

A Proton-Triggered ON–OFF–ON Fluorescent Chemosensor for Mg(II) via Twisted Intramolecular Charge Transfer

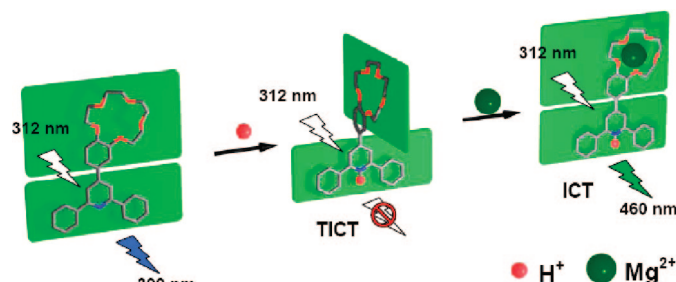
Yu Liu,* Min Han, Heng-Yi Zhang, Li-Xu Yang, and Wei Jiang

Department of Chemistry, State Key Laboratory of Elemento-Organic Chemistry,
Nankai University, Tianjin 300071, PRC

yuliu@nankai.edu.cn

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ABSTRACT



A novel fluorescent chemosensor has been synthesized and shows interesting fluorescent ON–OFF–ON processes through mediating its twisted intramolecular charge transfer (TICT) state. An exclusively fluorescent enhancement is observed for Mg²⁺.

Fluorescent chemosensors are receiving increasing attention due to their potential in analytical chemistry, the life sciences, medical analysis, and environmental monitoring.^{1–3} Sensitive magnesium ion sensors are extensively required because this biologically most abundant divalent cation plays vital roles in many cellular processes.⁴ As a result, intensive efforts have been devoted to the design and synthesis of sensitive

and selective fluorescent sensors for Mg²⁺.^{5–7} These chemosensors, which are mainly based on the fluorescence signaling mechanisms of photoinduced electron transfer (PET) and internal charge transfer (ICT), usually exhibit poor selectivity for Mg²⁺ due to the interference of related cations, such as Ca²⁺ and Ba²⁺.⁸ Herein, we report the novel fluorescent chemosensor **1**, which can signal Mg²⁺ selectively after its

(1) (a) *Fluorescent Chemosensors for Ion and Molecule Recognition*; Czarnik, A. W., Eds.; ACS Symposium Series 538; American Chemical Society: Washington, DC, 1993. (b) Valeur, B.; Leray, I. *Coord. Chem. Rev.* **2000**, *205*, 3–40. (c) de Silva, A. P.; Fox, D. B.; Huxley, A. J. M.; Moody, T. S. *Coord. Chem. Rev.* **2000**, *205*, 41–57. (d) 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. (e) Löhr, H.-G.; Vögtle, F. *Acc. Chem. Res.* **1985**, *18*, 65–72.

(2) (a) Wiegmann, T. B.; Welling, L. W.; Beatty, D. M.; Howard, D. E.; Vamos, S.; Morris, J. A. *J. Physiol.* **1993**, *265*, C1184–C1190. (b) Salvador, J. M.; Inesi, G.; Rigaud, J. L.; Mata, A. M. *J. Biol. Chem.* **1998**, *273*, 18230–18234. (c) Vo-Dinh, T.; Viallet, P.; Ramirez, L.; Pal, A.; Vigo, J. *Anal. Chim. Acta* **1994**, *295*, 67–75. (d) Hirshfeld, K. M.; Toptygin, D.; Grandhige, G.; Packard, B. Z.; Brand, L. *Biophys. Chem.* **1998**, *71*, 63–72. (e) Yuasa, J.; Fukuzumi, S. *J. Am. Chem. Soc.* **2006**, *128*, 15976–15977. (f) Yuasa, J.; Fukuzumi, S. *J. Am. Chem. Soc.* **2008**, *130*, 566–575.

