A molecular tool kit for the variable design of logic operations (*NOR*, *INH*, *EnNOR*)†

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Received (in Cambridge, UK) 23rd January 2006, Accepted 23rd March 2006
First published as an Advance Article on the web 10th April 2006
DOI: 10.1039/b600932h

A simple set of five components was used to design molecular logic gates based on phthalimide-sensitised Tb(III) luminescence, including the first report of an enabled *NOR* (*EnNOR*) gate.

The fluorescence properties of many chromophores are influenced by variations in their chemical environment, *e.g.*, changes of pH, presence of oxygen, addition of metal ions or quenchers.[1] Combinations of these variations can be potentially interpreted in terms of logic operations.[2–5] Hence, the molecular design of basic logic operations (*AND*, *OR*, *NOT*, *NAND*, *NOR*, *XOR*, *XNOR*) and therefrom derived combinatorial functions like *INHIBIT* and *EnOR* has attracted considerable attention in recent years.[6–20] We introduce a system which relies on a simple set of five components, capable of mimicking *NOR*, *INHIBIT*, and enabled *NOR* (*EnNOR*) operations based on Tb(III) luminescence as output signal. Noteworthy, the enabled *NOR* operation (*EnNOR*) was not demonstrated before at the molecular level, while *INHIBIT* gates have been reported rather scarcely.[9,14,15,18–20]

Light emission in form of very long-lived luminescence has the advantage of detecting the output signal in a time-gated manner without the disturbing influence of shorter-lived auto-fluorescence from the sample. In this respect, molecular logic gates with lanthanide luminescence as output signal have been realised before, although much less than with shorter-lived organic fluorophores.[14,15,18]

However, one major drawback of lanthanides is their poor light absorption ($\varepsilon < 1\ \mathrm{M^{-1}\ cm^{-1}}$). To circumvent this obvious disadvantage organic antenna chromophores are used, which are better light absorbers and whose excited triplet states can photosensitise the luminescence of lanthanides *via* electronic energy transfer (EET).[21] Recently, we and others have shown that aromatic dicarboximides, *i.e.*, a 1,8-naphthalimide derivative and a dendrimer with appended 2,3-naphthalimide residues, are suitable for this purpose.[18,22]

In the present work we applied the phthalimide derivative **1** (Chart 1) for the sensitisation of Tb(III) luminescence. Compound **1** was synthesised by condensation of phthalic anhydride with *N*,*N*-dimethylethylenediamine, akin to an earlier published procedure.[23] As additional structural asset this compound has an amino function, which is attached *via* an alkyl spacer to the imide nitrogen and serves as coordination site for the lanthanide ion. Potentially, the imide carbonyl oxygen atom can also participate in the binding of lanthanide ions.

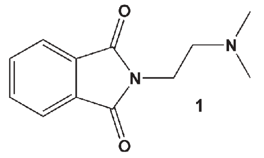

Chart 1

In the absence of lanthanide ions, intramolecular photoinduced electron transfer (PET) quenching of the excited phthalimide chromophore dominates [$\Delta G_{\mathrm{PET}} = -1.19$ and -0.76 eV for the excited singlet (S_1) and triplet state (T_1), respectively, *cf.* ESI†]. Laser-flash photolysis ($\lambda_{\mathrm{exc}} = 308$ nm) of deaerated solutions of **1** in acetonitrile (MeCN) yielded a very weak spectrum shown in Fig. 1. Addition of one equivalent of trifluoroacetic acid led to the observation of a transient absorption with a much stronger maximum at 340 nm, typical for the triplet-triplet absorption of phthalimides (ESI,† Fig. S1).[24–26] Protonation of the amine causes a switch-off of PET in the excited singlet state S_1 of **1** and leads consequently to an efficient population of the excited triplet state T_1 (*e.g.*, $\Phi_{\mathrm{ISC}} = 0.70$ for *N*-methylphthalimide).[25] A similar effect (see Fig. 1) was observed upon addition of Tb(III) triflate to a

