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A fluoroionophore for detection of potassium ions: 9-anthryl-substituted azacrown ether covalently linked to a 1,3-alternate calix[4]arene

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Abstract

N-(9-methyl-anthracene)-25,27-bis(1-propyloxy)calix[4]arene azacrown-5 (**II**) and its model compound *N*-(9-anthrylmethyl)aza-18-crown-6 (**I**) were synthesized and tested as fluoroionophores for the selective detection of potassium ions with a view to the use of **II** in the fabrication of potassium ion sensors. Compound **II** consists of a 1,3-alternate calix[4]arene group covalently linked to an azacrown ether that is *N*-substituted with a fluorescent anthracene group. This compound acts as an 'off–on' fluorescent indicator for ion complexation. In dichloromethane solution, compound **II** exhibits good sensitivity to potassium ions and forms a 1:1 fluoroionophore–ion complex. Studies demonstrate that **II** is selective for potassium over other alkali metal cations, with excellent selectivity over sodium and lithium ($\log K_{K,Na} \sim \log K_{K,Li} \leq -3.5$) and moderate selectivity over rubidium and cesium ($\log K_{K,Rb} \sim \log K_{K,Cs} \sim -1$). Sensitivity of **II** to potassium is considerably enhanced in dichloromethane in comparison to methanol/dichloromethane mixtures, presumably due to two effects: a hydrogen-bonding interaction of methanol with the azacrown nitrogen atom, and poor solvation of the ion by dichloromethane, the latter creating a driving force for complexation.

Keywords: Fluoroionophore; Calix[4]arenes; Photoinduced electron transfer

1. Introduction

The use of crown ethers that are covalently bound to calix[4]arenes to selectively complex with specific ions has been studied extensively [1–15]. Reinhoudt and co-workers [1,2] reported selective binding of potassium ions (relative to sodium or lithium) to calix[4]crown-5 structures, noting that the K^+/Na^+ selectivity was dependent on the calix[4]crown conformation (i.e., cone, partial cone or 1,3-alternate).

Since these early reports, studies have expanded to include benzocrown and azacrown structures and their selectivity and sensitivity for binding a wide variety of metal cations and their practical application as sensors, particularly optical sensors. For example, Dabestani and co-workers [3–6] reported the synthesis and characterization of an *o*-benzocrown-6-calix[4]arene structure consisting of a 9-cyanoanthryl chromophore covalently linked through a methylenic bridge to the benzo group. This fluoroionophore acts as an off–on fluorescence switch that is triggered by ion complexation. In the absence of cation, the benzocrown group quenches the cyanoanthryl excited singlet state by photoinduced electron transfer (PET), while in the presence of complexed cation, the electrostatic field of the ion disrupts this PET process. This particular system exhibited high sensitivity for cesium ions (important in the detection of radioactive contamination) and relatively good selectivity for cesium over other alkali metal ions. Similar structures make use of azacrown rings instead of benzocrowns [7–14], presumably because the lower oxidation potential of the amine (1.15 V [16]) relative to the benzo group (1.45 V [16]) allows greater flexibility in the selection of the fluorophore used in the system, i.e., the amine provides greater driving force for the electron transfer process. Kim et al. [10] have synthesized azacrown-5 calix[4]arenes where the nitrogen of the azacrown is substituted with benzyl or picolyl groups. In the picolyl systems, selectivity for silver ions was found to be an order of magnitude higher than for other cations measured. The presence of the pyridinyl ring apparently contributes to the metal ion binding.

More recently, Dabestani and co-workers [8] suggested that a structure consisting of separate binding sites for cesium and potassium cations could function as a proton-activated logic device. This structure consists of a benzocrown-6 calix[4]arene covalently linked through the benzo group to an anthryl azacrown-6. The anthryl azacrown structures (crown-5, crown-6) have been shown previously to be sensitive to sodium and potassium cations among

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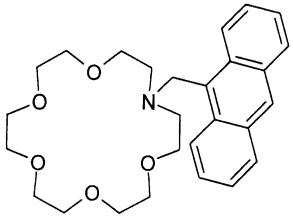
others, although the selectivity for these ions over other alkali metal ions is only modest [14].

Our focus in this work and in earlier studies has been the construction of fluoroionophores specific for potassium and sodium cations in the human physiological range that can be incorporated into solid-state optical sensors for clinical diagnostic measurements. To this end, we have synthesized **II** (and its model compound **I**), which combines the known optical response of anthryl azacrown-6 to potassium ions with expected enhanced selectivity provided by coupling the azacrown to a 1,3-alternate calix[4]arene. Described here are the results of these initial studies, potentially promising increased selectivity for potassium over sodium and other alkali metal ions and good sensitivity for potassium ions in the human physiological range.