(3) *New Trends in Fluorescence Spectroscopy: Applications to Chemical and Life Sciences*; Valeur, B.; Brochon, J.-C., Eds.; Springer: Berlin, 2001. More specific reviews are referenced in the various chapters

(4) (a) Rude, G. A. *Am. J. Cardiol.* **1989**, *63*, 316–321. (b) Grubb, R. D.; Maguire, M. E. *Magnesium* **1987**, *6*, 113–127. (c) Hartwig, A. *Mutat. Res.* **2001**, *475*, 1133–1143.

(5) Bühlmann, P.; Pretsch, E.; Bakker, E. *Chem. Rev.* **1998**, *98*, 1593–1688.

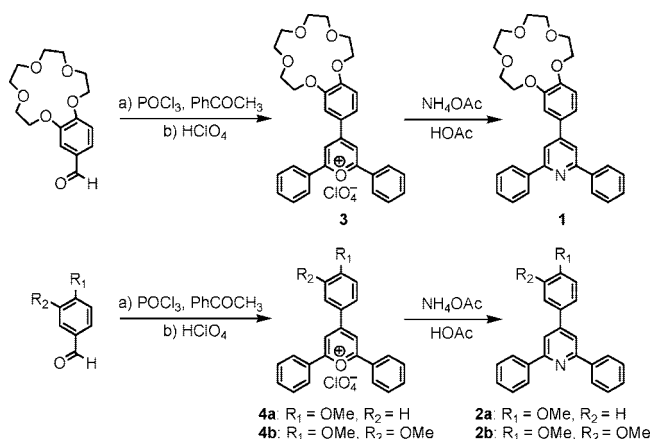
(6) (a) Farruggia, G.; Iotti, S.; Prodi, L.; Montalti, M.; Zaccheroni, N.; Savage, P. B.; Trapani, V.; Sale, P.; Wolf, F. I. *J. Am. Chem. Soc.* **2006**, *128*, 344–350. (b) Yang, Q.-Z.; Wu, L.-Z.; Zhang, H.; Chen, B.; Wu, Z.-X.; Zhang, L.-P.; Tung, C.-H. *Inorg. Chem.* **2004**, *43*, 5195–5197. (c) Arunkumar, E.; Chithra, P.; Ajayaghosh, A. *J. Am. Chem. Soc.* **2004**, *126*, 6590–6598. (d) Ajayaghosh, A.; Arunkumar, E.; Daub, J. *Angew. Chem., Int. Ed.* **2002**, *41*, 1766–1769. (e) Gromov, S. P.; Ushakov, E. N.; Fedorova, O. A.; Baskin, I. I.; Buevich, A. V.; Andryukhina, E. N.; Alfimov, M. V.; Johnels, D.; Edlund, U. G.; Whitesell, J. K.; Fox, M. A. *J. Org. Chem.* **2003**, *68*, 6115–6125.

(7) (a) Liu, Y.; Duan, Z.-Y.; Zhang, H.-Y.; Jiang, X.-L.; Han, J.-R. *J. Org. Chem.* **2005**, *70*, 1450–1455. (b) Mello, J. V.; Finney, N. S. *Angew. Chem., Int. Ed.* **2001**, *40*, 1536–1538.

protonation. For the first time, the proton-triggered ON–OFF and the OFF–ON response induced by Mg^{2+} are based on the TICT mechanism. The concept of twisted intramolecular charge transfer (TICT), first suggested by Lippert and co-workers for explaining the dual fluorescence phenomenon of *p*-(*N,N*-dimethylamino)-benzointrile,⁹ has frequently been invoked to interpret the photophysical properties of fluorophores.¹⁰ The degree of electron transfer and the change of molecular geometry are two crucial factors for the resulting TICT state. If one could control these factors by molecular recognition, the TICT theory might become another important tool for designing novel chemosensors in addition to PET and ICT.^{8c,11}

