A Pyrenyl-Appended Triazole-Based Calix[4]arene as a Fluorescent Sensor for Iodide Ion†

Jong Seung Kim,* Sun Young Park, Sang Hoon Kim, Pierre Thuéry,‡ Rachid Souane,§ Susan E. Matthews,* and Jacques Vicens*#

Department of Chemistry, Korea University, Seoul 130-701, Korea. *E-mail: jongsKim@korea.ac.kr

†CEA, IRAMIS, SCM, LLCEF (CNRS URA 331), Bât. 125, 91191 Gif-sur-Yvette, France

‡School of Chemical Sciences and Pharmacy, University of East Anglia, Norwich NR4 7TJ, U.K.

§E-mail: susan.matthews@uea.ac.uk

#IPHC-UdS-ECPM-CNRS, 25 rue Becquerel, F-67087, Strasbourg, Cédex, France. *E-mail: vicens@chimie.u-strasbg.fr

Received November 10, 2009, Accepted November 18, 2009

The synthesis and evaluation of a novel calix[4]arene-based fluorescent chemosensor 1 for the detection of I⁻ is described. The fluorescent changes observed upon addition of various anions show that 1 is selective for I⁻ over other anions. Addition of I⁻ results in ratiometric measurements with 1 : 1 complex ratio.

Key Words: 1,2,3-Triazole, Calixarenes, Fluorescent sensors, Anion sensing, Iodide

Introduction

Iodide is recognized as an ion of significant physiological importance due to its essential role in the normal growth, development and functioning of the brain and body. Any deficiency of iodide can give rise to serious diseases such as enlarged goitres or mental retardation. Iodine is a biologically essential element in seawater, where it exists predominantly as the iodide ion. Similarly, Valiyaveettil and co-workers recently synthesized a Cu(II) complex of a tripodal receptor bearing anthracene moiety on one pod as the fluorophore. The anion recognition behaviour of the Cu(II) complex was evaluated in acetonitrile-water resulting in an extremely high selectivity for iodide over other anions such as F⁻, Cl⁻, Br⁻, NO₃⁻, CH₃COO⁻, and H₂PO₄⁻. A fluorescence turn-on probe for iodide based on the redox reaction between cupric and iodide has been recently published by Lin and coll. As part of our on-going studies on simple and easy-to-make fluorescent sensors for anion recognition, we present here the synthesis and anion binding studies of a pyrenyl-appended triazole-based calix[4]arenes as fluorescent sensors for anions.

The development of the Cu(I)-catalysed 1,3-dipolar cycloaddition of alkynes and azides by Meldal and Sharpless from the original thermal reaction of Huisgen has provided a straightforward molecular linking strategy which has been adopted in a wide range of applications. In addition, it has also been demonstrated that the triazoles formed during the coupling reaction are themselves excellent cation binding motifs and if suitably arranged can act cooperatively to provide receptors and sensors. Recently we and others have shown that when such arrays are incorporated onto a tailored calixarene scaffold can be useful for the selective binding of Cd²⁺, Ca²⁺, Pb²⁺, and Zn²⁺.

More recently it has been shown that triazole units can act as an amide mimics enabling protein folding by virtue of the polarized strong C-H hydrogen bond donors. This result has additionally opened up the potential of triazoles to act as anion binding motifs through C-H hydrogen bond donation. Thus, single triazoles, bistriazoles, rigid tetrameric triazole macrocycles, and triazole linked dendrimers have all been demonstrated to bind a range of anions including halides and phosphates. In this report we describe the synthesis, via the click reac-

†This paper is dedicated to Professor Sunggak Kim on the occasion of his honorable retirement.
tion, of two new calixarenes derivatives featuring pyrene reporting units and investigate their ability, along with previously prepared derivatives to act as fluorescent anion sensors.

Results and Discussion

Three potential fluorescent anion sensors were investigated in this study. We have synthesized a series of p-tert-butylcalix[4]arenes appending pyrene fluorophores 1-3 (Chart 1) incorporated into a 1,2,3-triazole spacer via the ‘click’ reaction and measured their optical properties and fluorescence changes upon anion binding.