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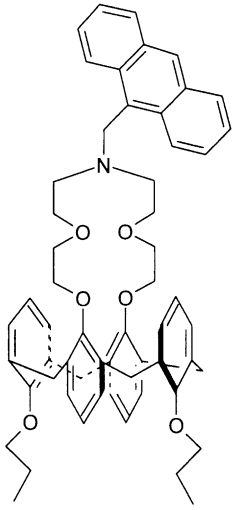

II

2. Experimental

2.1. General

Mass spectra were performed by SYNPEP Corporation, Dublin, CA. Melting point data was obtained using a Mel-Temp capillary melting point apparatus and is not corrected. ^{1}H and ^{13}C NMR spectra were recorded with a Bruker Avance 400 in $CDCl_3$. All solvents and reagents were used as supplied from Aldrich Chemical unless stated otherwise. Calix[4]arene was purchased from Acros.

2.2. Synthesis of *I*

*N-(9-anthrylmethyl) monoaza-18-crown-6 (**I**)*. The synthesis of **I** was based on a modified literature procedure [14]. 1-Aza-18-crown-6 (0.515 g, 1.95 mmol), 9-chloroanthracene (0.400 g, 1.76 mmol), and triethylamine (0.526 g, 0.74 ml) were refluxed in 1,4-dioxane (200 ml) for 24 h. The solvent was evaporated, and the product extracted with a 2:3 dichloromethane:water mixture. The organic phase was rinsed three times with water and then dried over anhydrous magnesium sulfate. Further purification was done using thin layer chromatography preparatory plates in the dark (dichloromethane:ethanol, 17:1 as eluent), to yield *N*-(9-anthrylmethyl) monoaza-18-crown-6 (0.176 g, 0.388 mmol). The product was then recrystallized with dichloromethane and ether to yield a yellow solid (22%). ^{1}H NMR ($CDCl_3$). δ 8.6–7.4 (m, 9H), 4.6 (s, 2H), 3.7–3.5 (m, 20H), 2.9 (t, 4H). ^{13}C NMR ($CDCl_3$). δ 52.4 (CH_2), 54.3 (CH_2), 71.3–70.6 (CH_2 crown), 131.8–124.8 (anthracene).

2.3. Synthesis of *II*

Preparation of 25,27-bis(1-propyloxy)calix[4]arene. The preparation of dipropyl-calix[4]arene followed a literature method [15]. In a 250 ml round bottom flask 5.08 g calix[4]arene (11.9 mmol), 4.87 g 1-iodopropane (28.6 mmol) and 3.95 g (28.6 mmol) K_2CO_3 were suspended in 150 ml dry acetonitrile and boiled under reflux for 24 h. The solvent was removed in vacuo and 50 ml 2 N HCl and 50 ml CH_2Cl_2 were added and the phases were separated. The aqueous phase was extracted two times with 30 ml CH_2Cl_2, the organic phases were combined dried with Na_2SO_4 and the solvent removed in vacuo. The crude product was recrystallized from methanol/CH_2Cl_2 (5:1) and gave 4.37 g (72%) of 25,27-bis(1-propyloxy)calix[4]arene as white crystals. The ^{1}H NMR spectrum corresponds to the published data [2]. ^{1}H NMR ($CDCl_3$) δ 1.32 (t, $J = 7.3$ Hz, 6H, $OCH_2CH_2CH_3$), 2.08 (m, 4H, $OCH_2CH_2CH_3$), 3.40 (d, $J = 12.9$ Hz, 4H, Ar–CH_2–Ar), 3.98 (t, $J = 6.2$ Hz, 4H, $OCH_2CH_2CH_3$), 4.35 (d, $J = 12.9$ Hz, 4H, Ar–CH_2–Ar), 6.65 and 6.74 (t, $J = 7.5$ Hz, 2H each, Ar*H* para), 6.92 and 7.06 (d, $J = 7.5$ Hz, 4H each, Ar*H* meta), 8.30 (s, 2H, O*H*).

Preparation of 2-(2-chloroethoxy)ethyl p-toluenesulfonate. Preparation was done according to a standard procedure for the preparation of *p*-toluenesulfonic esters [17]. In a round bottom flask 9.53 g (50 mmol) of *p*-toluenesulfonylchloride were mixed with 7.47 g (60 mmol) 2-(2-chloroethoxy)ethanol in 50 ml $CHCl_3$. The mixture was stirred and cooled below 5 °C and 10.1 g (100 mmol) triethylamine were added drop-wise at this temperature. After the addition was completed, the mixture was stirred for another 3 h at room temperature. At which point, a mixture of 50 g ice and 20 ml conc. HCl was added carefully and stirred for

30 min. The chloroform phase was separated, washed three times with 30 ml water, dried with Na_2SO_4 and the solvent removed in vacuo upon which 12.5 g (90%) of a yellowish oil was obtained. The product was used without further purification. ^{1}H NMR ($CDCl_3$) δ 2.45 (s, 3H, Ar–CH_3), 3.55 (t, J = 7.4 Hz, 2H, OCH_2CH_2Cl), 3.65–3.77 (m, 4H, $OCH_2CH_2OCH_2CH_2Cl$), 4.17 (t, J = 7.2 Hz, 2H, $SO_2OCH_2CH_2O$), 7.42 and 7.84 (2d, J = 7.5 Hz, 2H each, Ar*H* ortho and para).

