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COMMUNICATION

Cyclo[2]benzimidazole: luminescence turn-on sensing of anions†‡

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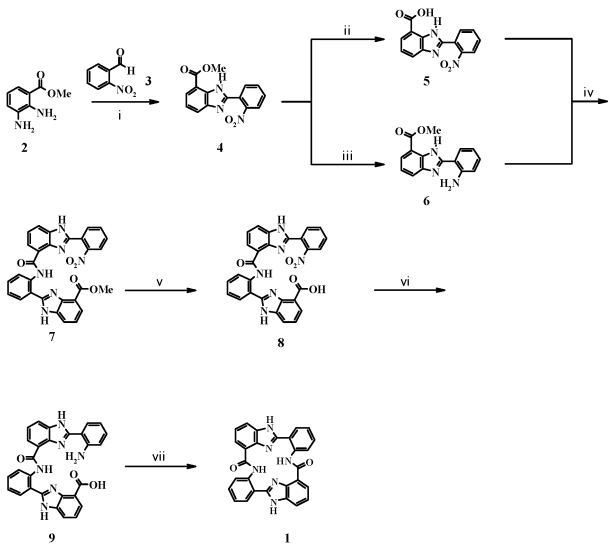
Cyclo[2]benzimidazole is a new host for anions that turns on its luminescence up to 150 fold upon binding. Photoexcited cyclo[2]benzimidazole undergoes an efficient non-radiative deactivation through an excited-state intramolecular proton-transfer (ESIPT) mechanism. Upon binding an anion, the ESIPT pathway is blocked, resulting in an increase in the luminescence efficiency.

Many real world sensors require fast and easily detectable means for reporting a molecular recognition event. Many chemosensors rely on transducing the recognition event through changes in the emission[1] properties. The use of luminescence for reporting a binding event has many advantages as it provides high sensitivity and instantaneous signal generation. Additionally, luminescence can be switched on or off and these changes may often be detected even by the naked eye. Binding dependent luminescence may rely on different mechanisms such as intramolecular charge transfer processes (ICT),[2] photoinduced electron transfer processes (PET),[3] metal-to-ligand charge transfer processes (MLCT),[4] excimer/exciplex formation[5] and guest induced changes in the rigidity of the host.[6]

Another, less common, report mechanism is the Excited-State Intramolecular Proton Transfer (ESIPT) process.[7]

ESIPT occurs in systems having intramolecular hydrogen bonds between hydrogen-bond donors such as –OH and –NH_2 and hydrogen-bond acceptors such as N: and C=O.[8] Upon photoexcitation, the *enol* S_0 ground state form transforms into the *enol* S_1 excited state which in turn transforms into the more stable *keto* S_1 photo excited tautomer. In most cases, this species decays to the ground state in a radiative way. Due to the tautomeric relaxation, the typical Stokes shifts of such a process are in the range of 6000–12 000 cm^{-1}. In view of the fact that anion binding is based on the formation of hydrogen bonds, harnessing the ESIPT process for the development of new anion binding signaling systems seems promising.



Scheme 1 (i) nitrobenzene, reflux 4 d, 70%; (ii) NaOH, MeOH/H_2O, reflux 12 h, 95%; (iii) H_2, Pd/C, MeOH, 3 h rt, 98%; (iv) BOP/NMM, DCM, reflux, 6 d, 53%; (v) NaOH, MeOH/H_2O, reflux 5 h, 80%; (vi) H_2, Pd/C, MeOH, 5 h rt, 98%; (vii) BOP/NMM, DCM, reflux, 6 d, 30%.[9]

Here we report on a new cyclic amidophenyl benzimidazole-based anion binding system, **1**, that exhibits a dramatic luminescence turn-on upon binding fluoride, bifluoride and the oxo anions dihydrophosphate and benzoate, probably through the inhibition of an ESIPT process.

Cyclo[2]benzimidazole, **1**, that was prepared according to Scheme 1, may exist in a wealth of possible tautomeric forms.

Electronic energy calculations (gas phase)[10] predict that the three tautomers **1-2H$_{in}$**, **1-4H$_{in}$** and **1-3H$_{in}$** are the most stable ones, Fig. 1. The calculations predict that the stability order is **1-2H$_{in}$** > **1-3H$_{in}$** > **1-4H$_{in}$**. In the **1-2H$_{in}$** conformer the protons inside the cavity interact with the free nitrogen atoms of the benzimidazole moieties, upon adding protons to the cavity, forming **1-4H$_{in}$** and **1-3H$_{in}$**, these attractive interactions are replaced by repulsive H–H interactions.

