Synthesis and Study of A Molecular Fluorescent Chemosensor For Potassium

Wen-Sheng Xia,[a] Russell H. Schmehl,*[a] and Chao-Jun Li*[a]

Keywords: Fluorescent sensor / Potassium / Dendrimers / Self-assembling

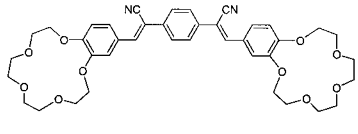
A potassium selective fluorescent chemosensor, **2**, was designed and synthesized. The molecular sensor is weakly luminescent in acetonitrile solution, but exhibits a significant increase in intensity upon addition of K^+. The luminescence intensity increases reach a plateau when the K^+/**2** ratio is 3:2. The sensor shows a linear fluorescent enhancement with the concentration of potassium ion in the presence of a large excess of sodium ion.

Introduction

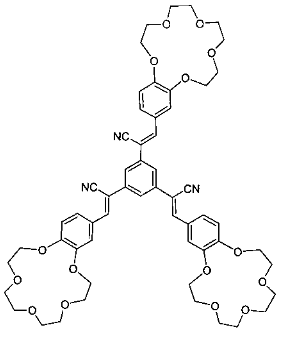
The rapid, selective, and sensitive determination of alkali and alkaline earth ions has important environmental and biological applications. Among them, the measurement of potassium is an important clinical process, for example during open-heart surgery.[1] Currently, such a measurement is carried out by using ion selective electrodes.[2] Optical sensors have received great interest in the last decade due to their often simple design and ease of handling.[3] These sensors are increasingly important for clinical and environmental analysis[4] as well as for pharmaceutical applications.[5] Among the various optical molecular sensors, extensive interest has been focused on fluorescent probes due to their very sensitive detection ability.[6] These sensor molecules exhibit large changes in their fluorescence behavior during interaction with analytes.

A challenge in the development of K^+ chemosensors for biological applications is the presence of Na^+. Because the concentration of sodium is much higher than that of potassium in human blood ($Na^+/K^+ = 30:1$), effective chemosensors must be unaffected by sodium and have a linear response to potassium when a large excess of sodium is present. Masilamani and co-workers reported that a cryptand-based fluorescent molecular sensor shows moderate selectivity towards K^+ over Na^+.[7] However a potassium-selective fluorescent chemosensor with a practical selectivity over sodium is yet to be developed. Recently, we reported the highly selective fluorescent chemosensor **1**, a dicyano-substituted distyrylbenzene derivative containing two 15-crown-5 rings, for potassium over sodium ions.[8] Studies showed that the high potassium selectivity of the sensor arises from *Self-Assembling induced Fluorescence-Enhancement (SAFE)* upon complexation with potassium.

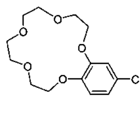
Herein we wish to report the synthesis and study of the potassium-selective fluorescent molecular sensor **2**. The chemosensor shows a linear fluorescence enhancement with increasing potassium concentration in acetonitrile; the response is observed even in highly concentrated sodium ion solutions. In addition, this chemosensor also exhibits a better-defined stoichiometry of the saturation response to potassium than **1**. This tris-crown molecular sensor represents the simplest member of much larger dendritic structures which can be prepared using similar chemistry. There is currently much interest applying dendritic structures for sensing purposes due to their well-defined structures, fixed molecular weights, and potential for the generation of new materials.[9]



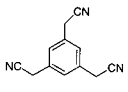
1



2



3



4

Results and Discussion

The reaction of 4-formylbenzo-15-crown-5 (**3**) with 1,3,5-(tricyanomethyl)benzene (**4**) in ethanol with a small amount of tetrabutylammonium hydroxide generated **2** in 34% isolated yield. In acetonitrile, **2** shows a broad absorption with a maximum at 362 nm. No significant change of the absorption was observed by changing the solvent polarity. Upon the addition of aqueous K^+,[10] the main absorption peak slightly blue-shifts to 358 nm together with a slight increase in absorbency (Figure 1). There are more distinct changes in the absorption spectrum in the band around 250 nm, where a distinct isobestic point is observed. The absorption obtained both in the absence of K^+ and in the presence of saturation levels of K^+ is linear with concentration over a broad concentration range of **2**. Upon excitation of **2** in acetonitrile, a weak and broad emission is