Preparation of 25,27-bis(1-propyloxy)-26,28-bis(5-chloro-3-oxapentyloxy)calix[4]arene. A solution of 2.54 g (5 mmol) 25,27-bis(1-propyloxy)calix[4]arene, 5.57 g (20 mmol) 2-(2-chloroethoxy)ethyl *p*-toluenesulfonate and 3.36 g (10 mmol) Cs_2CO_3 in 150 ml dry acetonitrile was heated at reflux under nitrogen for 24 h. The solvent was removed in vacuo and 50 ml 2 N HCl and 50 ml CH_2Cl_2 were added and the phases were separated. The aqueous phase was extracted two times with 30 ml CH_2Cl_2, the organic phases were combined dried with Na_2SO_4 and the solvent removed in vacuo. The crude product was recrystallized twice from methanol/CH_2Cl_2 (5:1) and gave 3.07 g (85%) of 25,27-bis(1-propyloxy)-26,28-bis(5-chloro-3-oxapentyloxy) calix[4]arene as white crystals. The ^{1}H NMR spectrum corresponds to the published data [10]. ^{1}H NMR ($CDCl_3$) δ 0.93 (t, J = 7.2 Hz, 6H, $OCH_2CH_2CH_3$), 1.65 (m, 4H, $OCH_2CH_2CH_3$), 3.50–3.80 (m, 28H), δ 6.67–6.72 (m, 4H, Ar*H* para), 6.97 and 7.05 (d, J = 7.6 Hz, 4H each, Ar*H* meta).

Preparation of N-tosyl 25,27-bis(1-propyloxy)calix[4] arene azacrown-5. A solution of 1.446 g (2 mmol) 25,27-bis(1-propyloxy)-26,28-bis(5-chloro-3 oxapentyloxy)-calix [4]arene, 0.343 g (2 mmol) *p*-toluenesulfonamide and 1.38 g (10 mmol) K_2CO_3 in 70 ml dry DMF was heated at reflux under nitrogen for 24 h. The solvent was removed in vacuo and 50 ml 2 N HCl and 50 ml CH_2Cl_2 were added and the phases were separated. The aqueous phase was extracted two times with 30 ml CH_2Cl_2, the organic phases were combined dried with Na_2SO_4 and the solvent removed in vacuo. The crude product was purified by column chromatography using ethyl acetate:hexane 1:4 (R_f = 0.4) to provide 1.15 g (70%) *N*-tosyl 25, 27-bis(1-propyloxy)calix[4]arene azacrown-5. The ^{1}H NMR spectrum corresponds to the published data [10]. ^{1}H NMR ($CDCl_3$) δ 0.72 (t, J = 7.3 Hz, 6H, $OCH_2CH_2CH_3$), 1.28 (m, 4H, $OCH_2CH_2CH_3$), 2.45 (s, 3H, ArCH_3), 3.20–3.80 (m, 28H), 6.74–6.82 (m, 4H, Ar*H* para), 7.01–7.06 (m, 8H, Ar*H* meta) 7.34 (d, 2H, J = 7.4 Hz TosAr*H* ortho), 7.74 (d, 2H, J = 7.4 Hz, TosAr*H* meta).

Preparation of 25,27-bis(1-propyloxy)calix[4]arene azacrown-5. The reductive detosylation of *N*-tosyl 25,27-bis (1-propyloxy)calix[4]arene azacrown-5 followed the procedure described by Quici et al. [17]. Under nitrogen, 380 mg (10 mmol) $LiAlH_4$ was added carefully to a solution of 410 mg (0.5 mmol) *N*-tosyl 25,27-bis(1-propyloxy)calix[4] arene azacrown-5 in 80 ml dry THF. The suspension was heated to reflux for 24 h and then allowed to cool to RT, and the excess $LiAlH_4$ was decomposed with stoichiometric amounts of water. The aluminum oxide was filtered off and carefully washed with 80 ml THF and the solvent evaporated. The crude product was purified on prep. TLC using ethyl acetate:hexane 1:1 (R_f = 0.2) to afford 203 mg (61%) 25,27-bis(1-propyloxy)calix[4]arene azacrown-5 as a pale yellow solid. The ^{1}H NMR spectrum corresponds to the published data [10]. ^{1}H NMR ($CDCl_3$) δ 0.82 (t, J = 7.3 Hz, 6H, $OCH_2CH_2CH_3$), 1.52 (m, 4H, $OCH_2CH_2CH_3$), 2.77 (s, 4H, –$OCH_2CH_2NCH_2$–), 3.43–3.60 (m, 16H, –CH_2–), 3.77 (s, 8H, Ar–CH_2–Ar), 6.78 and 6.83 (t, J = 7.5 Hz, 2H each, Ar*H* para), 7.03 and 7.13 (d, J = 7.5 Hz, 4H each, Ar*H* meta).

