J. Am. Chem. Soc. **1999,** *121,* 5599−5600

A Highly Selective Fluorescent Chemosensor for K^+ from a Bis-15-Crown-5 Derivative

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Received December 31, 1998
Revised Manuscript Received April 27, 1999

There has been a great deal of interest in recent years in exploiting fluorescence changes in luminescent molecular systems to signal the presence of particular substances in solution and at interfaces.[1] Rapid growth in the development of supramolecular assemblies has provided a large feedstock of molecular ensembles having a fluorescent component and a receptor capable of selectively binding substrates.[2] Such systems often make excellent sensors because of the sensitivity of fluorescence detection and the selectivity of particular substrate receptors associated with the supramolecule. A substrate of particular interest is K^+; in biological systems it is often difficult to detect because of competition with Na^+ which is generally present in much larger concentrations (i.e., $Na^+/K^+ \approx 30$ in human serum).[3] Among molecular systems available to distinguish alkali ions, crown ethers have proven effective. Recently, a few systems have been prepared that exhibit good selectivity for K^+ over Na^+ in ion transport across membranes.[4] Such systems have two crown ethers attached to a flexible hydrocarbon; K^+ complexation involves formation of a sandwich complex with the crowns. We wish to report here the fluorescence behavior of a distyryl benzene derivative, **1** (Figure 1), having two 15-crown-5 groups attached.[5] The bis-crown-distyryl benzene system forms intermolecular sandwich complexes with K^+ (but not Na^+) that result in a dramatic increase in the fluorescence intensity of the chromophore and provide excellent selectivity for K^+ over Na^+. Evidence suggests the selective enhancement of the fluorescence of the bis-crown derivative in the presence of K^+ is the result of formation of a complex that inhibits *Z*−*E* isomerization of excited **1**.

The ligand **1** is isolated as a pale yellow crystalline solid, and ^{1}H NMR analysis indicates that it is exclusively the *Z*−*Z* (trans-trans) isomer.[5] Irradiation of solutions of *Z,Z*-**1** with either room light or >400 nm light from arc lamps results in a change in the absorption consistent with formation of the *Z*−*E* (trans-cis) isomer (blue shift in the maximum and decrease in molar absorptivity).

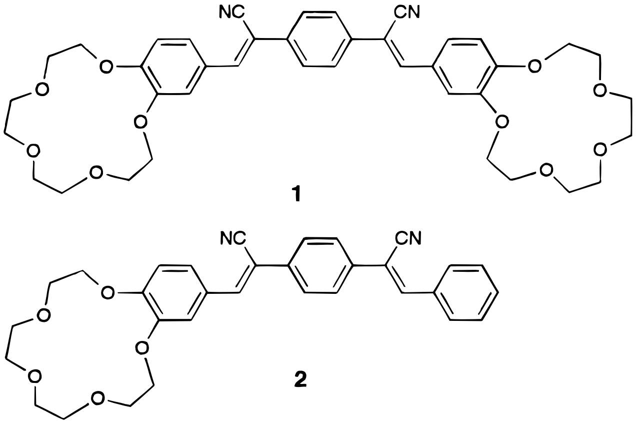

Figure 1. Drawing of sensor molecule **1** and analogue compound **2**.

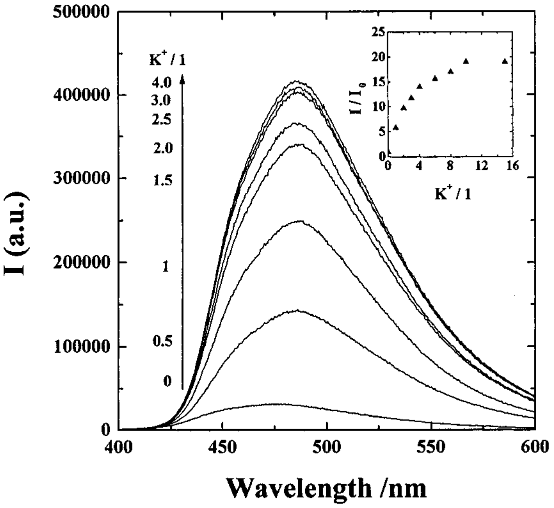

Figure 2. Emission spectra of **1** in the presence of varying amounts of K^+ in methanolic acetonitrile solutions following 325-nm excitation. Inset: integrated intensity of emission as a function of K^+ concentration.