---

[a] Tulane University, Department of Chemistry,
New Orleans, LA, U.S.A.
Fax: (internat.) +1-504/865-5596
E-mail: cjli@mailhost.tcs.tulane.edu
schmehl@mailhost.tcs.tulane.edu

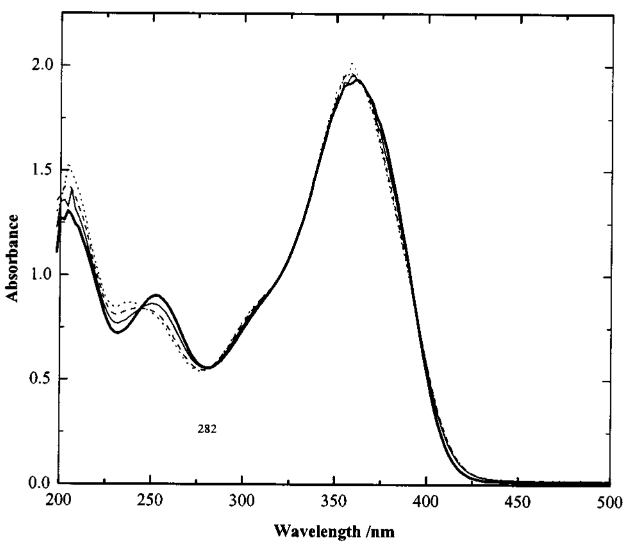


Figure 1. Fluorescence spectral changes with the addition of K^+ into a solution of **2** in acetonitrile: [**2**] = 2 · 10^{-5} M; Ratio of **2**/K+ given in the figure. Insert: titration curve of **2** in acetonitrile for M^+; observe at 468 nm.

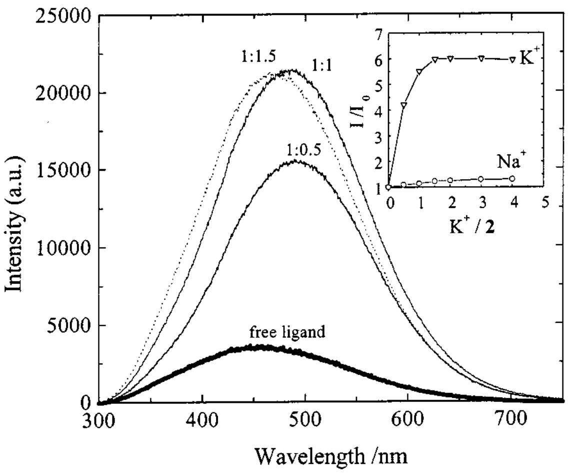
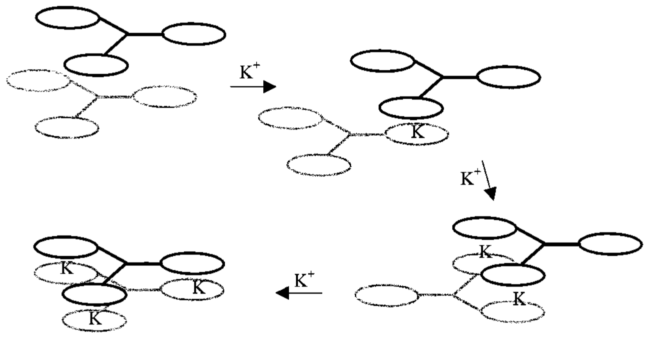


Figure 2. Absorption spectra of compound **2** in the presence (dashed line) and absence (solid line) of K^+ at several concentrations.