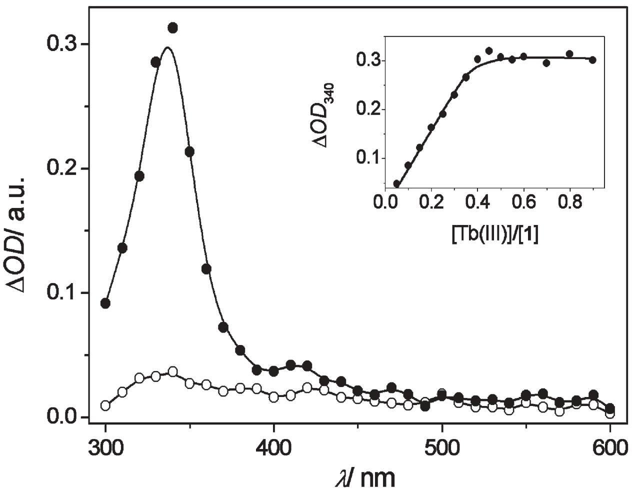

Fig. 1 Transient absorption (deaerated MeCN, $\lambda_{\mathrm{exc}} = 308$ nm, 500 ns after laser flash) of **1** (150 μM) in absence (open circles) and presence (filled circles) of 1 eq. Tb(III). Inset: transient signal at 340 nm as function of the Tb(III) concentration, and the corresponding fit.

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† Electronic supplementary information (ESI) available: Synthesis and characterisation of **1**, experimental details of photophysical measurements. See DOI: 10.1039/b600932h

deaerated solution of **1** in MeCN. This is in agreement with the complexation of the lanthanide ion by the amine nitrogen, akin to the situation for protonation. Furthermore, it should be stressed that the recovery of the phthalimide excited triplet state is a precondition for the occurrence of antenna-to-lanthanide EET (see below). The observation of the amplitude of the triplet–triplet absorption signal at 340 nm as a function of added Tb(III) yielded the curve shown in the inset of Fig. 1 (see also ESI†). Using HYPERQUAD 2003,[27] log β values of 5.7, 12.6 and 18.5 (T = 298 K, MeCN) were extracted for the complex formation of Tb**1**, Tb$\mathbf{1}_2$ and Tb$\mathbf{1}_3$, respectively.

Excitation in the phthalimide absorption band (λ_{exc} = 285 nm) of a 1:1 mixture of **1** and Tb(III) triflate yielded the typical line-like emission spectrum of Tb(III) with maxima at 486, 544, 587 and 623, which were assigned to $^5D_4 \rightarrow {}^7F_J$ (J = 6, 5, 4, 3) transitions, respectively (Fig. 2). The luminescence excitation spectrum (λ_{obs} = 544 nm) and absorption spectrum of **1** coincide virtually, which confirms the role of the phthalimide chromophore as energy donor (Fig. 2). The luminescence lifetime was measured as 1.1 ms and the quantum yield was Φ_{lum} = 0.002 in aerated MeCN solution. However, removal of oxygen by argon-outgassing yielded a five-fold larger quantum yield (Φ_{lum} = 0.01). Back-EET from the lanthanide to the antenna, as has been often claimed as reason for the oxygen sensitivity of some antenna chromophore-Tb(III) conjugates, does not play any role in this case.[8,14,15] Simply, the energy gap between the T_1 state of the antenna and the $^5D_4$ state of Tb(III) is too large (2900 cm^{-1}) to account for such a thermally-activated process.‡ Instead, a slow forward electronic energy transfer is postulated which competes with the oxygen quenching of the phthalimide triplet state. Indeed, the measured rates of both pathways confirm this assumption, with EET (k_{EET} = 1.3 × 10^5 s^{-1}) being one order of magnitude slower than oxygen quenching ($k_q[O_2]$ = 1.2 × 10^6 s^{-1}).§ A slow energy transfer (k_{EET} = 6 × 10^4 s^{-1}) from phthalimide to Tb(III) has also been reported for phthalimide-containing dendrimers.[28]

As shown above for the case of oxygen, the luminescence of lanthanides can be indirectly influenced *via* quenching of the excited triplet state of the antenna chromophore. Presumably, the triplet-excited state of the phthalimide antenna can be quenched *via* intermolecular PET by external addition of electron-donating triethylamine (TEA) to a 1:1 mixture of Tb(III) triflate and **1**. This pathway leads to reduced Tb(III) luminescence, akin to the *intramolecular* PET quenching of lanthanide luminescence, which has been demonstrated earlier.[29] A combination of the two influence factors (oxygen and triethylamine) results in a *NOR* operation. In other words, in absence of oxygen and triethylamine the strongest Tb(III) luminescence was observed (ESI,† Fig. S3). All other combinations led to weaker signals (<30%). *NOR* gates (and also *NAND* gates) are of potential interest because they are considered as universal gates, which enable the combinatorial creation of all other basic Boolean operations.

