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Selective chromogenic response via regioselective binding of cations: a novel approach in chemosensor design

Demet Ataman and Engin U. Akkaya*

Department of Chemistry, Middle East Technical University, TR 06531 Ankara, Turkey

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Abstract—A calixdiquinone bis-indoaniline derivative with two kinds of potential binding sites, discriminates cations according to their charge/size ratio. Harder and highly oxophilic Eu(III) preferentially interacts with the lower rim quinone oxygens; whereas Na(I) binds to the azacrown moieties. As a consequence of the chromogenic sensor's design, these two binding events result in two different responses, Eu(III) causes a remarkable auxochromic change, but Na(I) produces a significant anti-auxochromic effect. © 2002 Elsevier Science Ltd. All rights reserved.

The construction of ion selective molecular sensors continues to attract attention due to potential applications and as a testing ground for molecular recognition and signal transduction schemes. Progress in the field has been reviewed in recent years.[1–3] In conjugated donor–acceptor chromophores or fluorophores (internal charge transfer-ICT sensors), if the receptor is a part of the donor moiety, cation binding induces a blue-shift with a decrease in the extinction coefficient (anti-auxochromic effect); however, if the acceptor group is part of the receptor then there is a red-shift with an increase in extinction coefficient results (auxochromic effect) on cation binding.[4]

Selective response is one of the most important issues for all chemosensors. This issue has been addressed, at least in part, by designing selective receptor units with varying degrees of success.[1] In our own attempts in achieving selective chemosensor response, we reasoned that the selectivity would be drastically improved if there were not one, but two competing potential receptor sites, one with donor and one with acceptor characteristics. If the cation shows a preference for the donor–receptor, it will cause a blue shift, whereas if the preference is for the acceptor–receptor, there will be a red shift. In recent years, there have been reports of ditopic (bifunctional) fluorophores acting as molecular equivalents of logic gates.[5–8] In one case, a bifunctional fluoroionophore with D_1-A-D_2 constitution was reported,[7] but both of the receptor units were donor substituents. Consequently, the receptors displayed differential affinity for cations, but the spectral shifts were in the same direction. de Silva's quinoline–BAPTA conjugate[8] is particularly relevant, because Ca(II) and H^+ ions were shown to produce blue and red shifts, respectively, interacting with either the donor or the acceptor part of the push–pull system. Thus, it is clear that judicious choice of receptors would yield chemosensors of broad spectral response range.

Indoaniline derivatives have been used[9,10] as chromogenic sensors for some time. These intense blue dyes can be easily prepared by the reaction of (*N*,*N*-dialkylamino)anilines with phenols under oxidative conditions.[11] In recent studies on chromogenic sensors, calixarenes, which proved themselves to be very useful scaffolds for sensor design, were coupled with indoaniline structures to yield remarkable chromogenic chemosensors.[12–15] In these studies, lower rim diquinone binding is strengthened by further functionalization of the other two hydroxyls. Pronounced red shifts in the absorption spectrum were observed when the calixdiquinone carbonyls coordinate to a number of alkaline and alkaline-earth cations, especially the high charge density Ca(II) cation.

In this study, we targeted a calixdiquinone derivative with an azacrown modification on the *N*,*N*-dialkylaminostructure. To that end, our synthesis started with 4-fluoronitrobenzene. In analogy to a recently reported method,[16] we simply carried out an S_NAr reaction of

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* Corresponding author. E-mail: akkayaeu@metu.edu.tr

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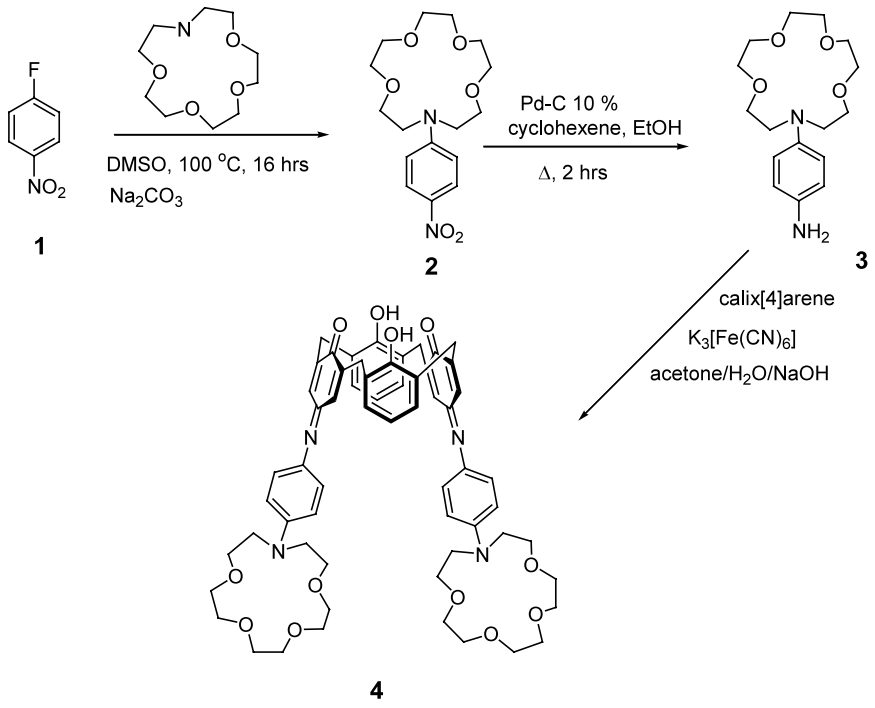

the azacrown (1-aza-15-crown-5) with the fluoroarene in DMSO. Usual work-up, followed by a silica-gel column purification yielded compound **2**. The reduction of the nitro group was accomplished using 10% Pd–C in refluxing ethanol with cyclohexene as the hydrogen source.