observed with a maximum of 458 nm and a quantum yield of approximately 0.001. The addition of a small amount of K^+ (< 0.5 equiv.) results in a significant enhancement of the fluorescence, which is accompanied by a red-shift of the emission maximum to 492 nm. Upon increasing the concentration of potassium, the emission maximum blue-shifts to 485 nm (K^+/**2** = 1) and finally to 468 nm (K^+/**2** = 1.5) to reach a saturation state as shown in Figure 2. The titration curve for K^+, Figure 2 insert, shows the saturation ratio of K^+/**2** as 3:2. The saturation fluorescence intensity, monitored at 468 nm, is about six times that of the free **2**. Excitation spectra obtained while monitoring the emission at 460 nm, 468 nm, 485 nm, and 492 nm are essentially identical in the 300 to 450 nm range (regardless of K^+ concentration). On the other hand, the addition of Na^+ only causes very slight fluorescent enhancement (25–30% of the initial value). Unlike the fluorescent change observed with the addition of potassium, a gradual red-shift from 458 nm to 480 nm is observed with the increasing concentrations of Na^+. Other alkali or alkaline earth metal ions such as Li^+, Cs^+, Mg^{2+}, and Ca^{2+} do not show any response upon their addition.



Scheme 1

The emission spectral changes observed upon addition of K^+ are unusual. The changes in the luminescence and the K^+/**2** stoichiometry beyond which no further changes are observed can be used to provide an explanation for the observed behavior. It is well-known that absorption and luminescence changes observed upon aggregation of chromophores can be related to the relative orientation of the transition dipoles of the interacting molecules.[11] It is also known that K^+ forms sandwich complexes with benzo-15-crown-5.[12] In solutions having a K^+/**2** ratio of 1, on average there will be two sandwiches per molecule of **2**. A representation of the structure formed between two K^+ and two **2** is given in Scheme 1.[13] Increasing the K^+ : **2** ratio to 1.5 should yield the tris-sandwich molecule of Scheme 1. While the orientation of the transition dipole for the emitting excited state of **2** is not clear, it is possible that discrete bis and tris sandwich complexes are formed which have significantly different electronic interactions that give rise to the observed spectroscopic behavior. An alternate explanation may be that, upon complexation of one or two K^+ ions, each chromophore has a significantly different dipole in the ground state than the uncomplexed **2**; this may give rise to charge transfer interactions that lower the transition energy. Upon complexation of all three crowns of **2** by K^+, the symmetry of the molecule is restored and the transition reverts to higher energy.

An important characteristic of any potassium chemosensor is its functioning ability in the presence of excess amounts of sodium ions. For the present system, it was found that Na^+ only slightly perturbed the response of the sensor molecule for K^+ when both ions were present in the same solution. Figure 3 shows the fluorescence response of **2** with added K^+ in the presence a large excess (60–120 folds) of Na^+. It is clear that the fluorescence response is not significantly affected by the addition of Na^+. Most interestingly, about 4.5 to 6 times of increase in the fluorescent intensity was observed when 2 equivalent of K^+ (per

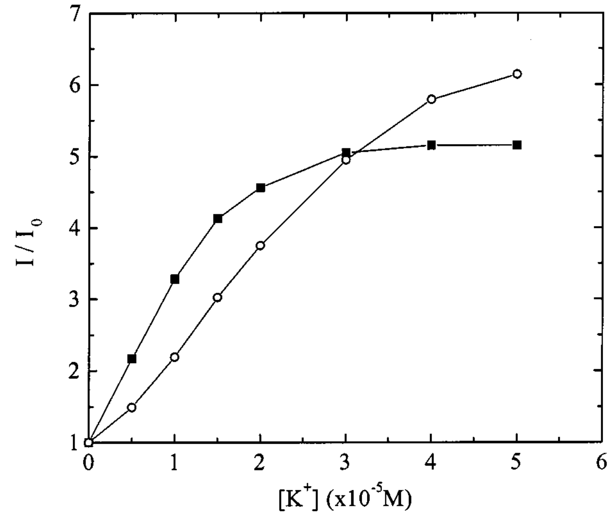


Figure 3. Fluorescence intensity of **2** with increasing amounts of added K^+ in the presence of $1.2 \cdot 10^{-3}$ M Na^+ (– ■–) and $2.4 \cdot 10^{-3}$ M Na^+ (–o–) in acetonitrile. The excitation wavelength is 360 nm and emission was monitored at 468 nm.

crown) was added in a solution with 30 fold excess of Na^+ over K^+ present.