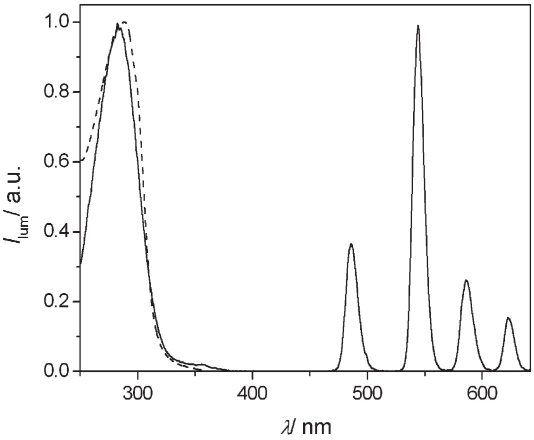


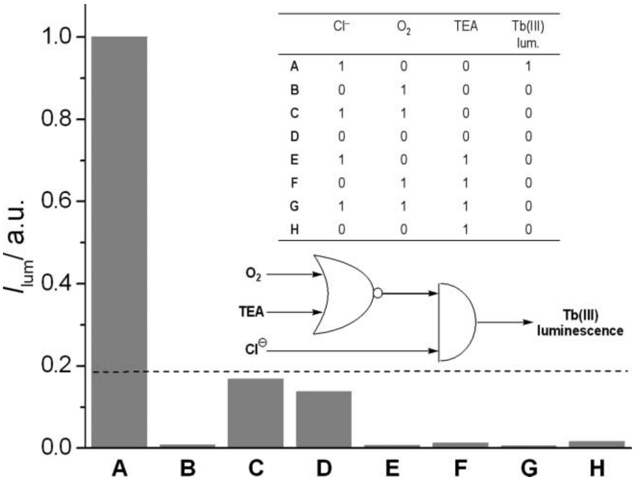
Fig. 2 Normalised luminescence spectrum (right, solid line, λ_{exc} = 285 nm) and excitation spectrum (left, solid line, λ_{obs} = 544 nm) of a 1:1 mixture of **1** (75 μM) with Tb(III) in MeCN. The dotted line (left) shows the normalised absorption spectrum of **1**.

It is generally accepted that triflate anions do not coordinate to lanthanide ions.[30–32] On the other hand, titration of a 1:1 Tb(III) triflate–**1** mixture in MeCN with different inorganic anions led to dramatic luminescence increases for $H_2PO_4^-$, Cl^- and NO_3^-. The enhancement factors were *ca.* 62 (for 3 eq. $H_2PO_4^-$) and *ca.* 7 (for 2 eq. Cl^- or 2 eq. NO_3^-). Thus, for $H_2PO_4^-$ a quite large Tb(III) luminescence quantum yield of Φ_{lum} = 0.13 (aerated solution) can be extrapolated. However, Br^- and I^- anions showed no luminescence increase. The observed anion effects on Tb(III) luminescence can be rationalised by assuming the removal of solvent molecules or residual water from the coordination sphere of the lanthanide by anion coordination, which diminishes quenching by OH or CH oscillators (for lifetime measurements see ESI,† Table S1). This has been extensively studied for related antenna–lanthanide conjugates.[30–32] Noteworthy, high luminescence quantum yields are usually only observed for lanthanide complexes where the ligand offers efficient shielding from water quenching.[33,34] For example, for imidodiphosphinate ligands Tb(III) luminescence quantum yields around Φ_{lum} = 0.19 have been reported.[33] In this respect the observed effect upon addition of $H_2PO_4^-$ is striking and will be further explored for anion sensing purposes.

The combination of oxygen and for instance chloride anions as input signals led to a logic operation characteristic for a two-input *INHIBIT* gate. An *INHIBIT* function is basically an *AND* operation where one input is reversed, *i.e.*, in our case oxygen. In the absence of oxygen and the presence of chloride ions the strongest luminescence signal of phthalimide-sensitised Tb(III) luminescence was observed, while all other combinations of these two inputs led to much weaker signals (<20%; see ESI,† Fig. S4).