*Preparation of N-(9-methyl-anthracene)-25,27-bis(1-propyloxy)calix[4]arene Azacrown-5 (**II**)*. A solution of 100 mg (0.15 mmol) 25,27-bis(1-propyloxy)calix[4]arene azacrown-5, 35 mg (0.15 mmol) 9-(chloromethyl)anthracene and 46 mg (0.45 mmol) triethylamine in 50 ml of dry dioxane was refluxed for 24 h. The solvent was removed in vacuo and 50 ml 2 N HCl and 50 ml CH_2Cl_2 were added and the phases were separated. The aqueous phase was extracted two times with 30 ml CH_2Cl_2, the organic phases were washed once with 30 ml of 2 N NaOH, separated, dried with Na_2SO_4 and the solvent was evaporated in vacuo. The crude product was purified on prep. TLC using CH_2Cl_2 (R_f = 0.3) to afford 23 mg (18%) *N*-(9-methyl-anthracene)-25,27-bis(1-propyloxy)calix[4]arene azacrown-5, the title compound, as white crystals. m.p. 188–190; ^{1}H NMR ($CDCl_3$) δ 0.70 (t, J = 7.3 Hz, 6H, $OCH_2CH_2CH_3$), 1.21 (m, 4H, $OCH_2CH_2CH_3$), 2.70–3.85 (m, 28H), 4.57 (s, 2H, ArCH_2NR_2), 6.77–6.97 (m, 4H, Ar*H* para), 7.01–7.08 (m, 8H, Ar*H* meta) 7.46–8.79 (m, 9H, Anthr-Ar*H*). ^{13}C NMR ($CDCl_3$) δ 10.42 ($OCH_2CH_2CH_3$), 22.80 ($OCH_2CH_2CH_3$), 38.57 ($OCH_2CH_2CH_3$), 54.03 (ArCH_2Ar), 70.167, 70.89, 71.23, 72.39 (O–CH_2–CH_2–O–CH_2–CH_2–N) 122.59, 122.69, 125.31, 125.67, 126.07, 129.42, 130.12, 130.23, 131.85, 134.18, 134.50, 157.24, 157.47 (Ar-carbon). MS m/z (M^+) calcd. 856.11 found 856.4.

2.4. Fluorescence measurements

Fluorescence emission and excitation spectra were obtained with a Perkin Elmer LS-50B Fluorimeter in dichloromethane. Fluorescence was measured as a function of metal ion concentrations where the metal ions were added as the acetate salts. Fluorescence areas were determined by integrating the spectrum over a fixed wavelength range.

2.5. Calculations

Molecular modeling was preformed on an SGI 320 running Windows NT. Calculations were carried out using the molecular operating environment (MOE) ver. 2000.02 computing package (Chemical Computing Group Inc., Montreal, Quebec, Canada). Structures were minimized first using the

AMBER94 potential control under a solvent dielectric of 5. PEF95SAC was used to calculate partial charges. Minimized structures were then subjected to a 30 ps molecular dynamics simulation employing the NVT statistical ensemble. The structures were heated to 400 K, equilibrated at 310 K and cooled to 290 K in the dynamics thermal cycle at a rate of 10 K/ps. The lowest energy structures obtained from these dynamics calculations were then minimized again. Electrostatic calculations were then performed on the molecules using the default parameters.

3. Results and discussion

3.1. Emission spectra of *I* and *II*

Fig. 1 shows the fluorescence spectra obtained for *N*-(9-anthrylmethyl) monoaza-18-crown-6, **I**, in the absence and presence of added concentrations of potassium acetate in dichloromethane. We consider **I** as a model for **II** since it contains the same chromophore/amine electron transfer system as **II** and the size and electrostatic characteristics of the complexation sites are qualitatively similar in both compounds as determined by molecular modeling. This model compound was synthesized in order to serve as a baseline in the determination of whether the selectivity and sensitivity of the azacrown moiety is increased by the incorporation of the calix[4]arene group.

The fluorescence behavior of **I** clearly demonstrates that the PET off–on switching mechanism that occurs in response to ion complexation is operative. In the absence of ions, the anthryl fluorescence is at a minimum and increases linearly with addition of potassium acetate up to a concentration marginally higher than the concentration of **I**, after which it begins to plateau. This indicates that the ion and ionophore are likely forming a 1:1 complex in solution as expected given the reported behavior of similar azacrowns [14]. The results obtained show a ca. 50-fold enhancement of the fluorescence intensity upon addition of potassium ions. This is consistent with previously published data [14] and certainly indicates sufficient sensitivity and dynamic range for further study following incorporation of the calix[4]arene group.