Conclusion

In conclusion, tris-crown potassium selective fluorescent chemosensor has been synthesized which can be used to detect trace amount of potassium in the presence of a large excess amount of sodium in solution. Further studies on dendrimeric chemosensors for various analytes are in progress.

Experimental Section

General Remarks: The preparation of compound **1** was reported earlier. α,α',α''-Trichloromesitylene[14] and 1,3,5-benzenetriacetonitrile[15] were synthesized according to literature methods. – Infrared spectra were measured using a Mattson Instruments Cygnus 100 FTIR. – UV-visible absorption spectra were obtained with a Varian 100 scanning spectrophotometer. – Emission spectra were measured with a SPEX Fluorolog spectrofluorimeter equipped with a 450 W Xe arc lamp and a cooled photomultiplier housing. Spectra were not corrected for response of the PMT (Hammamatsu R 928).

(2): Compound **2** was synthesized by coupling 1,3,5-tricyanonethylbenzene (38 mg, 0.18 mmol) with 4'-formyl 15-crown-5 (160 mg, 0.54 mmol) using 4 drops of Bu_4NOH as catalyst in ethanol under reflux for 3 h. The green precipitate was filtered and purified by column chromatography with silica gel using $CHCl_3$/CH_3OH (9:1) as eluent. The product, a yellow solid, was obtained as the second column fraction (68 mg, 34%). – FTIR(film) $\tilde{\nu}$ = 2867, 2209, 1586, 1514, 1436, 1274, 1140, 1051, 936 cm^{-1}. – ^1H NMR (400 MHz, $CDCl_3$, ppm): 7.82 (s, 3 H), 7.68 (s, 3 H), 7.56 (s, 3 H), 7.45 (d, J = 8 Hz, 3 H), 6.91 (d, J = 8 Hz, 3 H), 4.32 (d, J = 14 Hz, 12 H), 3.94 (s, 12 H), 3.77 (s, 24 H). – ^{13}C NMR(100 MHz, $CDCl_3$, ppm): 151.7, 144.8, 144.1, 136.7, 126.4, 125.1, 123.2, 118.4, 113.4, 112.8, 106.9, 71.1, 70.3 (d), 69.3, 69.2, 68.8, 68.6. – $C_{57}H_{63}N_3O_{15} \cdot 2 H_2O$: calcd. C 64.23, H 6.29, N 3.94; found: C 64.61, H 6.21, N 3.85.

Acknowledgments

We are grateful to the Center of Bioenvironmental Research at Tulane University (DoD) for support of this research.

---

[1] B. Eggins, *Biosensors: An Introduction*, John Wiley Sons, Chichester, **1996**.

[2] See: K. Kimura, T. Shono, in: *Cation Binding by Macrocycles: Complexation of Cationic Species by Crown Ethers* (Eds.: Y. Inoue, G. W. Gokel), Marcel Dekker, New York **1990**.

[3] For recent examples, see: H. F. Ji, G. M. Brown, R. Dabestani, *Chem. Commun.* **1999**, 609; K. Ver Heyen, E. Clelen, G. J. Hoornaert, *Tetrahedron* **1999**, *55*, 5207; I. Leray, F. O'Reilly, B. Valeur, *Chem. Commun.* **1999**, 795; U. Oguz, E. U. Akkaya, *Tetrahedron Lett.* **1998**, *39*, 857; M. Engeser, L. Fabbrizzi, D. Sacchi, *Chem. Commun.* **1999**, 1191.

[4] For examples, see: D. Branton, J. Golovchenko, *Nature* **1999**, *398*, 660; M. A. Mortellaro, D. G. Nocera, *J. Am. Chem. Soc.* **1996**, *118*, 7414.

