2002**, 1450–1451 and references cited therein.
12. Mak, T. C. W.; Xue, F. *J. Am. Chem. Soc.* **2000**, *122*, 9860–9861.
13. Quinn, R.; Appleby, J. B.; Pez, G. P. *J. Am. Chem. Soc.* **1995**, *117*, 329–335.
14. Shenderovich, I. G.; Tolstoy, P. M.; Golubev, N. S.; Smirnov, S. N.; Denisov, G. S.; Limbach, H.-H. *J. Am. Chem. Soc.* **2003**, 11710.