Protonation of the nitrogen atom in the azacrown can potentially block the electron transfer process and for this reason, the organic base, benzyltrimethylammonium hydroxide (BTMAH), was added to minimize protonation. In fact, the addition of base to solutions of **I** in the absence of potassium ions causes a 4-fold decrease in the fluorescence intensity, consistent with this protonation effect. Nevertheless, some fluorescence is still observed. It is difficult to unambiguously determine the origin of this fluorescence, i.e., whether it reflects the intrinsic rate constants for fluorescence and electron transfer in this molecule or whether there is a low background concentration of potassium, sodium or other cations present as impurities. Indeed, the intensity of the fluorescence emission in the presence of base and in the absence of added potassium is somewhat variable and it is possible to reduce this intensity by using rigorously cleaned glassware during sample preparation, suggesting that at least some of the effect is due to impurity ions.

Fig. 2 shows the fluorescence spectra obtained for **II** in the absence and presence of added potassium acetate in dichloromethane solution. In order to compare directly the behavior of **I** and **II**, the spectrum for **II** in the absence of potassium ions was normalized to that of **I** to account for differences in sample absorbance at the excitation wavelength. As with **I**, the fluorescence intensity of **II** in the presence of added base, increases dramatically with addition of potassium ions, although both the rate of increase as a function of ion concentration and the dynamic range for **II** is

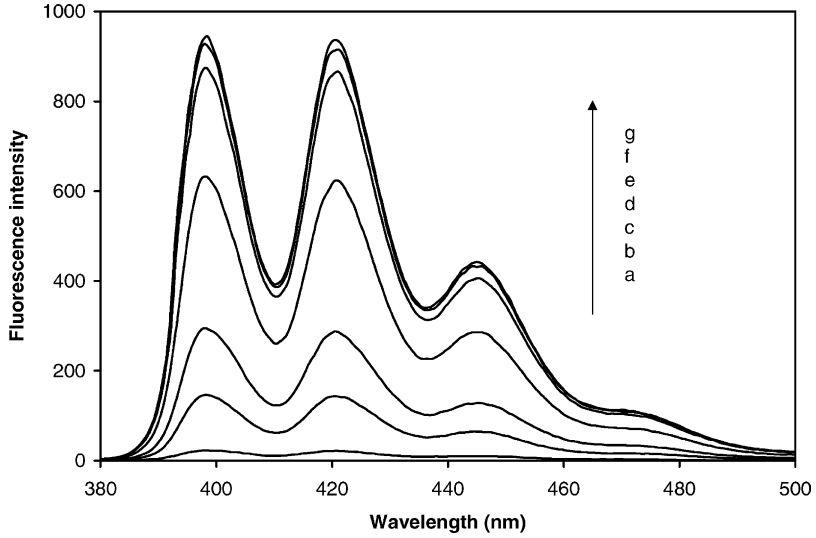

Fig. 1. Fluorescence emission spectra (λ_{ex} 355 nm) of **I** (5.5×10^{-6} M) in dichloromethane with added BTMAH (9.0×10^{-7} M) as a function of [K^+]. a: 0 μM, b: 1.25 μM, c: 2.5 μM, d: 5 μM, e: 7.5 μM, f: 10 μM, g: 11.3 μM.

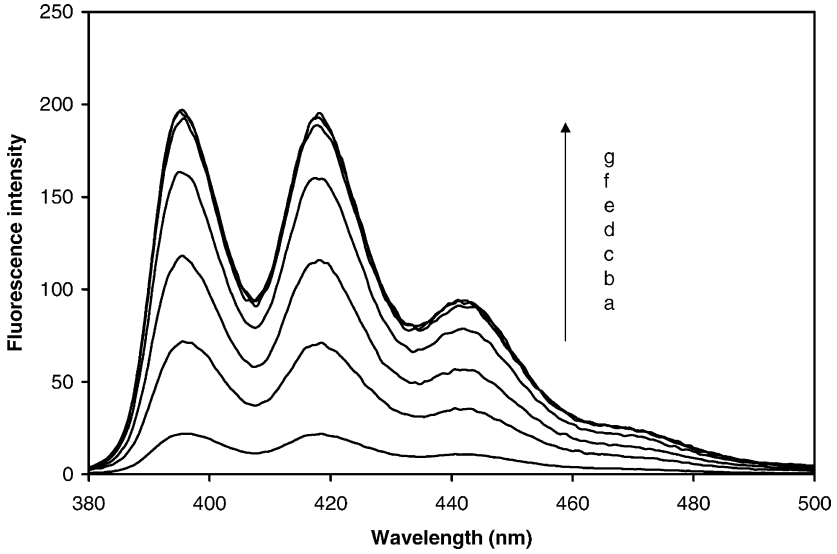

Fig. 2. Fluorescence emission spectra (λ_{ex} 355 nm) of **II** (1.1×10^{-6} M) in dichloromethane with added BTMAH (1.0×10^{-7} M) as a function of [K^+]. a: 0 μM, b: 0.5 μM, c: 1 μM, d: 1.5 μM, e: 2 μM, f: 2.5 μM, g: 3 μM.

considerably less than for **I** (8.5-fold and 50-fold increases, respectively).