The biarylpyridine signaling unit presents an attractive fluorophore because of its visible emission from a locally excited (LE) state and a longer-wavelength visible emission band arising from a charge transfer (CT) state which can be induced by coordination of an ion to the pyridine nitrogen.^{7b,12,13} The synthetic pathways for the target compound **1** and the reference compounds **2a/2b** are shown in Scheme 1. The

Scheme 1. Synthetic Routes for **1** and **2**



intermediates **3** and **4** were prepared by heating a mixture of 4-formylbenzo-15-crown-5 and 4-methoxybenzaldehyde or 3,4-dimethoxybenzaldehyde with acetophenone in the presence of POCl_3 . The products reacted with ammonium acetate in glacial acetic acid to give **1** and **2a/2b**.

When alkali and alkaline earth cations were added to a CH_3CN solution of **1**, its original absorption bands signifi-

cantly changed in both intensity and location, and the relative emission intensity also decreased accompanied by a blue shift (Figure 1a). The replacement of **1** by either **2a** or **2b** did not

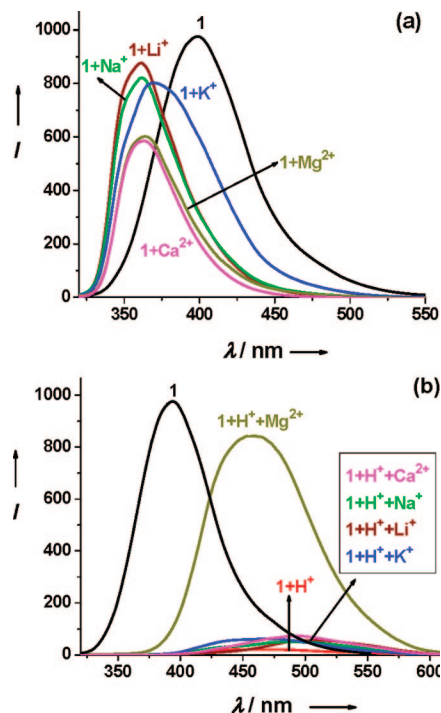


Figure 1. Emission spectra of (a) **1** (0.02 mM) with various alkali and alkaline earth cations and (b) **1** (0.02 mM) with various alkali and alkaline earth cations in the presence of 15 equiv of HClO_4 , $\lambda_{\text{ex}} = 312 \text{ nm}$.

result in significant changes in both absorption and emission spectra under the same conditions, suggesting that characteristic spectral responses are the complexation between the crown ether moiety in **1** and the cations.¹⁴ This complexation was validated by ^1H NMR experiments (Supporting Information). The data of the association constants¹⁵ for complexation of **1** with the cations indicate that the compound does not show the significant selectivity against these alkali and alkaline earth cations estimated.

Upon addition of HClO_4 to the CH_3CN solution of **1**, a remarkable bathochromic shift of the absorption maximum

(8) (a) Mashraqui, S. H.; Sundaram, S.; Bhasikuttan, A. C.; Kapoor, S.; Sapre, A. V. *Sens. Actuators, B* **2007**, *122*, 347–350. (b) Hama, H.; Morozumi, T.; Nakamura, H. *Tetrahedron Lett.* **2007**, *48*, 1859–1861. (c) Yang, J.-S.; Hwang, C.-Y.; Chen, M.-Y. *Tetrahedron Lett.* **2007**, *48*, 3097–3102. (d) Farruggia, G.; Iotti, S.; Prodi, L.; Montalti, M.; Zaccheroni, N.; Savage, P. B.; Trapani, V.; Sale, P.; Wolf, F. I. *J. Am. Chem. Soc.* **2006**, *128*, 344–350.

(9) Lippert, E.; Lüder, W.; Moll, F.; Nagele, H.; Boos, H.; Prigge, H.; Siebold-Blankenstein, I. *Angew. Chem.* **1961**, *73*, 695–706.