These changes are accompanied by changes in the ^{1}H NMR spectrum that indicate *Z* to *E* isomerization in the ligand.[5] Ligand *Z,Z*-**1** is weakly luminescent. The emission maximum in CH_3CN solution, 476 nm, does not change upon irradiation, and the excitation spectrum indicates that emission arises from the *Z*−*Z* isomer. In fact, measurements by Sandros and co-workers indicate that, for a related distyrylbenzene derivative, the *E*−*E* (trans-trans) isomer emission quantum yield is 9 times greater than the *Z*−*E* (cis−trans) and 200 times greater than the *Z*−*Z* (cis-cis).[7]

The luminescence intensity of dilute solutions of **1** (either preirradiated or unirradiated) in acetonitrile increases by a factor of nearly 20 upon addition of a 10-fold molar excess of potassium.[6] Figure 2 shows emission spectra obtained for pre-irradiated solutions of **1** with varying amounts of added K^+; the inset shows the integrated intensity as a function of the K^+/**1** ratio. A small redshift of the emission maximum relative to the free ligand is observed. When solutions containing **1** and K^+ are irradiated, no change in the emission maximum of the K^+ adduct is observed. The excitation spectrum of **1** in the absence of K^+ has a maximum at 375 nm; following addition of excess K^+ the

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[1] See Fabbrizzi, L.; Poggi, A. *Chem. Soc. Rev.* **1995**, *24*, 197. (b) Bissell, R. A.; de Silva, A. P.; Nimal, G. H. Q. *Chem. Soc. Rev.* **1992**, *21*, 187. (c) Mortellaro, M. A.; Nocera, D. G. *CHEMTECH* **1996**, *2*, 17. (d) Bissell, R. A.; deSilva, A, P.; Gunaratne, H. Q. N.; Lynch, P. L. M.; Maguire, G. E. M.; McCoy, C. P.; Sandanayake, K. R. A. *Top. Curr. Chem.* **1993**, *168*, 223.

[2] See Inoue, Y.; Gokel, G. W. “Cation Binding by Macrocycles: Complexation of Cationic Species by Crown Ethers”, Dekker: New York, 1990. (b) Bradshaw, J. S.; Krakowiak, K. E.; Izatt, R. M. *Aza Crown Macrocycles* John Wiley and Sons: New York, 1993.

[3] Masilamani, D.; Lucas, M. E. In *Flourescent Chemosensors for Ion and Molecule Recognition*; Czarnik, A. W., Ed.; American Chemical Society: Washington, DC, 1992.

[4] Ueno, A.; Osa, T. In *Photochemistry in Organized and Constrained Media*; Ramamurthy, V., Ed.; VCH Publishers: New York, 1991; Chapter 16.

[5] The crown **1** was prepared by reaction of 4-formylbenzo-15-crown-5 and 1,4-phenylenediacetonitrile in methanol with a small amount of tetrabutylammonium hydroxide. A yellow solid product was obtained with yields typically around 40%. ^{1}H NMR ($CDCl_3$, δ ppm) 3.77 (16 H, d), 3.94 (8 H, t), 4.2 (8 H, h), 6.9 (2 H, d), 7.4 (2 H, d), 7.5 (2 H, s), 7.7 (6 H, d). ^{13}C NMR ($CDCl_3$, δ ppm) 151.56, 148.97, 142.40, 135.05, 126.69, 126.24, 125.07, 118.41, 113.11, 112.81, 107.51, 71.18, 70.38(d), 69.32(d), 68.85(d). Anal. Calcd. for $C_{40}H_{46}O_{10}N_2$: C, 67.42; H, 6.18; N, 3.93. Found: C, 67.38; H, 6.15; N, 3.77. ^{1}H NMR spectra of closely related cyanostilbene derivatives (vinylic proton chemical shifts ($E = 7.33$, $Z = 7.52$) were used to aid in assignment of the geometry of compound **1**. See Bottino, F. A.; Scarlata, G.; Sciotto, D.; Torre, M. *Tetrahedron* **1982**, *38*, 3712.

[6] The 325-nm isobestic point in the absorption spectrum was used for excitation to avoid changes in the luminescence intensity due to changes in absorption of the solution.

[7] (a) Sandros, K.; Sundahl, M.; Wennerstrom, O.; Norinder, U. *J. Am. Chem. Soc.* **1990**, *112*, 3082. (b) Bush, T. E.; Scott, G. W. *J. Phys. Chem.* **1981**, *85*, 144−146.

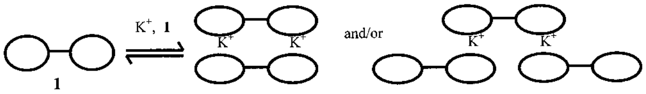
10.1021/ja984462c CCC: $18.00

maximum shifts to 362 nm, consistent with emission from a complex of **1** with K^+. Addition of Na^+ to acetonitrile solutions of **1** results in a very slight increase in the fluorescence intensity and virtually no change in the emission spectral band shape. Other alkali ions induce only very slight changes in luminescence intensity and absorption spectra. It is clear that the fluorescence response of **1** to K^+ is unique.