The room temperature absorption and emission spectra of **1** in 0.1% H_2O:DMSO reveal a large Stokes shift ($\Delta\lambda$ = 158 nm, 10 775 cm^{-1}), which is commonly observed in 2-aminophenyl and 2-hydroxyphenyl benzimidazole derivatives and is attributed to the significant structural reorganization upon photoexcitation associated with an Excited State Proton Transfer (ESPT) process.[11]

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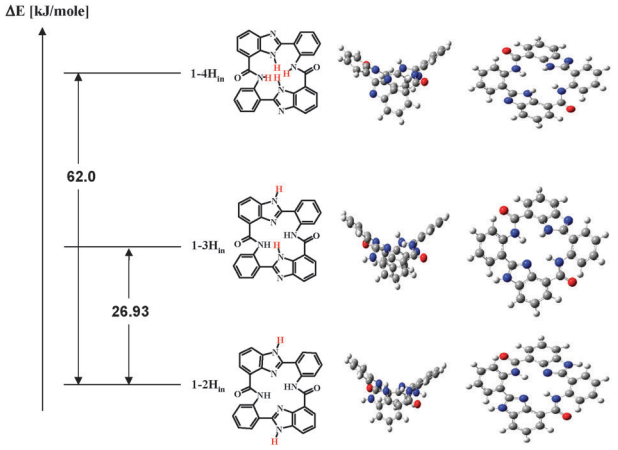

Fig. 1 Energy diagram and structures of the low energy tautomeric structures of **1** obtained from electronic energy calculations (Gaussian 03 suite programs,[10] DFT, B3LYP, 6-311G*).

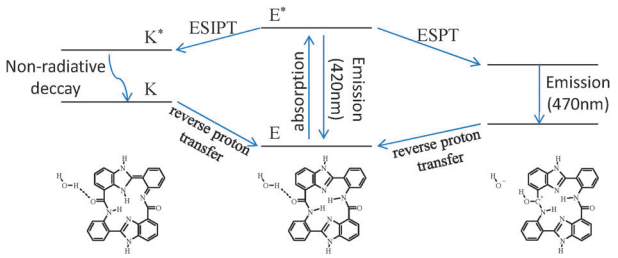

Fig. 2 Proposed tautomeric forms and decay pathways of **1** in water containing DMSO.

Low temperature fluorescence spectroscopy of **1** in 0.1% H_2O:DMSO reveals that upon cooling the dominant emission is a new luminescence peak centred at ~420 nm, while the 470 nm emission does not seem to vary in intensity. This type of temperature dependent luminescence spectrum is also indicative of an ESIPT process.

The probability of the ESIPT process decreases with the temperature, through gradually blocking the tautomerism relaxation pathways and enabling the relaxation of the S_1 *enol* tautomer to relax radiatively to the *enol* S_0.[12,13] Fig. 2 presents the proposed tautomeric forms and decay pathways of **1**.

The anion binding ability of cyclo[2]benzimidazole, **1**, was studied in 0.1% H_2O:DMSO using spectrophotometric and spectrofluorimetric titration experiments. Various anions were added as their tetrabutyl ammonium (TBA) salts to solutions of **1** in 0.1% H_2O:DMSO and the relevant spectral changes were monitored. The most significant changes were recorded upon adding fluoride and basic oxo-anions.

Fig. 3 presents the absorption and emission spectra of cyclo[2]benzimidazole, **1**, in the presence of different concentrations of tetrabutyl ammonium fluoride in 0.1% H_2O:DMSO. Addition of fluoride induces the formation of a new absorption peak at 340 nm, while the peak at 309 nm decreases.