According to scheme 1, compound 1 was prepared in a short synthetic sequence from the known dipropargyl derivative of p-tert-butylcalix[4]arene (4). Firstly, the two ester binding moieties were introduced through exhaustive alkylation with methyl bromoacetate in the presence of NaH to give the tetrafunctionalised calix[4]arene (5) in 74% yield. The fluorescent pyrene reporting units were then incorporated using our previously developed conditions for the Cu(I)-catalysed 1,3-dipolar cycloaddition of calix[4]arene alkynes and azides, namely reaction of 5 with 1-azidomethyl pyrene (6) in the presence of CuI in DMF for 2 h at 90 °C.

We have previously described the synthesis of 2, the mono ester mono pyrene receptor, through a cycloaddition between 7 and 6. The synthesis of 8 from the common precursor 7 was achieved through the introduction of the amine binding group on treatment with commercial dimethylethyleneamine. The importance of amine binding in enhancing Cu(I) mediated click reactions was verified through the observation that introduction of the pyrene reporting unit to prepare sensor 3 proceeded swiftly at room temperature in this case which can be proposed to be due to intra/intermolecular formation of amine copper complexes.

The conservation of the original fixed cone conformation of the calix[4]arene was confirmed by the presence of doublets for 

---

**Chart 1. Structures of fluorescent sensors 1-3**

---

**Scheme 1. Synthesis of 1, 3, 5, and 8**
the ArCH2Ar protons at ~3 and 4 ppm. The formation of the 1,2,3-triazole rings was shown from appearance of the triazole-
H signal as a singlet within the range at 7.52 ppm for 1 and
7.88 ppm for 3 and the down-field shift of the OCH2-triazole
linker. All analytical data of 1, 3, 5, and 8 are given in the experi-
mental section. The cone conformation of 5 was also confirmed
by the determination of its crystal structure (Figure 1).

The fluorescence properties of 1-3 were investigated in ace-
tonitrile (Figure 2). On excitation at 343 nm, the maximum ab-
sorption wavelength of the pyrene, 1 displays monomer and ex-
cimer bands at 395 and 475 nm, respectively, whereas 2 and 3
both exhibit only the monomer band at 395 nm. Compared with
2, 3 shows a relatively weaker emission, which is attributable
to the fact that the pendent amide group (-CH2CONH-) takes
part in a PET (photo-induced electron transfer) process: an elec-
tron transfer from a lone-pair electron of the nitrogen atom (HOMO)
to the pyrene unit of 3 (LUMO).

UV/vis absorption and fluorescence changes have been inves-
tigated on the addition of tetrabutylammonium (Bu4N+) salts of
MO) to the pyrene unit of 1. UV/vis absorption and fluores-
cence changes have been investigated on the addition of tetrabutylammonium (Bu4N+) salts of F-, Cl-, Br-, I, CH3CO2-, OH-, HSO4-, and H2PO4- to CH3CN solutions of 1-3. From UV/vis and fluorescence spectral chang-
es of 1-3 (Figure 3), we found that only 1 exhibits I selectivity
over the other anions tested. Addition of I to the CH3CN solution
of 1 induced a marked ratiometry where the monomer emis-
sion of 1 increases as its excimer emission concomitantly declin-
es (Figure 4 (a)). In contrast, 2 and 3 bearing only one pyrene
unit, show no significant spectral changes upon addition of any
anions.

Figure 4 shows the titration profiles of 1 on I addition. When
the concentration of I ion is increased up to 1.2 x 10^-4 M, the
intensity is decreased by 6.2-fold in excimer emission. Addition
of more than 200 equiv of I to 1 resulted in both the monomer
and excimer emission becoming quenched, due to the heavy
atom effect imparted by I. The association constant (Kassoc) of 1
with I was determined to be 979.25 M^-1 for a 1:1 complex. The
quantum yields (Φq) of 1, and 1-I-, referenced to anthracene,
were also determined and found to be 0.176, and 0.074, respec-
tively.

