COMMUNICATION

ChemComm
www.rsc.org/chemcomm

Strong fluorescence enhancement of 2-bromo-3-(1*H*-indol-3-yl)maleimide upon coordination to a Lewis-acidic metal complex

Başak Kükrer Kaletaş,[a] René M. Williams,[a] Burkhard König[b] and Luisa De Cola*[a]

[a] *Universiteit van Amsterdam, Institute of Molecular Chemistry, Molecular Photonic Materials Group, Nieuwe Achtergracht 166, 1018 WV Amsterdam, The Netherlands. E-mail: ldc@science.uva.nl*

[b] *Institut für Organische Chemie, Universität Regensburg, D-93040 Regensburg, Germany. E-mail: Burkhard.Koenig@chemie.uni-regensburg.de*

Received (in Cambridge, UK) 21st December 2001, Accepted 19th February 2002

The emission intensity of an indolyl maleimide derivative increases ~80-fold by reversible coordination to (1,4,7,11-tetraazacyclododecane)zinc(II), which makes the system a promising new signalling motif for molecular sensors.

Changes in photophysical properties, which occur upon formation of a reversible assembly, are widely used in molecular chemosensors.[1,2] In particular, enhancement of emission upon chemical recognition is one of the most interesting and challenging processes, because of the high sensitivity and simplicity of detection.[2,3] Both Lewis acid (*e.g.* BF_3 with acridine)[4] and cation induced fluorescence enhancement[5] have received a lot of attention. We report in this communication a new structural motif which may find applications in this context.

Bis-indole-maleimides are common substructures of natural products[6] and their biological activity as potent inhibitors of protein kinase C (PKC)[7] stimulated their application as lead structures in drug discovery. Asymmetrically substituted indole-maleimide systems however have been studied less intensively. Investigations on the photophysical properties of such compounds have not been reported till now. Only some recent reports on related naphthalimide derivatives which address their use in fluorescence signalling are present in the literature.[8] In this communication, we report the photophysical properties of 2-bromo-3-(1*H*-indol-3-yl)maleimide (**1**) and in particular a strong emission enhancement, upon reversible coordination to (1,4,7,11-tetraazacyclododecane)zinc(II) (**2**) (Fig. 1).

Compound **1** was prepared according to a known procedure[9] employing the reaction of indolyl magnesium bromide with a 2,3-dibromomaleimide in THF. Crystals of the compound, suitable for X-ray structure analysis, were obtained by slow evaporation from an acetone–hexane solution.† The photophysical properties of **1** were determined in different solvents and the data are summarised in Table 1. Absorption and emission maxima show slight solvatochromic effect but our study was limited to the solvents in which compound **1** dissolves. Compound **1** can be considered as a push–pull type system consisting of the well-known electron acceptor, maleimide, and the electron donor, indole moiety. Therefore a π–π* state with a charge transfer (CT) character would be expected to be the lowest excited state in such a polar system, as was also suggested by the blue shift (1819 cm^{-1}) of the emission maximum at 77 K in a butyronitrile matrix. The emission properties of **1** (see Table 1) show that the compound is very weakly emitting in all of the solvents investigated except in dicholoromethane which is the least polar among the solvents studied (ϕ_{em} = 0.0140).

Coordination of the imide group with the zinc(II) azamacrocycle has been intensively studied[10] and the formation of a bond between the deprotonated imide nitrogen atom and the zinc(II) atom was confirmed by X-ray structures.[11]

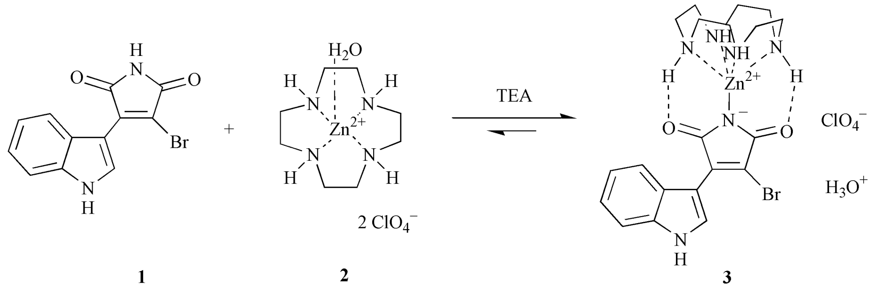
In our investigation, the titration of a 2.5×10^{-5} mol L^{-1} solution of **1** with (1,4,7,11-tetraazacyclododecane)zinc(II) bis perchlorate **2** leads to the formation of assembly **3** (see Fig. 1). In aereated acetonitrile solution, the adduct formation was followed by UV–Vis absorption and emission spectroscopy (Fig. 2). For **1**, in the presence of a weak base (1 equivalent of triethylamine, TEA), upon addition of **2** a blue shift (775 cm^{-1}) was observed for the absorption band centred at 416 nm. This was accompanied by a decrease in the molar extinction coefficient of the band and the appearance of a new band in the UV region (Fig. 2). The assembly **3** obtained by coordination of **1** with **2** has a clear 1:1 stoichiometry as confirmed by a Job plot. The changes in emission properties of **1** upon binding are even more interesting, since a strong increase in emission intensity was observed.