The reason for this reduced response is unclear. One potential explanation is that the ion occupies a site in **II** relative to the electron lone pair on the azacrown nitrogen atom as well as to the anthryl fluorophore that is different than in **I**. For example, if the most stable position of the ion in the complex is at a greater distance from the nitrogen lone pair in **II**, this could lead to a weaker electrostatic interaction and result in less effective interference with the electron transfer quenching process. Such an effect could conceivably be caused by an interaction between the ion and the π-systems of the phenyl rings of the calixarene group. The binding of cations through π interactions has been observed for other host–guest molecules [22–24] as well as the 1,3 alternate calix[4]arenecrown-5 used in the present study [1]. In fact, electrostatics calculations on the potassium ion–**II** complex point out significant changes in charge density in the calixarene phenyl rings upon complexation. Additionally, it was found that when the structure of **I** complexed with potassium ion was minimized, a $K^+ \cdots N$ distance = 3.00 Å was optimal, whereas a $K^+ \cdots N$ distance of 3.48 Å was observed for **II**. Therefore, a weaker interaction with the amine electron donor and consequently a reduction in the fluorescence response would be expected for **II** compared to **I**.

3.2. Selectivity

Since it is our eventual intention to use molecules similar to **II** as a sensor for the detection of potassium ions in blood samples, the selectivity of **II** for potassium over other analytes is an important consideration. Given the structural similarities between **II** and 1,3-alternate calix[4]arenes [1], it is reasonable to expect similar binding properties. Therefore, we expect that metal ion complexation in **II** is governed by electrostatic interactions, particularly with the azacrown oxygen atoms, and through cation–π interactions, but selectivity is controlled primarily by a size fit effect and steric effects from the propyl substituents appended to the two rotated aryl rings of the calix[4]arene [1]. Fig. 3 shows the dependence of the emission intensity of **II** on cation concentration. (The values in the plot are normalized to the fluorescence intensity in the absence of ion.) These results suggest high selectivity of **II** to potassium in comparison with the other alkali metal cations studied, including sodium. This is an important property for blood analysis applications since sodium is present in relatively high concentrations in whole blood.

Selectivity was calculated by a method (illustrated in Fig. 4) that is similar to the fixed interference method (FIM) used in ion selective electrode applications [25]. Fig. 4 shows a hypothetical plot of fluorescence emission intensity as a function of ion concentration for primary and 'interfering' ions. Selectivity is calculated from the following equation and is represented as a logarithmic value:

$$\log K_{i,j} = \log\left(\frac{[i]}{[j]}\right) \quad (1)$$

where [j] is the concentration of the interfering ion in the plateau region of the plot and for sensor applications is normally chosen to fall within a physiological concentration range for that ion. This is the concentration of interfering ion that provides the maximum fluorescence response. [i] is the concentration of the primary ion that produces the same fluorescence response as the maximum fluorescence produced by the interfering ion and as such represents a minimum unambiguous detection limit for the primary ion. From Fig. 3, it is clear that sodium and lithium ions produce virtually no

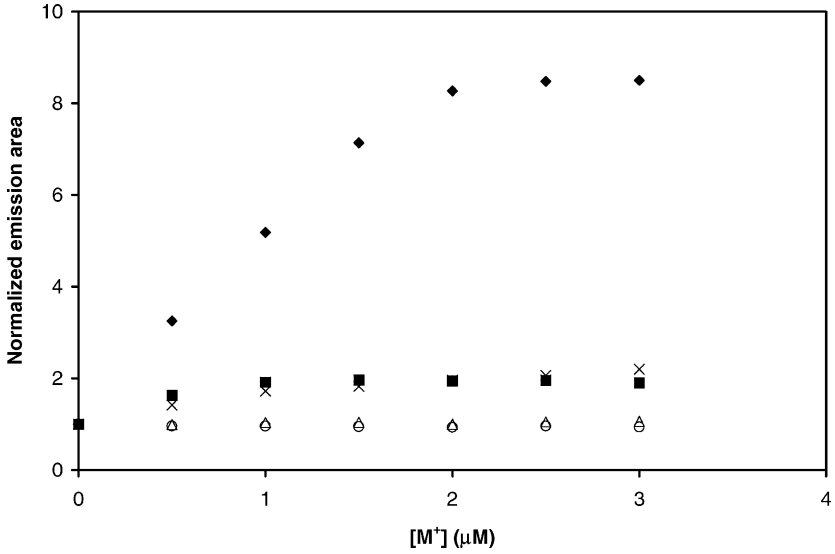

Fig. 3. Emission area of **II** versus the concentration of various alkali metal ions: Li (○), Na (△), K (◆), Rb (■), Cs (×).