The 1:1 stoichiometry was confirmed by the MALDI-TOF
mass spectrometry technique. The MALDI-TOF mass spectrum
of a mixture of 1 with an excess of I as its Bu4N+ salt showed the
formation of 1-Bu4NI complex with a peak at m/z = 1624.0202
for a calculated molecular weight = 1626.18 (Figure 4 (b)). This
may correspond to the detection of 1-Bu4NI in which iodide
is not seen. To compare a similar experiment was done with
Bu4N+X (X=F-, Cl-, Br-) which were shown to not induce fluo-
rescent changes. And indeed no detection was made of the pre-

cence of 1-Bu4NI complex evidencing the complexation of I
and not of other halide anions by 1. This suggested the fluo-
rescent changes of 1 upon addition of I to be due partly due to
complexation.

In conclusion, new fluorogenic calix[4]arene (1) bearing two
methyl ester and two pyrene triazole groups in opposite dis-
positions has been prepared. It was shown to be selective for the
binding of I. When I is bound to 1, the pyrene monomer emis-
ion increased while the excimer emission declined in a rati-
ometric manner. This ratiometric change is probably due to the
encapsulation of I in the cavity, delineated by the ester and tria-
zole functionality, to form a 1:1 complex. This encapsulation
induces conformational changes of the frame which removes
one pyrene residue from the other. The 1:1 stoichiometry of the
complex was confirmed by mass spectrometry.

Experimental Section

5,11,17,23-Tetra-tert-butyl-25,26-dihydroxy-27,28-dipro-
pargylcalix[4]arene (1) and 5,11,17,23-tetra-tert-butyl-25,
(7) are known compounds.

Synthesis of 5,11,17,23-tetra-tert-butyl-25,27-dimethylace-
tate-26,28-di(1,2,3-triazol-1-methyl pyrene) calix[4]arene (1).
Copper iodide (10 mg) was added to 5 (505 mg, 0.59 mmol) and
6 (300 mg, 1.18 mmol) in DMF (6 mL) and the mixture heated at
90°C for 2 h. The resulting solution was cooled and diluted with
water. The mixture was filtered, the residue washed with water
and then taken up in dichloromethane and dried. The desired
material was isolated as a pale cream solid following pre-
cipitation from dichloromethane / acetone (370 mg, 46%). mp...
Figure 3. UV/vis and fluorescence spectra of (a) 1, (b) 2, and (c) 3 (absorption: 15 µM, emission: 6 µM) in CH₃CN in the presence of various anions, including F⁻, Cl⁻, Br⁻, I⁻, OH⁻, CH₃COO⁻, HSO₄⁻, and H₂PO₄⁻ (200 equiv, as Bu₄N⁺ salts).

153 - 155 °C. ¹H NMR (300 MHz) δ 7.85-8.29 (9H, m), 7.59 (2H, s), 6.71 (4H, s), 6.45 (4H, s), 6.10 (4H, s), 5.08 (4H, s), 4.44 (4H, s), 3.45 (6H, s), 2.88 (2H, d, J = 12 Hz), 1.05 (18H, s), 0.87 (18H, s). ¹³C NMR (400 MHz) δ 31.2, 31.3, 31.6, 31.8, 33.8, 34.0, 51.6, 52.0, 66.0, 71.7, 94.5, 122.3, 124.6, 124.7, 125.0, 125.3, 125.8, 125.9, 126.4, 127.4, 127.4, 127.8, 128.0, 128.9, 129.2, 130.7, 131.3, 131.9, 132.4, 135.2, 144.8, 145.2, 145.5, 152.6, 153.0, 171.0. IR v = 2953, 1752, 1735, 1479, 1439, 1360, 1300, 1196, 1123 cm⁻¹. MALDI-TOF MS (CHON =1383.71) 1406.68 [M + Na⁺]. Anal. Calcd for C₉₀H₉₀N₁₆O₈: C, 78.12; H, 6.56; N, 6.07. Found: C, 72.33; H, 6.15; N, 5.70.