The solutions were excited at the isosbestic point (380 nm) and the complex formation resulted in an ~*80-fold* increase in emission quantum yield. The association constant calculated on

Table 1 Photophysical properties of compound **1** in different solvents

Solvent	Absorption, λ_{max}/nm (ε/ $M^{-1}cm^{-1}$)	Emission, λ_{max}/ nm	ϕ_{em}[a]
CH_2Cl_2	422 (7907)	554	0.0140
C_2H_5OH	426 (8229)	535	0.0022
CH_3CN	416 (7460)	559	0.0009
$(CH_3)_2NCOH$	424 (7528)	543	0.0024
CH_3NHCOH	426 (7670)	532	0.0018

[a] Total emission quantum yield calculated relative to $[Ru(bpy)_3]Cl_2$ in aerated acetonitrile solution.



1 **2** **3**

Fig. 1 Reversible formation of a coordinative bond between 2-bromo-3-(1*H*-indol-3-yl)maleimide (**1**) and (1,4,7,11-tetraazacyclododecane)zinc(II) (**2**).

DOI: 10.1039/b111599e

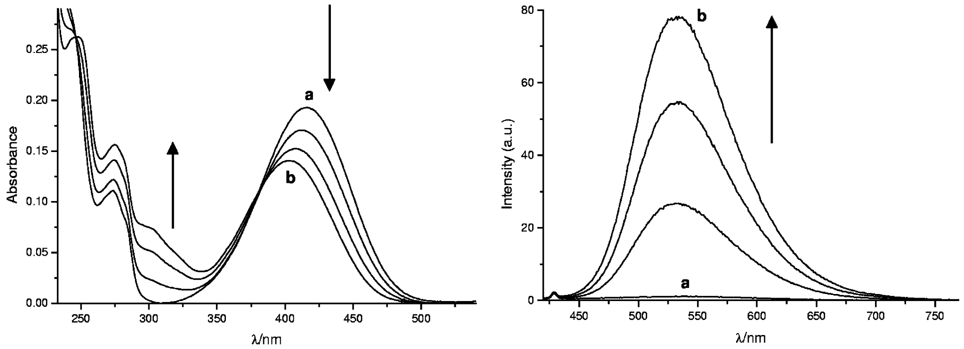


Fig. 2 Changes in the absorption (left) and emission (right) spectra of **1** upon addition of **2** in acetonitrile solution. (a) Compound **1** (2.5×10^{-5} mol L^{-1}), (b) complex **3**, obtained from a 1 : 1 mixture of **1** and **2** in the presence of 1 equiv. of TEA.

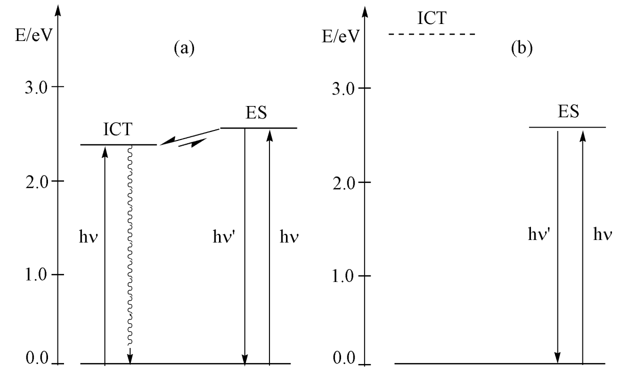


Fig. 3 Schematic diagram of the energy levels of **1** (a) in polar solvents and (b) at low temperature and upon coordination with **2**.

the basis of the change in absorption and in emission is 2×10^6 L mol^{-1}.

The reason of this emission enhancement and blue shift in the absorption maximum lies in a strong perturbation of the excited state upon coordination of the Zn moiety. As pointed out earlier, a low lying internal charge transfer state (ICT) due to the presence of an electron donor (indole) and an electron acceptor (maleimide) is the lowest excited state in polar solvents. This state is, however, a non-emitting state and it is in thermal equilibrium with π–π* excited state of the molecule (see Fig. 3a), responsible for the fluorescence of the compound at low temperature or in low polarity solvent. Upon coordination of **1** with **2**, the ICT interaction becomes weaker since the electron withdrawing group, the imide unit, is now an electron rich moiety due to the deprotonation of the NH group necessary to coordinate the metallo macrocycle **2**. The ICT state, therefore, in the assembly **3** is no longer in equilibrium with the emitting state (ES) (Fig. 3b), leading to a decrease of the dark process and to a higher emission quantum yield of the ES. This new electronic situation results in a decrease of the oscillator strength of the visible band in the absorption spectra (because of the disappearance of the ICT component of the band) and in an increase in the emission quantum yield of compound **1**. Such energetic ordering of the locally excited states relative to the CT state has been observed before for singly bonded D–A systems.[12] In order to support our explanation, the absorption and emission spectra of compound **1** in the absence and presence of a strong base, potassium carbonate, were recorded in acetonitrile solution. For the deprotonated species, we observed the same trend in the photophysical behaviour as in the low temperature experiment and upon coordination with **2**, even though the emission enhancement upon deprotonation was very moderate. This evidence and the strong enhancement in emission intensity upon coordination of a Lewis-acidic metal complex creates new opportunities for the use of these systems in the design of new sensor molecules.