(10) (a) Grabowski, Z. R.; Rotkiewicz, K. *Chem. Rev.* **2003**, *103*, 3899–4031. (b) Rurack, K.; Resch-Genger, U. *Chem. Soc. Rev.* **2002**, *31*, 116–127.

(11) (a) Aoki, S.; Kagata, D.; Shiro, M.; Takeda, K.; Kimura, E. *J. Am. Chem. Soc.* **2004**, *126*, 13377–13390. (b) Morozumi, T.; Anada, T.; Nakamura, H. *J. Phys. Chem. B* **2001**, *105*, 2923–2931.

(12) (a) Mello, J. V.; Finney, N. S. *J. Am. Chem. Soc.* **2005**, *127*, 10124–10125. (b) McFarland, S. A.; Finney, N. S. *J. Am. Chem. Soc.* **2001**, *123*, 1260–1261. (c) Fang, A. G.; Mello, J. V.; Finney, N. S. *Org. Lett.* **2003**, *5*, 967–970. (d) Fang, A. G.; Mello, J. V.; Finney, N. S. *Tetrahedron* **2004**, *60*, 11075–11087.

(13) Kollmannsberger, M.; Rurack, K.; Resch-Genger, U.; Rettig, W.; Daub, J. *Chem. Phys. Lett.* **2000**, *329*, 363–369.

(14) (a) Cielen, E.; Tahri, A.; Heyen, K. V.; Hoornaert, G. J.; de Schryver, F. C.; Boens, N. *J. Chem. Soc., Perkin Trans. 2* **1998**, 1573–1580. (b) Ushakov, E. N.; Gromov, S. P.; Fedorova, O. A.; Pershina, Y. V.; Alfimov, M. V.; Barigelletti, F.; Flamigni, L.; Balzani, V. *J. Phys. Chem. A* **1999**, *103*, 11188–11193.

(15) The association constants are measured by means of titration fluorimetry with a 1:1 binding stoichiometry, and the values obtained are respectively $3.50 \times 10^4 \text{ M}^{-1}$ for 1-Li^+ , $1.19 \times 10^4 \text{ M}^{-1}$ for 1-Na^+ , $3.83 \times 10^3 \text{ M}^{-1}$ for 1-K^+ , $8.55 \times 10^4 \text{ M}^{-1}$ for 1-Mg^{2+} , and $1.64 \times 10^5 \text{ M}^{-1}$ for 1-Ca^{2+} .

was observed, and an isobestic points appeared at 312 nm (Supporting Information). Obviously, the new long-wavelength absorption band originates from the ICT process. Protonation of the pyridine group by HClO₄ leads to a decrease in the oxidation potential of the pyridine receptor, which triggers charge transfer from the benzocrown ether to the pyridine moiety.¹⁶ It is noteworthy that the emission spectra of both **1** and **2b** were almost quenched upon addition of acid ($\Phi_1 = 0.387$, $\Phi_{2b} = 0.405$ vs $\Phi_{1\cdot H^+} = 0.039$ and $\Phi_{2b\cdot H^+} = 0.037$), while that of **2a** significantly shifted from 356 to 469 nm ($\Phi_{2a} = 0.273$, $\Phi_{2a\cdot H^+} = 0.495$). The combined results can be due to a TICT fluorescence quenching process occurring between the biarylpyridine moiety and the phenyl groups for **1**·H⁺ and **2b**·H⁺, but for **2a**·H⁺, a simple ICT process occurs for **2a**. In fact, the very weak emission in the **1**·H⁺ or **2b**·H⁺ system is a combination of the LE state of the biphenylpyridine fluorophore and the TICT state, as confirmed by fluorescence lifetime measurements.