Finally, all three beforehand discussed inputs, *i.e.*, oxygen, triethylamine, and chloride anions, were applied (Fig. 3). The deduced logic scheme corresponds to a *NOR* function (oxygen and triethylamine as inputs) which is only activated in the presence of the third input (chloride anions). The presence of chloride has the function of a control signal: whenever it is positive (*i.e.*, 1) the *NOR* gate is open (*i.e.*, 1), whenever it is negative (*i.e.*, 0) the *NOR* gate is closed (*i.e.*, 0). This behaviour is typical for an enabled *NOR* (*EnNOR*) gate. Although the enabled *OR* function (*EnOR*) has been demonstrated in one example before,[10] to the best of our knowledge this is the first example of a molecular *EnNOR* gate.

In summary, we showed that photophysical engineering of the energy transfer efficiency (*via* intermolecular quenching of the antenna chromophore by oxygen and triethylamine) and lanthanide luminescence (*via* anion-induced removal of solvent molecules from the coordination sphere of the lanthanide) can lead to several logic gates with different levels of complexity.



	Cl^-	O_2	TEA	Tb(III) lum.
A	1	0	0	1
B	0	1	0	0
C	1	1	0	0
D	0	0	0	0
E	1	0	1	0
F	0	1	1	0
G	1	1	1	0
H	0	0	1	0

Fig. 3 Normalised Tb(III) luminescence intensities of a 1:1 mixture with **1** (75 μM, MeCN) at λ_{obs} = 544 nm with different chemical inputs [Cl^-: 150 μM; O_2: 1.9 mM (air-equilibrated); TEA: 75 μM]. The dashed line marks the threshold. The insets show the logic table and the respective symbolic representation of the *EnNOR* function.

We acknowledge financial support by the Fundação para a Ciência e Tecnologia, Lisbon (Grant No. POCI/QUI/58535/2004 for U. P.). Further, we thank Dr C. Baleizão (Instituto Superior Técnico, Lisbon, Portugal) for phosphorescence measurements and Prof. W. M. Nau (International University Bremen, Germany) for making his laser-flash-photolysis-setup available.

Notes and references

‡ The measurement of the phosphorescence spectrum of **1** at 77 K in presence of 1 eq. Gd(III), whose energy levels are too high-lying to quench *via* energy transfer, yielded a triplet energy of E_T = 23 400 cm^{-1} (ESI,† Fig, S5). The energy of the $^5D_4$ level of Tb(III) was taken as 20 500 cm^{-1} (*cf.* ref. 8).

§ The rate constant for electronic energy transfer (k_{EET}) from phthalimide to Tb(III) was calculated with $k_{EET} = 1/\tau_{obs} - 1/\tau_0$ (with τ_{obs} = 2.4 μs in presence of 1 eq. Tb(III) and τ_0 = 3.5 μs in presence of 1 eq. H^+). The bimolecular oxygen quenching constant ($k_q = 6.3 \times 10^8$ M^{-1} s^{-1}) of the triplet state of **1** in presence of 1 eq. Tb(III) was determined *via* lifetime measurements with laser-flash-photolysis (ESI,† Fig. S6). The pseudo-unimolecular rate constant was calculated with [O_2] = 1.9 mM (air-equilibrated MeCN solution).