The emission quantum yield of solutions of **1** irradiated to steady state at an excitation wavelength of 340 nm (the isobestic point) in the absence of K^+ is 0.001 and increases to 0.019 when solutions contain >2 equiv of K^+ per **1**. The emission quantum yield of the distyryl benzene derivative in the absence of K^+ is much lower than the near unity yields measured by Sandros and co-workers for the $Z-Z$ isomer of the related tetra-*tert*-butyldistyrylbenzene derivative and other distyrylbenzene derivatives, including a di-alkoxy derivative.[7] The luminescence lifetimes of both **1** and the K^+ complex are less than or equal to the resolution of the apparatus used (approximately 1.5 ns); thus, nonradiative relaxation is rapid enough to exclude the possibility of bimolecular interactions of excited **1** and K^+.[8]

How can these observed fluorescence intensity changes be rationalized? Other fluorescence sensors for Na^+ and K^+ that use 15-crown-5 as the receptor for the alkali ion exhibit increases in fluorescence associated with inhibition of quenching of the fluorophore emission by reductive electron transfer. Coordination of the alkali ion to the oxygens of the crown raises the one-electron oxidation potential of the dialkoxy benzene of the crown, effectively shutting down photoinduced electron transfer to the excited fluorophore (which is, for example, cyanoanthracene).[9] In these systems, the ion that fits best into the crown ring, Na^+, provides the greatest fluorescence enhancement. Other systems responsive to alkali ions exhibit luminescence changes linked to conformational changes in the fluorophore.[10,11] All of these systems exhibit a much greater selectivity for Na^+. A recent report of a system having a [2.2.2] cryptand ionophore and a coumarin flourophore shows selectivity for K^+. However, the increase in fluorescence intensity upon complexation of the alkali ion is modest.[1] The change in fluorescence intensity in the cryptand system also involves inhibition of reductive photoinduced electron-transfer quenching of the coumarin excited state by the cryptand alkylamino functionality.

Scheme 1



In the system reported here, the large fluorescence enhancement is consistent with formation of a complex in which $Z-E$ isomerization of the $Z-Z$ excited state is inhibited. The luminescence data obtained for **1** and the K^+ adduct suggests that only the $Z-Z$ isomer is luminescent. It is well-known that 15-crown-5 forms sandwich complexes in which K^+ is coordinated to two crowns.[2,3] A large increase in the fluorescence quantum yield could occur in a double sandwich if isomerization pathways for nonradiative deactivation of the $Z-Z$ excited state become less favorable.[12] Formation of K^+ sandwich complexes must involve at least two molecules of **1** since intramolecular formation of K^+ sandwiches is only possible for the $E-E$ isomer. As shown in Scheme 1 above, the adduct could either be a 2:2 complex of K^+ and **1** (a discrete complex) or a complex in which each crown of one molecule of **1** forms K^+ sandwich complexes with crowns from two other moles of **1** (which could lead to K^+ sandwich bridged oligomers in solution). Recently, the crystal structure of a closely related bis-15-crown-5 compound was reported as a 2:2 adduct with K^+, indicating such adducts can form.[13] While the assignment of the structure of the K^+ adduct in the system reported here is not definitive, it is consistent with the data and serves to explain the remarkable difference in the fluorescence behavior between adducts with K^+ and those with other ions. Complexes of **1** with Na^+ do not produce bridged sandwiches[2,3] and very little change in the fluorescence behavior is observed.

To examine the importance of having two crowns per chromophore, we prepared compound **2**, which has only a single crown, and examined its luminescence behavior in the presence and absence of alkali ions. This crown exhibits no change in luminescence intensity upon addition of both Na^+ and K^+. Thus, this related chromophore having only a single crown exhibits entirely different luminescence behavior and is independent of the presence of alkali ions. Without the possibility of forming a conformationally constrained complex with K^+, the luminescence of the K^+ complex does not differ from that of the other alkali ions.

We are presently attempting to better characterize the K^+/**1** adducts and more thoroughly define the photophysical behavior of each geometric isomer of **1**. Also, we are preparing other systems that are likely to exhibit large changes in luminescence intensity when intramolecular photoreaction paths are inhibited by either intra- or intermolecular ion complexation.

Acknowledgment. The authors wish to thank the Tulane Center for Bioenvironmental Research for support of this work. C.J.L. is an NSF CAREER Awardee.

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(8) Lifetimes were measured by time-correlated single-photon counting; the limit of resolution of the system is approximately 1.5 ns.

(9) See for example Bissell, R. A.; de Silva, P.; Gunaratne, H. Q.; Lynch, P. L.; Maguire, G. E.; McCoy, C. P.; Sandanayake, K. S. *Top. Curr. Chem.* **1993**, *168*, 223, and references therein.

(10) Shizuka, H.; Takada, K.; Morita, T. *J. Phys. Chem.* **1980**, *84*, 994.

(11) Minta, A.; Tsien, R. Y. *J. Biol. Chem.* **1989**, *264*, 19449.

(12) It could be argued that the increase in luminescence is due to formation of an excimer. However, since the change in the emission maximum upon binding K^+ is very small and the ligand with a single crown, **2**, exhibits emission at the same wavelength as the bis-crown ligand, independent of the presence of K^+, excimer emission is unlikely. For stilbene, there is nearly a 100-nm difference in emission maxima between the excimer and the monomer (see Letsinger, R. L.; Wu, T. *J. Am. Chem. Soc.* **1994**, *116*, 811−812, and references therein).

(13) Wang, D.; Sun, X.; Hu, H.; Liu, Y.; Chen, B. *Polyhedron* **1989**, *8*, 2051.