response. These results allow only a lower limit to the selectivity to be calculated. Thus $\log K_{K,Na} \sim \log K_{K,Li} \leq -3.5$, a value similar to that obtained for valinomycin and considerably larger than obtained for **I**. For cesium and rubidium, $\log K_{K,Cs} \sim \log K_{K,Rb} \sim -1$, a value that is comparable to that obtained for **I** [14]. These results are summarized in Table 1. For comparison, Table 1 also shows selectivity results obtained previously for related calixarene crown ethers.

Since the complexes apparently have a 1:1 ion/ionophore stoichiometry as suggested by similar calix[4]crowns [1,18–21] and molecular modeling, ion concentrations much higher than the concentration of **II** do not result in further increases in fluorescence intensity. The concentration of **II** in turn is limited by the requirement that absorbances at the excitation wavelength in our fluorescence experiments must be less than 0.04 in order to obtain a linear fluorescence response. Therefore, the concentration of **II** used in these measurements is limited and by necessity the ion concentrations are well below physiological norms. However, in the eventual sensor configuration, considerably shorter path lengths will make much higher ionophore concentrations possible, possibly giving sensitivity in the physiological

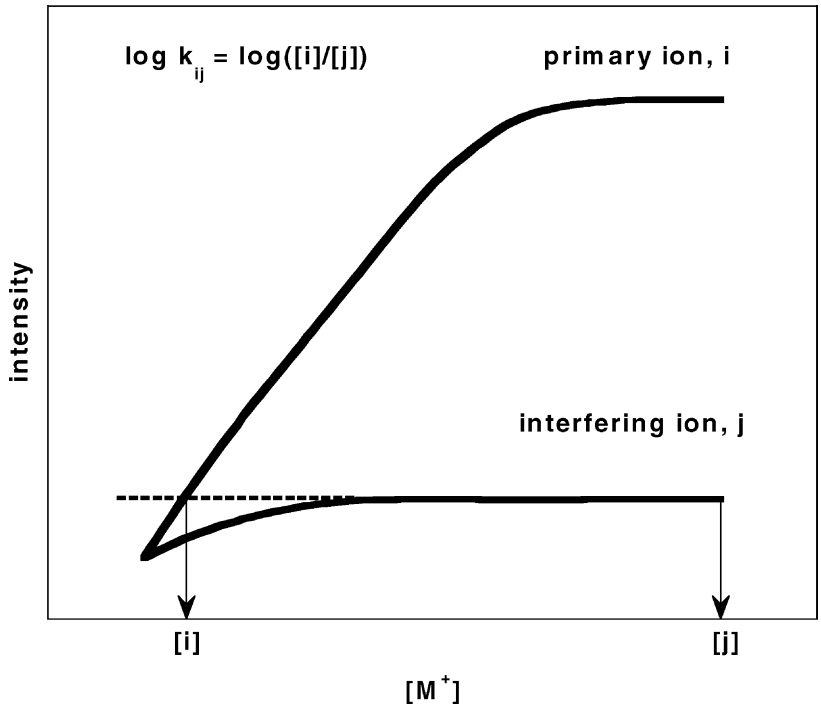

Fig. 4. Hypothetical plot of fluorescence emission intensity as a function of ion concentrations for primary (*i*) and interfering (*j*) ions.

Table 1
Selectivity data ($\log K_{ij}$) as calculated from Eq. (1) for **II** (this work) and related compounds

Compound	Li^+	Na^+	Rb^+	Cs^+
I	–	−1.3	–	–
II	≤−3.5	≤−3.5	∼−1	∼−1
Ref 1[a]	−4.84	−5.39	−0.48	−2.25
Ref 1[b]	−3.52	−3.26	−0.48	−0.38
Ref 1[c]	−3.7	−3.2	–	–
Ref 1[d]	−3.5	−3.1	–	–

[a] 1,3 alternate calix[4]arenecrown-5 in $CHCl_3$.
[b] Valinomycin in $CHCl_3$.
[c] $\log K_{i,j}^{pot}$ of 1,3 alternate calix[4]arenecrown-5 as CHEMFET.
[d] $\log K_{i,j}^{pot}$ of valinomycin as CHEMFET.

range. It should also be pointed out that considerable increases in selectivity have been achieved by incorporation of fluoroionophores into polymer membranes where factors such as solvation and diffusivity have much different effects than in solution. Thus it is not inconceivable that we will observe improved selectivity for **II** in membranes. In fact, in a previous study we have incorporated a calix-rhodamine fluoroionophore into a variety of polymer matrices with varying degrees of lipophilicity and have observed good selectivity [26]. It should be noted that while in general fluoroionophore-membrane compatibility is a serious consideration, in this previous study we have been able to strike a balance between solubility and stability of the fluoroionophore in the membrane with the need for high aqueous diffusivity.