[5] For a recent monograph, see: M. C. Tran, *Biosensors (Sensor Physics and Technology Series)*, Chapman Hall, London, **1993**; D. Buerk, *Biosensors: Theory and Applications*, Technomic, Lancaster, **1993**; M. T. Jarvis, *Biosensors: today's technology, tomorrow's products*, SEAI Technical Publications, Madison, GA **1985**.

[6] For representitative examples, see: T. W. Bell, Z. Hou, Y. Luo, M. G. B. Drew, E. Chapoteau, B. P. Czech, A. Kumar, *Science*, **1995**, *269*, 671; Q. Zhou, T. M. Swager, *J. Am. Chem. Soc.* **1995**, *117*, 7017 and refs. cited therein; C. T. Chen, H. Wagner, W. C. Still, *Science*, **1998**, *279*, 851; R. Dagani, *CEN*, **1995**, July 17, 63; T. D. James, K. R. A. S. Sandanayake, S. Shinkai, *Nature*, **1995**, *374*, 345; M. A. Mortellaro, D. G. Nocera, *CHEMTECH* **1996**, *2*, 17; L. Fabbrizzi, A. Poggi, *Chem. Soc. Rev.* **1995**, *24*, 197; R. A. Bissell, deA. P. Silva, G. H. Q. Nimal, *Chem. Soc. Rev.* **1992**, *21*, 187; For recent monographs, see: A. W. Czarnik, (Eds.); *Fluorescent Chemosensors for Ion and Molecule Recognition*, Acs Symposium Series 538, American Chemical Society, Washington, DC, **1993**; J. P. Desvergne, A. W. Czarnik, (Eds.), *Chemosensors of Ion and Molecule Recognition*, NATO Advanced Study Institute, Ser. C, Kluwer Academic Publications, Dordrecht, NL, **1997**.

[7] D. Masilamani, M. E. Lucas, in: *Fluorescent Chemosensors for Ions and Molecule Recognition*, A. W. Czarnik (Ed.), American Chemical Society, Washington D.C. **1992**.

[8] W. S. Xia, R. H. Schmehl, C. J. Li, *J. Am. Chem. Soc.* **1999**, *121*, 5599; For a previous study on fluorescent chemosensor from this laboratory, see: D. Wang, T. J. Liu, W. C. Zhang, W. T. Slaven IV, C. J. Li, *Chem. Commun.* **1998**, 1748.

[9] For representative reviews, see: G. R. Newkome, C. N. Moorefiled, F. Vögtle, *Dendritic Molecules: Concepts, Syntheses, Perspectives*, VCH, Weinheim, **1996**; H. F. Chow, T. K. K. Mong, M. F. Nongrum, C. W. Wan, *Tetrahedron* **1998**, *54*, 8543; J. R. McElhanon, D. V. McGrath, *J. Am. Chem. Soc.* **1998**, *120*, 1647; D. K. Smith, F. Diederich, *Chem. Eur. J.* **1998**, *4*, 1353; A. W. Bosman, H. M. Janssen, E. W. Meijer, *Chem. Rev.* **1999**, *99*, 1665.

[10] KSCN and NaSCN was dissolved in water in high concentrations. No more than 10 μL aliquot was added into 3 mL of the measuring solution. The concentration of **2** in acetonitrile was kept at $2 \cdot 10^{-5}$ M.

[11] See for example: M. Kasha, *Rad. Research*, **1963**, *20*, 55.

[12] D. Wang, X. Sun, H. Hu, T. Liu, B. Chen, *Polyhedron*, **1989**, *8*, 2051.

[13] While oligomer formation is certainly possible, discrete dimeric structures are more likely to form in dilute solutions where association of K^+ with an existing sandwich is likely to lead to bis-sandwich molecules (Scheme 1).

[14] W. P. Cochrane, P. L. Pauson, T. S. Stevens, *J. Chem. Soc.*, **1968**. 630,

[15] M. Kanishi, J. Kunizaki, J. Inanaga, M. Yamaguchi, *Bull. Chem. Soc. Jpn.* **1981**, *54*, 3829.

Received August 18, 1999
[O99499]