Furthermore, the emission peak of **1** at 412 nm, recorded with excitation at the isosbestic point (322 nm), increases by up to 150 times while the broad emission peak at 470 nm is practically unchanged. The fluoride dependent spectral changes do not fit a 1 : 1 complex model nor any other simple

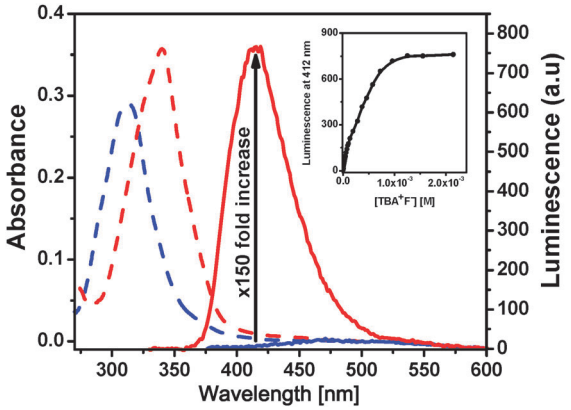

Fig. 3 Absorption (dashed curves) and emission (λ_{ex} = 322 nm) (solid curves) spectra of a solution of 1.5×10^{-5} M cyclo[2]benzimidazole, **1**, in 0.1% H_2O:DMSO before (blue) and after (red) adding excess tetrabutyl ammonium fluoride (TBAF). Inset: luminescence intensity of **1** as a function of added TBAF.

association model. NMR studies reveal that the complex behavior originates from the effective transformation of fluoride into bifluoride, HF_2^-.[13]

The association of HF_2^- with **1** is characterized by a high 1 : 1 association constant of 100 000 ± 10% M^{-1} and a 60 fold turn-on of the luminescence. The affinity of cyclo[2]-benzimidazole, **1**, to other anions is much weaker. For example, cyclo[2]benzimidazole, **1**, forms a 1 : 1 complex with tetrabutyl ammonium benzoate, TBABz, with an association constant of only 100 ± 10% M^{-1}. Here too, the luminescence turns on 130 fold upon complex formation, peaking at saturation. Similar results were obtained for $TBAH_2PO_4$. Table 1 depicts the association constants and luminescence turn on factors for the association of **1** with different anions in 0.1% H_2O:DMSO.‡

As can be seen in Fig. 3, the Stokes shift of complexed cyclo[2]benzimidazole, **1**, is significantly smaller than that of the free one, indicating the inhibition of the ESIPT process. The suggested mechanism for the fluorescence enhancement at the anion recognition event is through the stabilization of the **1-4H$_{in}$** tautomer due to the formation of four hydrogen bonds between the N–H groups of the molecule and the anion. Fig. 4 presents the energy minimized structure of the complex

Table 1 Association constants between cyclo[2]benzimidazole, **1**, and different anions in 0.1% H_2O:DMSO

Anion[a]	Stoichiometry	K_{ass}[b]	Lum. turn on factor
F^-	[c]	[d]	150
HF_2^-	1 : 1	100 000	60
$H_2PO_4^-$	1 : 1	280	137
$C_6H_5COO^-$	1 : 1	100	130
NO_3^-, Cl^-, Br^-, I^-, SCN^-, HSO_4^-, p-toluene sulfonate, PF_6^-, BF_4^-, BPh_4^-	—	< 5	No increase

[a] Anion added as their tetrabutyl ammonium salts. [b] Association constants were calculated using a non-linear curve-fitting software (see ESI‡) and are based on the fluorescence titration data. Estimated error < ± 10%. [c] Complex behaviour. [d] Not determined due to deprotonation and formation of HF_2^-.

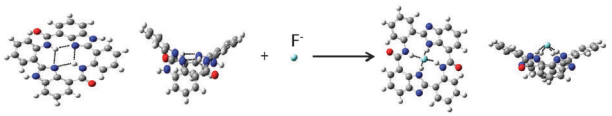

Fig. 4 Minimum energy optimized structures of free **1** and [1 − F^-] complex (B3LYP/6-31 + G*).

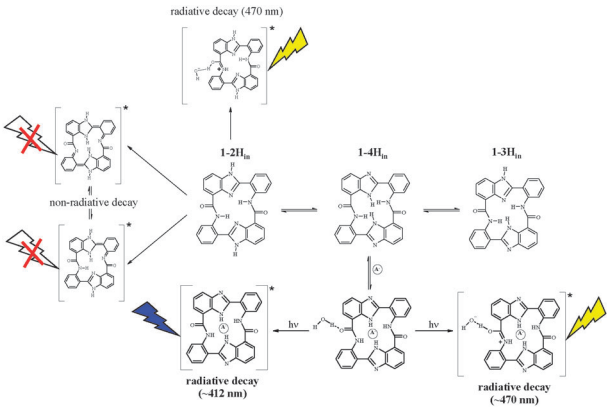

Fig. 5 Possible forms of free and bound **1** at the ground state and the excited state.