3.3. Solvent effects

Previous studies of analogous anthryl-benzocrown ether calixarenes indicated a considerable and complex solvent effect on the intensity of fluorescence in such compounds [6]. Specifically, addition of methanol to dichloromethane was observed initially to cause an increase in the fluorescence presumably due to complexation of the methanol with the oxygen atoms of the benzocrown ether, i.e., electron transfer was less efficient. With continued addition of methanol, the increase in polarity in turn increased the efficiency of electron transfer and led to a decrease in the fluorescence. Given this reported medium effect and its potential importance in the operation of a sensor based on this molecular structure, we have investigated the effect of solvent on **II**, both in the absence and presence of added potassium ions. In the absence of ions, the addition of methanol to the dichloromethane solutions caused an increase in the fluorescence intensity at small methanol concentrations and then a decrease as the methanol concentration was increased further. This behavior is similar to that reported for the benzocrown systems [6]. It is likely here that at low methanol concentrations, the increase in fluorescence intensity is due to a hydrogen bond interaction between methanol and the azacrown nitrogen. The fact that the effect of small concentrations of added methanol is more pronounced in **II** than in the previously studied benzocrown compounds is consistent with the fact that the nitrogen lone pair is a more localized source of electrons for the fluorescence quenching process than the 1,2-dimethoxybenzo moiety within benzocrown ethers. However, at higher methanol concentrations the drop in fluorescence intensity observed can be ascribed to an increase in the efficiency of electron transfer due to an increase in solvent polarity. This polarity effect overshadows the hydrogen-bonding effect.

In the presence of added potassium ions, an additional effect of solvent is observed. Fig. 5 shows the delta response of **II** as a function of the mole fraction of dichloromethane in methanol. The delta response is determined from the slope of the fluorescence intensity versus ion concentration curve at a specific solvent composition. It is clear that as

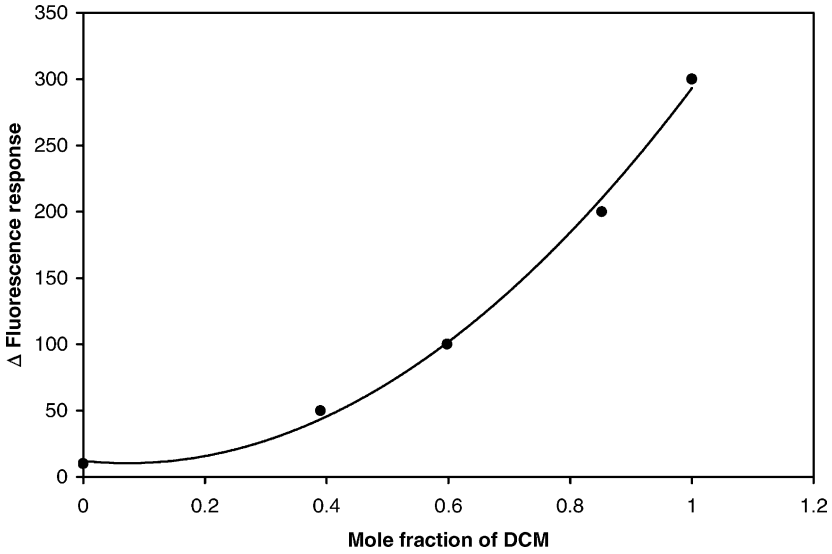

Fig. 5. Delta fluorescence response to K^+ of **II** as a function of the mole fraction of dichloromethane in methanol.

the mole fraction of methanol decreases, the delta response increases dramatically. We ascribe this behavior to a solvation effect in that, as the solvent polarity decreases with increased dichloromethane concentration, the potassium ions seek out a more energetically favorable solvation environment, namely the complexation site in **II**. This response to solvation is expected to have an important impact on the composition of the membrane that is eventually chosen to host **II** in sensor applications.

4. Conclusions

The anthryl azacrowncalix[4]arene, **II**, complexes with potassium ions in organic solution triggering a substantial increase in anthryl fluorescence emission through the disruption of the PET quenching process. Preliminary measurements indicate that the selectivity for potassium ions over other alkali metal cations particularly sodium and lithium for **II** is increased dramatically over that of the anthryl azacrown model compound, **I**. These preliminary solution phase studies indicate a 1:1 complexation between **II** and the ion, suggesting that **II** could be sensitive to potassium in the normal physiological concentration range once incorporated into a sensor. Furthermore, the observed fluorescence response to changes in solvent polarity suggests that the sensor substrate composition will have an important impact on the efficiency of **II** as an ionophore and could allow further optimization of sensitivity and selectivity.

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