In conclusion, we have shown that in general the photophysical properties, and in particular the fluorescence quantum yield, of a simple chromophore (**1**) can undergo major changes upon reversible coordination with a Lewis-acidic metallo macrocycle.

Support from the University of Amsterdam (UvA) and the Volkswagen Foundation is gratefully acknowledged. We thank Professor J. W. Verhoeven from UvA, Dr G. van der Zwan and Dr H. Joshi from Vrije Universiteit (VU) for valuable discussions.

Notes and references

† Synthetic and crystallographic data for **1** will be published elsewhere.

1 L. Prodi, F. Bolletta, M. Montalti and N. Zaccheroni, *Coord. Chem. Rev.*, 2000, **205**, 59; 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.
2 L. Fabbrizzi, M. Licchelli, P. Pallavicini, D. Sacchi and A. Taglietti, *Analyst*, 1996, **121**, 1763.
3 C. Bargossi, M. C. Fiorini, M. Montalti, L. Prodi and N. Zaccheroni, *Coord. Chem. Rev.*, 2000, **208**, 17; A. W. Czarnik, in *Fluorescent Chemosensors for Ion and Molecule Recognition*, ACS Symposium Series 538, ed. A.W. Czarnik, Oxford University Press, 1993.
4 R. Snyder and A. C. Testa, *J. Lumin.*, 1990, **47**, 35.
5 M. Kollmannsberger, K. Rurack, U. Resch-Genger, W. Rettig and J. Daub, *Chem. Phys. Lett.*, 2000, 363; S. A. Jonker, F. Ariese and J. W. Verhoeven, *Recl. Trav. Chim. Pays-Bas*, 1989, **108**, 109.
6 W. Steglich, B. Steffan and L. K. Eckhardt, *Angew. Chem.*, 1980, **92**, 463; S. Omura, I. Y. Wai, A. Hirano, A. Nakawaga, J. Awaya, H. Tsuchiya, Y. Takahashi and R. Masuma, *J. Antibiot.*, 1977, **30**, 275.
7 R. A. Bit, P. D. Davis, L. H. Elliott, W. Harris, C. H. Hill, E. Keech, H. Kumar, G. Lawton, A. Maw, J. S. Nixon, D. R. Vesey, J. Wadsworth and S. E. Wilkinson, *J. Med. Chem.*, 1993, **36**, 21; P. D. Davis, L. H. Elliott, W. Harris, C. H. Hill, S. A. Hurst, E. Keech, M. K. H. Kumar, G. Lawton, J. S. Nixon and S. E. Wilkinson, *J. Med. Chem.*, 1992, **35**, 994; R. T. Hendricks, D. Sherman, B. Strulovici and C. A. Broka, *Bioorg. Med. Chem. Lett.*, 1995, **5**, 67.
8 B. Ramachandram, N. B. Sankaran, R. Karmakar, S. Saha and A. Samanta, *Tetrahedron*, 2000, **56**, 7041; B. Ramachandram, G. Saroja, N. B. Sankaran and A. Samanta, *J. Phys. Chem. B*, 2000, **104**, 11824.
9 M. Faul, K. A. Sullivan and L. Winneroski, *Synthesis*, 1995, 1511.
10 B. Koenig, M. Pelka, H. Zieg, T. Ritter, H. Bouas-Laurent, R. Bonneau and J.-P. Desvergne, *J. Am. Chem. Soc.*, 1999, **121**, 1681; S. Aoki, C. Sugimura and E. Kimura, *J. Am. Chem. Soc.*, 1998, **120**, 10094; E. Kimura, H. Kitamura, K. Ohtani and T. Koike, *J. Am. Chem. Soc.*, 2000, **122**, 4668.
11 T. Koike, T. Gotoh, S. Aoki, E. Kimura and M. Shiro, *Inorg. Chim. Acta*, 1998, **270**, 424.
12 J. Daub, R. Engl, J. Kurzawa, S. E. Miller, S. Schneider, A. Stockmann and M. R. Wasielewski, *J. Phys. Chem. A*, 2001, **105**, 5655.