between fluoride and cyclo[2]benzimidazole, **1** (B3LYP/6-31+G*). The **1-4H$_{in}$** structure has no intramolecular hydrogen bonds, rendering the ESIPT process impossible. As the excited molecule cannot undergo the *enol* → *keto* tautomerization relaxation through intramolecular proton transfer, radiative relaxation from the **1-4H$_{in}$** excited-state is regained and a strong emission band at 412 nm is observed. Fig. 5 presents the proposed mechanism of fluorescence regain upon binding an anion by cyclo[2]benzimidazole, **1**.

In conclusion, a new host for anions, cyclo[2]benzimidazole, **1**, was prepared and characterized. Compound **1** was shown to be capable of reporting the presence of anions through fluorescence increase. The molecule was found to undergo an excited-state intramolecular proton transfer (ESIPT) process. This process provides the molecule with a non-radiative relaxation pathway which explains its low quantum yield. Upon binding an anion, the **1-4H$_{in}$** tautomer can no longer form intramolecular hydrogen bonds and thus the ESIPT pathway is blocked, allowing for the molecule to relax through emissive pathways.

Notes and references

1 (*a*) *Fluorescent Chemosensors for Ion and Molecular Recognition*, ed. A. W. Czarnik, American Chemical Society, Washington, DC, 1993; (*b*) A. P. de Silva, H. Q. N. Gunaratne, T. Gunnlaugsson, A. J. M. Huxley, C. P. McCoy, J. T. Rademacher and T. E. Rice, *Chem. Rev.*, 1997, **97**, 1515; (*c*) M. H. Keefe, K. D. Benkstein and J. T. Hupp, *Coord. Chem. Rev.*, 2000, **205**, 201; (*d*) F. P. Schmidtchen and M. Berger, *Chem. Rev.*, 1997, **97**, 1609; (*e*) J. F. Callan, A. P. de Silva and D. C. Magri, *Tetrahedron*, 2005, **61**, 8551; (*f*) J. Yoon, S. K. Kim, N. J. Singh and K. S. Kim, *Chem. Soc. Rev.*, 2006, **35**, 355; (*g*) P. A. Gale, *Acc. Chem. Res.*, 2006, **39**, 465.

2 (*a*) Z. C. Wen and Y. B. Jiang, *Tetrahedron*, 2004, **60**, 11109; (*b*) F. Y. Wu, Z. Li, L. Guo, X. Wang, M. H. Lin, Y. F. Zhao and Y. B. Jiang, *Org. Biomol. Chem.*, 2006, **4**, 624; (*c*) X. Qian, Y. Xiao, Y. Xu, X. Guo, J. Qian and W. Zhu, *Chem. Commun.*, 2010, **46**, 6418; (*d*) R. M. Duke and T. Gunnlaugsson, *Tetrahedron Lett.*, 2010, **51**, 5402; (*e*) C. Hertzog-Ronen, E. Borzin, Y. Gerchikov, N. Tessler and Y. Eichen, *Chem.–Eur. J.*, 2009, **15**, 10380–10386; (*f*) E. Borzin, A. Shemesh, C. Hertzog-Ronen, Y. Gerchikov, N. Tessler and Y. Eichen, *J. Phys. Org. Chem.*, 2010, **23**, 1108–1113.

3 (*a*) V. Thiagarajan, P. Ramamurthy, D. Thirumalai and V. T. Ramakrishnan, *Org. Lett.*, 2005, **7**, 657; (*b*) T. Gunnlaugsson, M. Glynn, G. M. Tocci, P. E. Kruger and F. M. Pfeffer, *Coord. Chem. Rev.*, 2006, **250**, 3094; (*c*) Z. Xu, S. Kim, K.-H. Lee and J. Yoon, *Tetrahedron Lett.*, 2007, **48**, 3797; (*d*) Luminescence Applied in Sensor Science, *Top. Curr. Chem.*, **300**, 2011, P. Luca, M. Marco, Z. Nelsi (Eds.); (*e*) J. Geng, P. Liu, B. Liu, G. Guan, Z. Zhang and M.-Y. Han, *Chem.–Eur. J.*, 2010, **16**, 3720; (*f*) H. Salman, Y. Abraham, S. Tal, S. Meltzman, M. Kapon, N. Tessler, S. Speiser and Y. Eichen, *Eur. J. Org. Chem.*, 2005, 2207–2212.

