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A Squaraine-based Sodium Selective Fluorescent Chemosensor

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Abstract: A novel squaraine with a lariat-crown ether cation-receptor unit was synthesized and shown to selectively respond to Na⁺ ions in polar protic solvents. The selectivity of the novel ligand, together with the impressive spectroscopic properties of squaraines yields a promising chemosensor. © 1998 Elsevier Science Ltd. All rights reserved.

Fluorescent chemosensor design is a very active field.¹ The final potential of the chemosensor is determined mostly by the choice made for the signalling process. A number of highly successful chemosensors were obtained by employing either photo-induced electron transfer² (PET) or photo-induced charge transfer³ (PICT) processes. For an on-off switching of the signal, PET design has proved to be more appropriate, whereas for designing wavelength-ratiometric chemosensors PICT-based design is preferred. Among the parameters to be optimized for a successful chemosensor, high quantum yields, high extinction coefficients, long excitation and emission wavelengths, long lifetimes, chemical and photostability, some proved to be antagonistic. One certainty is that the choice of fluorophore is very important in determining the above mentioned properties of the chemosensor. Squaraines, a class of organic dyes and pigments with impressive spectral properties, have not been exploited in the chemosensor design area excluding a few recent cases.⁴⁻⁷ The squaraines typically have large extinction coefficients (log $\varepsilon = 5.3-5.5$) and high quantum yields (0.4-0.85, in organic solvents) and absorptions and emissions in red to NIR region of the spectrum.⁸ Considering the multitude of advantages⁹ of working in the red region of the spectrum, our group is focused⁴⁻⁶ on the squaraines as long wavelength fluorophore base.

We have recently reported⁴ that azacrown appended squaraines can be synthesized in a one-pot reaction starting from squaric acid, phloroglucinol and the desired azacrown. This very facile synthesis proved to be widely applicable, and as a next step we have targeted a sodium selective chemosensor. The diazacrown 1 is known¹⁰ to have a preference for Na⁺ over K⁺, and further derivatization to lariat crown ether 2, in analogy with the previous work¹¹ is likely to improve both the binding constant and selectivity by forming a more defined cavity for the Na⁺ ions. An additional advantage of using 2 instead of 1 is that, in the former, the second amine function is protected and thus possible complications in the reaction with phloroglucinol is avoided.

The synthesis starts with 1,7-diaza-4,10,13-trioxacyclopentadecane. The reaction of this diazacrown with 2-methoxybenzylchloride, followed by purification with Silica-gel column chromatography using 10 % $Et_3N/CHCl_3$ results in compound 2 in 52% yield. Then the lariat crown ether was treated with phloroglucinol in 50/50 n-BuOH/Toluene in a Dean-Stark apparatus, removing the water formed azeotropically. The reaction was complete in 4 hours, the half equivalent of squaric acid was added and the reflux was continued for 8 hours.



Scheme 1. Synthesis of the sodium selective chemosensor: (i) 2-methoxybenzylchloride, (ii) phloroglucinol, n-BuOH/PhCH₃, reflux, (iii) squaric acid, n-BuOH/PhCH₃, reflux.



Figure 1. Absorption spectrum of the sodium selective chemosensor as a function of increasing concentrations of Na⁺: (a) 0 mM, (b) 0.5 mM, (c) 0.6 mM, (d) 0.7 mM, (e) 1 mM, (f) 2 mM, (g) 4 mM.

The squaraine dye formed precipitates as the reaction progresses. The dye was then collected by filtration and washed with isopropyl alcohol. The overall yield for the synthesis is 40%. Squaraine **3** is soluble in DMF and isopropyl alcohol, the absorption spectrum shows an intense peak at 642 nm and the emission is maximum at 651 nm. As the concentration of Na⁺ is increased, absorption at 642 nm decreases, while a broad new peak forms at 604 nm with a clean isosbestic point at 614 nm (Figure 1). The decrease in emission intensity parallels (Figure 2) that of absorption changes, the sodium bound form is very weakly fluorescent.



Figure 2. Emission spectrum of 3 as a function of increasing Na⁺ concentrations: (a) 0 mM, (b) 0.5 mM, (c) 0.7 mM, (d) 1 mM, (e) 2 mM, (f) 3 mM, (g) 4 mM. Excitation is at 642 nm.

The averaged dissociation constant is 0.7 mM in isopropyl alcohol. Saturated solutions of potassium nitrate, perchlorate or thiocyanate salts has no affect on either the absorption or emission spectrum, revealing the selective nature of the interaction.

Various derivatives of the parent azacrown unit (1) has been utilized in Tsien's work,¹⁰ yielding a Na⁺- selective chemosensor that works in aqueous media; however, extension of the sensing action to the red-NIR region of the spectrum appears to be possible by appropriate derivatization of the squaraines. As demonstrated in this work, with judicious choice of the receptor units attached, squaraines are likely to yield interesting fluorescent chemosensors.

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