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Click synthesis of a quinoline-functionalized hexahomotrioxacalix[3]arene: A turn-on fluorescence chemosensor for Fe^{3+}

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ABSTRACT

A novel quinoline-functionalized hexahomotrioxacalix[3]arene **L** was synthesized via Click chemistry and its chemosensing properties with various metal ions were investigated. The chemosensor **L** exhibited a high selectivity for Fe^{3+} with little interference from other environmentally and biologically relevant metal ions, leading to a prominent 'off-on' type fluorescent signalling behaviour. Our studies demonstrated that the detection limit on fluorescence response of the sensor to Fe^{3+} is in the 10^{-7} M range. The mechanism of the interaction between the **L** and Fe^{3+} has been investigated in detail by ^{1}H NMR spectroscopic titration experiments.

1. Introduction

The development of chemosensors capable of recognizing and sensing metal ions has attracted considerable attention because of their fundamental role in biological, environmental, and chemical processes [1–5]. As one of the most essential trace elements, the ferric ion (Fe^{3+}) plays important roles in oxygen metabolism, enzyme catalysis, and DNA synthesis [6–9]. Deficiency or overloading of iron can result in various pathological disorders, such as anemia, liver and kidney damages, diabetes, and heart diseases [10,11]. Therefore, the development of simple and effective chemosensors for the detection of Fe^{3+} is of great importance in environmental and life sciences.

A fluorescent chemosensor strategy has proven to be a convenient and efficient approach for metal ion detection due to its superiority over other methods, for example this approach possesses high sensitivity and selectivity, ease of manipulation, non-destructive analysis, and a rapid response [12–14]. Given the paramagnetic nature of Fe^{3+}, most reported Fe^{3+} fluorescent chemosensors are based on a fluorescence quenching mechanism, whereas sensors exhibiting fluorescence enhancement (turn-on) sensing behaviour are somewhat limited [15–20]. Nevertheless, turn-on sensors do have some advantages not so easily attainable by turn-off sensors, including the ease of detecting low concentrations against a dark background, reduced false-positive signals, and enhanced sensitivity [21–24]. Thus, the development of chemosensors that exhibit fluorescence enhancement upon binding with Fe^{3+} would be an attractive target.

Homooxacalixarenes incorporate extra ethereal linkages which makes them relatively flexible and thus they can provide a suitable binding environment for species that require trigonal-planar, tetrahedral, or octahedral coordination [25–28]. Based on this excellent structural versatility, homooxacalixarenes have been used as molecular platforms for the development of receptors in the molecular recognition of chemical and biological targets [29–32]. On the other hand, we have noted that quinoline derivatives possess desirable photo-physical properties, and that they are usually employed as fluorophores to construct fluorescence chemosensors for heavy and transition metal ions. In particular, the nitrogen atom of the heterocyclic quinoline can act as a chelating site towards metal ions [33–37]. Recently, Rao and co-workers reported the incorporation of the triazole–CH_2–quinoline fluoroionophores onto the lower-rim of calix[4]arene, which exhibited a turn on fluorescence response for Fe^{3+} [38]. Taking advantage of the easily-synthesized triazole binding site, we were able to readily synthesize the quinoline-functionalized hexahomotrioxa-

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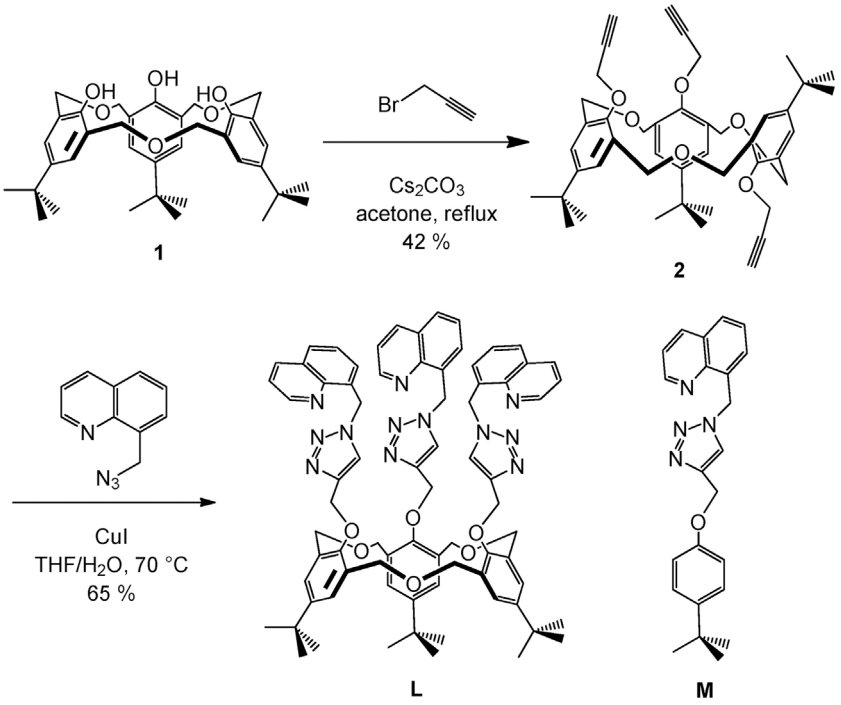

Scheme 1. The synthetic route to chemosensor **L**.

calix[3]arene by Click chemistry. In the present manuscript, we report a quinoline-functionalized triazole linked hexahomotrioxacalix[3]arene **L**, which was found to be a selective fluorescence turn on chemosensor for Fe^{3+} with little interference from the other metal ions studied. The role of the calixarene platform has been addressed by making a non-calixarene-based analogue.