Synthesis of of 5,11,17,23-tetra-tert-butyl-25,27-dihydroxy-26-dimethylethyleneamine-28-(1,2,3-triazol-1-methyl pyrene) calix[4]arene (3). Copper iodide (10 mg) was added to 8 (200 mg, 0.24 mmol) and 6 (157 mg, 0.61 mmol) in DMF (6 mL) and
the mixture stirred at room temperature for 2 h. The resulting solution was cooled and diluted with water. The mixture was filtered, the residue washed with water and then taken up in dichloromethane and dried. The desired material was isolated as a buff solid following column chromatography in dichloromethane : acetone = 5 : 1 (178 mg, 68%). mp 147 - 149 °C. 1H NMR (300 MHz) δ 8.53 (1H, t, J = 6 Hz), 7.98-8.29 (9H, m), 7.88 (1H, s), 7.02 (2H, br s), 6.90 (4H, s), 6.75 (2H, s), 6.66 (2H, s), 6.34 (2H, s), 5.17 (2H, s), 4.35 (2H, s), 4.03 (2H, d, J = 12 Hz), 3.75 (2H, d, J = 12 Hz), 3.36 (2H, m), 3.12 (4H, d, J = 12 Hz), 2.43 (2H, br t), 2.17 (6H, s), 1.25 (18H, s), 0.94 (9H, s), 0.86 (9H, s). 13C NMR (75 MHz) δ 30.8, 30.9, 31.6, 31.7, 33.8, 33.9, 33.9, 45.0, 52.7, 57.8, 70.1, 74.3, 121.9, 125.0, 125.1, 125.2, 125.7, 125.8, 125.9, 125.92, 126.3, 127.1, 127.1, 127.3, 127.4, 128.1, 128.4, 129.0, 132.2, 132.5, 142.1, 149.0, 149.1, 149.7, 168.6. IR ν = 3364, 2952, 2857, 1736, 1672, 1539, 1481, 1460. Synthesis of 5,11,17,23-tetra-tert-butyl-25,27-dihydroxy-26-dimethylthyleneamino-28-propargylicalix[4]arene (5). A suspension of sodium hydride (95%, 790 mg, 32.92 mmol) and 4 (4.00 g, 5.41 mmol) in DMF (80 mL) was stirred at room temperature for 1 h. Methyl bromoacetate (5.07 g, 33.2 mmol) was added and the suspension stirred for a further 18 h. Water (50 mL) was added and the resulting precipitate collected and dissolved in dichloromethane (50 mL). The organic solution was washed with 10% HCl and then dried with magnesium sulphate. Evaporation of the solvent gave a crude white solid which on precipitation from dichloromethane-methanol yielded the title compound (3.58 g, 74%). mp 173 - 175 °C. 1H NMR (300 MHz) δ 7.02 (4H, s), 6.39 (4H, s), 5.07 (2H, d, J = 2.5 Hz), 4.54 (4H, d, J = 13 Hz), 4.42 (4H, s), 3.76 (6H, s), 3.08 (4H, d, J = 2.5 Hz), 2.29 (2H, d, J = 12 Hz), 2.23 (18H, s), 0.74 (18H, s). 13C NMR (100 MHz) δ 31.2, 31.9, 32.1, 33.8, 34.4, 52.0, 60.2, 72.1, 74.2, 82.3, 124.9, 125.6, 132.0, 136.4, 145.3, 146.0, 152.3, 152.9, 170.44. IR ν = 3285, 2954, 2909, 2868, 1756, 1756, 1479, 1435, 1362, 1300, 1196, 1125, 1071, 1009 cm⁻¹. Synthesis of 5,11,17,23-tetra-tert-butyl-25,27-dihydroxy-26-

References


Acknowledgments. The authors wish to acknowledge the financial support of the Creative Research Initiative project, SRC (20090063001), KRF-2008-313-C00501 of the National Research Foundation of Korea (JSK) and the University of East Anglia (SEM).

5. Rostovtsev, V. V.; Green, L. G.; Fokin, V. V.; Sharpless, K. B. Angew. Chem. Int. Ed. 2002, 41, 2596.