4 (*a*) R. B. P. Elmes and T. Gunnlaugsson, *Tetrahedron Lett.*, 2010, **51**, 4082; (*b*) K. K.-W. Lo, M.-W. Louie and K. Y. Zhang, *Coord. Chem. Rev.*, 2010, **254**, 2603; (*c*) J.-C. G. Bünzli, *Chem. Rev.*, 2010, **110**, 2729.

5 (*a*) S. K. Kim, J. H. Bok, R. A. Bartsch, J. Y. Lee and J. S. Kim, *Org. Lett.*, 2005, **7**, 4839; (*b*) J. S. Wu, J. H. Zhou, P. F. Wang, X. H. Zhang and S. K. Wu, *Org. Lett.*, 2005, **7**, 2133.

6 (*a*) J. Bourson, J. Pouget and B. Valeur, *J. Phys. Chem.*, 1993, **97**, 4552; (*b*) S. Watanabe, O. Onogawa, Y. Komatsu and K. Yoshida, *J. Am. Chem. Soc.*, 1998, **120**, 229; (*c*) Z. H. Lin, Y. G. Zhao, C. Y. Duan, B. G. Zhang and Z. P. Bai, *Dalton Trans.*, 2006, 3678.

7 L. G. Arnaut and S. J. Formosinho, *J. Photochem. Photobiol., A*, 1993, **75**, 1.

8 S. G. Schulman, in *Acid–Base Chemistry of Excited Singlet States. In Modern Fluorescence Spectroscopy*, ed. E. L. Wehry, Plenum Press, New York, 1976, p. 239.

9 Starting materials were made according to: (*a*) A. W. White, R. Almassy, A. H. Calvert, N. J. Curtin, R. J. Griffin, Z. Hostomsky, K. Maegley, D. R. Newell, S. Srinivasan and B. T. Golding, *J. Med. Chem.*, 2000, **43**, 4084; (*b*) U. Tawar, A. K. Jain, B. S. Dwarakanath, R. Chandra, Y. Singh, N. K. Chaudhury, D. Khaitan and V. Tandon, *J. Med. Chem.*, 2003, **46**, 3785; (*c*) T. Fekner, J. Gallucci and M. K. Chan, *J. Am. Chem. Soc.*, 2004, **126**, 223.

10 Gaussian, DFT B3LYP, 6-311G*, M. J. Frisch, *et al.*, *Gaussian 03, Revision C.02*, Gaussian, Inc., Wallingford CT, 2004.

11 (*a*) K. Das, N. Sarkar, A. K. Ghosh, D. Majumdar, D. N. Nath and K. Bhattacharyya, *J. Phys. Chem.*, 1994, **98**, 9126; (*b*) S. Santra and S. K. Dogra, *Chem. Phys.*, 1998, **226**, 285; (*c*) D. LeGourrierec, V. A. Kharlanov, R. G. Brown and W. Rettig, *J. Photochem. Photobiol., A*, 2000, **130**, 101; (*d*) S. Santra and S. K. Dogra, *J. Mol. Struct.*, 1999, **476**, 223; (*e*) F. S. Rodembusch, F. P. Leusin, L. F. C. Medina, A. Brandelli and V. Stefani, *Photochem. Photobiol. Sci.*, 2005, **4**, 254; (*f*) T. Iijima, A. Momotake, Y. Shinohara, T. Sato, Y. Nishimura and T. Arai, *J. Phys. Chem. A*, 2010, **114**, 1603.

12 (*a*) J. S. Stephan and K. H. Grellmann, *J. Phys. Chem.*, 1995, **99**, 10066; (*b*) S. Tobita, M. Yamamoto, N. Kurahayashi, R. Tsukagoshi, Y. Nakamura and H. Shizuka, *J. Phys. Chem. A*, 1998, **102**, 5206; (*c*) F. Liang, L. Wang, D. Ma, X. Jing and F. Wang, *Appl. Phys. Lett.*, 2002, **81**, 4; (*d*) S. Oncul and A. P. Demchenko, *Spectrochim. Acta, Part A*, 2006, **65**, 179.

13 R. K. Sharma and J. L. Fry, *J. Org. Chem.*, 1983, **48**, 2112.