1 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**, 1515–1566.
2 F. M. Raymo, *Adv. Mater.*, 2002, **14**, 401–414.
3 V. Balzani, A. Credi and M. Venturi, *ChemPhysChem*, 2003, **4**, 49–59.
4 G. J. Brown, A. P. de Silva and S. Pagliari, *Chem. Commun.*, 2002, 2461–2463.
5 A. P. de Silva and N. D. McClenaghan, *Chem. Eur. J.*, 2004, **10**, 574–586.
6 A. Credi, V. Balzani, S. J. Langford and J. F. Stoddart, *J. Am. Chem. Soc.*, 1997, **119**, 2679–2681.
7 A. P. de Silva, H. Q. N. Gunaratne and C. P. McCoy, *J. Am. Chem. Soc.*, 1997, **119**, 7891–7892.
8 D. Parker and J. A. Gareth Williams, *Chem. Commun.*, 1998, 245–246.
9 A. P. de Silva, I. M. Dixon, H. Q. N. Gunaratne, T. Gunnlaugsson, P. R. S. Maxwell and T. E. Rice, *J. Am. Chem. Soc.*, 1999, **121**, 1393–1394.
10 A. Roque, F. Pina, S. Alves, R. Ballardini, M. Maestri and V. Balzani, *J. Mater. Chem.*, 1999, **9**, 2265–2269.
11 F. Pina, M. J. Melo, M. Maestri, P. Passaniti and V. Balzani, *J. Am. Chem. Soc.*, 2000, **122**, 4496–4498.
12 G. McSkimming, J. H. R. Tucker, H. Bouas-Laurent and J.-P. Desvergne, *Angew. Chem., Int. Ed.*, 2000, **39**, 2167–2169.
13 H. T. Baytekin and E. U. Akkaya, *Org. Lett.*, 2000, **2**, 1725–1727.
14 T. Gunnlaugsson, D. A. Mac Dónail and D. Parker, *Chem. Commun.*, 2000, 93–94.
15 T. Gunnlaugsson, D. A. Mac Dónail and D. Parker, *J. Am. Chem. Soc.*, 2001, **123**, 12866–12876.
16 S. Alves, F. Pina, M. T. Albelda, E. García-España, C. Soriano and S. V. Luis, *Eur. J. Inorg. Chem.*, 2001, 405–412.
17 G. Bergamini, C. Saudan, P. Ceroni, M. Maestri, V. Balzani, M. Gorka, S.-K. Lee, J. van Heyst and F. Vögtle, *J. Am. Chem. Soc.*, 2004, **126**, 16466–16471.
18 M. de Sousa, M. Kluciar, S. Abad, M. A. Miranda, B. de Castro and U. Pischel, *Photochem. Photobiol. Sci.*, 2004, **3**, 639–642.
19 J.-M. Montenegro, E. Perez-Inestrosa, D. Collado, Y. Vida and R. Suau, *Org. Lett.*, 2004, **6**, 2353–2355.
20 S. Banthia and A. Samanta, *Eur. J. Org. Chem.*, 2005, 4967–4970.
21 N. Sabbatini, M. Guardigli and J. M. Lehn, *Coord. Chem. Rev.*, 1993, **123**, 201–228.
22 J. P. Cross, M. Lauz, P. D. Badger and S. Petoud, *J. Am. Chem. Soc.*, 2004, **126**, 16278–16279.
23 J. H. Barlow, R. S. Davidson, A. Lewis and D. R. Russell, *J. Chem. Soc., Perkin Trans. 2*, 1979, 1103–1109.
24 J. D. Coyle, A. Harriman and G. L. Newport, *J. Chem. Soc., Perkin Trans. 2*, 1979, 799–802.
25 V. Wintgens, P. Valat, J. Kossanyi, L. Biczok, A. Demeter and T. Bérces, *J. Chem. Soc., Faraday Trans.*, 1994, **90**, 411–421.
26 H. Görner, A. G. Griesbeck, T. Heinrich, W. Kramer and M. Oelgemöller, *Chem. Eur. J.*, 2001, **7**, 1530–1538.
27 L. Alderighi, P. Gans, A. Ienco, D. Peters, A. Sabatini and A. Vacca, *Coord. Chem. Rev.*, 1999, **184**, 311–318.
28 R. C. Howell, S. H. Edwards, A. S. Gajadhar-Plummer, I. A. Kahwa, G. L. McPherson, J. T. Mague, A. J. P. White and D. J. Williams, *Molecules*, 2003, **8**, 565–592.
29 A. P. de Silva, H. Q. N. Gunaratne and T. E. Rice, *Angew. Chem., Int. Ed. Engl.*, 1996, **35**, 2116–2118.
30 M. Montalti, L. Prodi, N. Zaccheroni, L. Charbonnière, L. Douce and R. Ziessel, *J. Am. Chem. Soc.*, 2001, **123**, 12694–12695.
31 L. J. Charbonnière, R. Ziessel, M. Montalti, L. Prodi, N. Zaccheroni, C. Boehme and G. Wipff, *J. Am. Chem. Soc.*, 2002, **124**, 7779–7788.
32 T. Yamada, S. Shinoda and H. Tsukube, *Chem. Commun.*, 2002, 1218–1219.
33 S. W. Magennis, S. Parsons and Z. Pikramenou, *Chem. Eur. J.*, 2002, **8**, 5761–5771.
34 N. Chatterton, Y. Bretonnière, J. Pécaut and M. Mazzanti, *Angew. Chem., Int. Ed.*, 2005, **44**, 7595–7598.