2. Experimental section

2.1. General

Unless otherwise stated, all reagents were purchased from commercial sources and were used without further purification. All solvents were dried and distilled by the usual procedures before use. Melting points were determined using a Yanagimoto MP-S1. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Nippon Denshi JEOL FT-300 NMR spectrometer and a Varian-400MRvnmrs400 with $SiMe_4$ as an internal reference: *J*-values are given in Hz. UV spectra were measured by a Shimadzu UV-3150UV-vis-NIR spectrophotometer. Fluorescence spectroscopic studies of compounds in solution were performed in a semi-micro fluorescence cell (Hellma®, 104F-QS, 10 × 4 mm, 1400 μL) with a Varian Cary Eclipse spectrophotometer. Mass spectra were obtained on a Nippon Denshi JMS-01SG-2 mass spectrometer at an ionization energy of 70 eV using a direct inlet system through GLC.

2.2. General procedure for synthesis of sensor *L*

Compounds 8-azidomethyl quinoline [38] and **2** [39] were prepared following the reported procedures. Copper iodide (10 mg) was added to compound **2** (200 mg, 0.29 mmol) and 8-azidomethyl quinoline (177 mg, 0.96 mmol) in a 30 mL mixture of THF/H_2O (5:1, v/v) and the mixture was heated at 70 °C for 24 h. The resulting solution was cooled and extracted twice with CH_2Cl_2. The organic layers were combined, dried over $MgSO_4$ and the solvent was removed under reduced pressure. The residue obtained was purified using a silica gel column eluting with 1:1 hexane/ethyl acetate to give the desired compound **L** as a white solid in 65% yield. m.p. 146–147 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.03 (s, 27H, *t*Bu), 4.31–4.41 (ABq, 12H, ether bridge, *J* = 13.2 Hz), 4.54 (s, 6H, ArO–CH_2–triazole), 6.08 (s, 6H, triazole–CH_2–quinoline), 6.87 (s, 6H, Ar*H*), 7.39-7.45 (m, 6H, Quin–*H*), 7.50 (d, 3H, Quin–*H*, *J* = 6.8 Hz), 7.74 (d, 3H, Quin–*H*, *J* = 8.0 Hz), 7.84 (s, 3H, triazole–*H*), 8.10 (d, 3H, Quin–*H*, *J* = 8.4 Hz), 8.90 (d, 3H, Quin–*H*, *J* = 2.4 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 31.42, 34.16, 49.65, 67.36, 69.30, 121.50, 124.42, 125.86, 126.36, 128.20, 128.59, 129.59, 130.98, 133.51, 136.14, 143.96, 145.72, 146.21, 150.11, 152.00. HRMS *m*/*z* Calcd for $C_{75}H_{79}N_{12}O_6$ $[M+H]^+$: 1243.6246 Found: 1243.6246 $[M+H]^+$.

The monomeric compound **M** was also synthesized in 68% yield as a reference compound by following a similar protocol. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.28 (s, 9H, *t*Bu), 5.14 (s, 2H, ArO–CH_2–triazole), 6.24 (s, 2H, triazole–CH_2–quinoline), 6.88 (d, 2H, Ar*H*, *J* = 8.8 Hz), 7.26 (d, 2H, Ar*H*, *J* = 10.0 Hz), 7.48-7.54 (m, 2H, Quin–*H*), 7.64 (d, 1H, Quin–*H*, *J* = 6.8 Hz), 7.83 (d, 1H, Quin–*H*, *J* = 8.4 Hz), 7.86 (s, 1H, triazole–*H*), 8.19 (d, 1H, Quin–*H*, *J* = 8.4 Hz), 8.97 (d, 1H, Quin–*H*, *J* = 4.0 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 31.48, 34.05, 49.86, 62.14, 114.17, 121.62, 123.75, 126.21, 126.43, 128.36, 128.91, 129.91, 133.20, 136.39, 143.76, 144.18, 145.82, 150.17, 155.99. HRMS *m*/*z* Calcd for $C_{73}H_{24}N_4O$ $[M]^+$: 372.1950 Found: 372.1950 $[M]^+$.

2.3. General procedure for the UV–vis and fluorescence titrations

For absorption or fluorescence measurements, compounds were dissolved in acetonitrile to obtain stock solutions (1 mM). The stock solutions were diluted with acetonitrile to afford the desired concentration. Stock solutions (10^{-3} M) of perchlorate salts (Li^+, Na^+, K^+, Cs^+, Ag^+, Cu^{2+}, Pb^{2+}, Zn^{2+}, Co^{2+}, Ni^{2+}, Cr^{3+}, Al^{3+}, Cd^{2+}, Hg^{2+}, Fe^{2+} and Fe^{3+}) were prepared with water. In titration experiments, typically, aliquots of freshly prepared standard solutions (10^{-3} M to 10^{-6} M) of various analytes in water were added to record the UV–vis and fluorescence spectra. The fluorescence spectra were performed with the excitation wavelength 314 nm.

2.4. General procedure for the ^{1}H NMR titrations

To a $CDCl_3/CD_3CN$ (v/v 10:1, 550 μL) solution of **L** (5×10^{-3} M) in an NMR tube was added a CD_3CN solution of $Fe(ClO_4)_3$