Compound **3** obtained in this way, was then coupled with calix[4]arene under alkaline conditions with potassium ferricyanide as the oxidizing agent by an adaptation of the relevant literature procedures.[9] The major product which is 1,3-calixdiquinone bis-indoaniline **4** was collected following chromatography on silica-gel (chloroform–acetone, 50:1 v/v) and satisfactory analytical data were obtained. The calixdiquinone bis-indoaniline derivative **4** was moderately soluble in acetonitrile and the absorption spectrum showed a broad peak at 605 nm ($\varepsilon = 31{,}600\ cm^{-1}\ M^{-1}$). We studied the interaction of this novel chromophore with a number of cations (perchlorates or nitrates). It was expected that the harder calixdiquinone site would preferentially bind harder cations and large alkaline cations would preferentially interact with the azacrown units. Our experiments revealed that this is exactly the case. Apparently in aprotic acetonitrile, further functionalization of the lower rim is not necessary for binding to take place. The practical outcome of this sensor design is the broader palette of colors in response to the binding of different metal ions; for example, a dilute solution of **4** in acetonitrile is blue, but the addition of sodium perchlorate to yield a 9 mM solution creates a pink solution with a blue shift (–30 nm) in the absorption spectrum (Fig. 1). On the other hand,

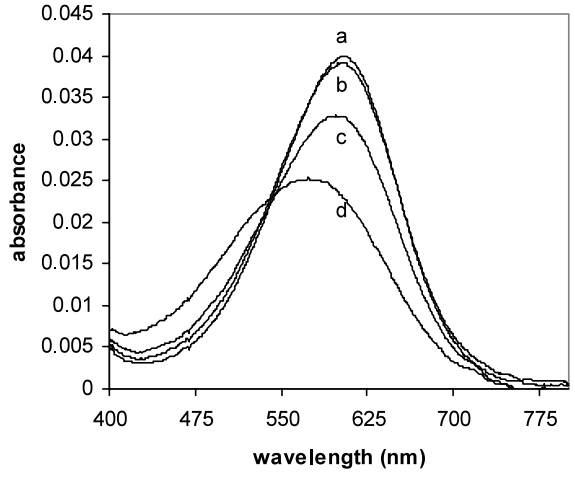

Figure 1. Absorption spectrum of 1.2 μM **4** in response to different concentrations of Na(I) in acetonitrile: (a) 0, (b) 1.0 mM, (c) 9.0 mM, (d) saturating.

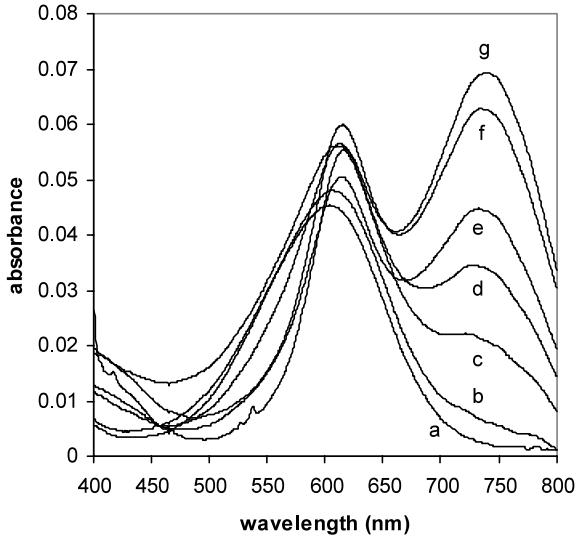

Figure 2. Absorption spectrum of 1.4 μM **4** in response to different concentrations of Eu(III) in acetonitrile: (a) 0, (b)1.0 μM, (c) 2.5 μM, (d) 5.0 μM, (e) 12.5 μM, (f) 100 mM, (g) saturating.

adding just 10 equiv. of a europium salt ($Eu(NO_3)_3$) generates a green solution with a strong red shift (+140 nm) in the absorption spectrum (Fig. 2). The lack of a clean isosbestic point in response to Eu(III) binding may be an indication of multi-cation or multi-mode binding. This seems to be more likely with calcium: Ca(II) also forms a green solution, but the absorption spectrum shows a very broad peak in the 400–750 nm range, suggesting a more complex pattern of binding interactions. Nevertheless, the principle of selective chromogenic response via regioselective binding of cations was shown to be valid. The work described here clearly points the direction for further development, as the receptor–ligand structure can be chosen in such a way that only very soft cations would bind to the donor–receptor site. In combination with a hard receptor site like the calixdiquinone unit of this work or others,[12,13] very cleanly separated metal ions responses would be obtained. Our own work to that end is in progress.

Acknowledgements

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