Interestingly, while the fluorescence spectrum of **1**·H⁺ hardly increased in the presence of Li⁺, Na⁺, K⁺, and Ca²⁺, a large fluorescence enhancement ($\Phi_{1\cdot H^+} + Mg^{2+} = 0.610$) was observed upon addition of Mg²⁺ (Figure 1b). The value of the fluorescence enhancement factor value (FEF) is 13 times larger than the other cations. Therefore, the protonation converts a general alkaline and alkaline earth metal ion sensor (fluorescence enhancement at 360 nm) into one which is highly selective to Mg²⁺ (large fluorescence enhancement at 460 nm). In fact, the complex of **1**·H⁺ with Mg²⁺ can be readily distinguished by the naked eye with a UV lamp (Supporting Information). In contrast, the nonfluorescent **2b**·H⁺ system did not become fluorescent in the presence of any of the metal ions. The exclusive selectivity for Mg²⁺ can be attributed to the lowest electron-donating ability of benzocrown ether because of its highest surface charge density.¹⁷

Table 1. Photophysical Data of the Investigated Species in CH₃CN

	λ_{em}/nm	Φ	FEF	τ_1/ns	τ_2/ns
1	399	0.387	-	2.70	-
1 ·Li ⁺	362	0.324	2.1	2.82	-
1 ·Na ⁺	362	0.313	2.2	2.83	-
1 ·K ⁺	370	0.354	2.1	2.71	-
1 ·Mg ²⁺	365	0.361	1.6	2.95	-
1 ·Ca ²⁺	363	0.336	1.6	2.97	-
1 ·H ⁺	475	0.039	-	0.57	4.65
1 ·H ⁺ ·Li ⁺	504	0.083	1.4	0.89	4.86
1 ·H ⁺ ·Na ⁺	488	0.068	2.1	0.68	4.71
1 ·H ⁺ ·K ⁺	477	0.079	2.9	0.76	4.69
1 ·H ⁺ ·Mg ²⁺	460	0.610	38	4.74	-
1 ·H ⁺ ·Ca ²⁺	493	0.077	2.5	0.59	4.55
2a	356	0.273	-	2.54	-
2a ·H ⁺	469	0.495	-	3.49	-
2b	393	0.405	-	2.82	-
2b ·H ⁺	564	0.037	-	0.28	4.94

To obtain in-depth mechanistic insight into the photo-physical effects allowing the operation of the novel sensor,

we performed time-resolved fluorescence experiments. As can be seen from Table 1, prior to the addition of acid, the fluorescence decays of both **1** and its complexes are monoexponential, and the observed lifetimes were all close to 3 ns. The same applies for the fluorescence decay of **2a** and **2b**. The minor differences between the lifetimes before

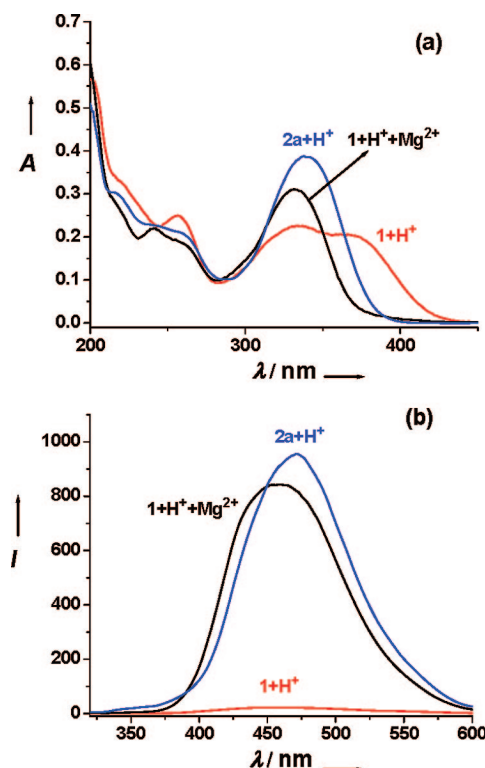


Figure 2. Absorption spectra (a) and emission spectra (b) of **1**·H⁺, **1**·H⁺·Mg²⁺, and **2a**·H⁺ in CH₃CN.

and after complexation with the cations are indicative for a retention of the nature of the electronic transition and the molecular geometry in **1**. Upon addition of acid, the fluorescence decays of **1**·H⁺, **1**·H⁺·Li⁺, **1**·H⁺·Na⁺, **1**·H⁺·K⁺, and **1**·H⁺·Ca²⁺ became biexponential. The two component decays are attributed to a mechanism involving the excitation of a single ground-state species to a fluorescent LE state followed by a fast reaction to a weakly fluorescent TICT state. The fast decay component (τ_1) corresponds to the LE state, and the slow one (τ_2) is attributed to the TICT state.¹⁸ In sharp contrast, the fluorescence decays of both **2a**·H⁺, which does not form a TICT but an ICT state, and **1**·H⁺·Mg²⁺ are monoexponential.

This observation suggests that the binding of Mg²⁺ with the crown ether prohibits TICT formation, such that the fluorescence occurs from an ICT state. The lifetime of 4.74 ns should correspond to an ICT state of **1**·H⁺. The similar

(16) (a) Zuccherro, A. J.; Wilson, J. N.; Bunz, U. H. F. *J. Am. Chem. Soc.* **2006**, *128*, 11872–11881. (b) Ihmels, H.; Meiswinkel, A.; Mohrschlacht, C. J.; Otto, D.; Waidelich, M.; Towler, M.; White, R.; Albrecht, M.; Schnurpfeil, A. *J. Org. Chem.* **2005**, *70*, 3929–3938.

(17) Geue, J. P.; Head, N. J.; Ward, A. D.; Lincoln, S. F. *Dalton Trans.* **2003**, 521–526.

(18) Kollmannsberger, M.; Rurack, K.; Resch-Genger, U.; Daub, J. J. *Phys. Chem. A* **1998**, *102*, 10211–10220.

absorption and emission changes of $1 \cdot H^+ \cdot Mg^{2+}$ with $2a \cdot H^+$ also conformed the occurrence of the ICT state (Figure 2). The schematic representation of the presumed coordination mode for the proton-triggered ON–OFF and the OFF–ON fluorescence response induced by Mg^{2+} is illustrated in Figure 3.

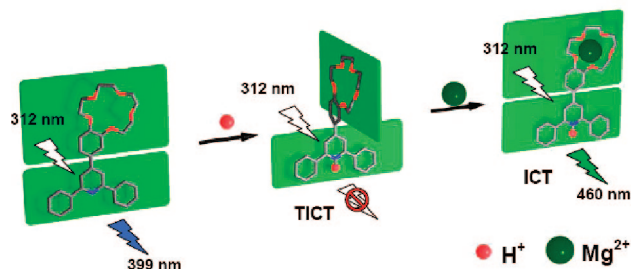


Figure 3. Schematic representation of the presumed coordination mode for the proton-triggered ON–OFF and the OFF–ON fluorescence response induced by Mg^{2+} .

In conclusion, the novel chemosensor **1** composed of biarylpyridine and crown ether moieties has been synthesized, and its spectral properties upon addition of alkali and alkaline

earth cations in neutral and acidic conditions have been investigated. In the absence of acid, the fluorescent sensor shows an unselective blue shift upon addition of all metal ions. Addition of acid efficiently quenches its emission spectrum, and the subsequent addition of metal ions which causes a fluorescent enhancement is exclusively for Mg^{2+} . Furthermore, we elucidated the mechanism that results in the ON–OFF–ON fluorescence response, indicating that the conversion to the TICT state in **1** plays an important role in the sensing. Although the application of **1** in organic solvents presents a drawback for direct implementation into potential applications, the design of related TICT sensors for different metal ions which results in improved water solubility appears to be promising in view of the present findings.

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Supporting Information Available: Experimental procedures and characterization data for the chemosensor **1** and the reference compounds **2a** and **2b**, UV–vis, fluorescence spectra, and 1H NMR spectra. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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