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ARTICLE

Naphthyl "capped" triazole-linked calix[4]arene hosts as fluorescent chemosensors towards Fe^{3+} and Hg^{2+}: an experimental and computational study

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Four new naphthyl "capped" 1,2,3-triazole-linked receptors **6a-d** have been synthesized and characterized. Their binding properties towards different metal ions have been studied by ^{1}H NMR and fluorescence spectroscopy and the association constants were analysed by a non-linear global fit method. The fluorescent spectral changes show that **6a-d** are sensitive and selective towards Fe^{3+} and Hg^{2+} ions. DFT calculations of the binding modes of **6a-d** with these metal ions are also presented.

1. Introduction

Many studies have been conducted on the use of triazole-functionalized calixarenes as highly selective and sensitive chemosensors.[1a] Calixarenes offer several advantages over other molecular systems and these advantages include their relatively easy functionalization at their lower- and upper-rims, the presence of hydrophobic cavities, and the presence of flexible core/scaffolds that can be modified for target substrate binding.[1b] The design and synthesis of new receptors for metal ions such as those of iron and mercury is of current ongoing interest in supramolecular chemistry due to the roles that these ions play in biological, environmental, and chemical processes.[2-5]

Biologically, iron is the most essential transition-metal since it plays an essential role in carrying oxygen in the heme molecule. It acts also as a cofactor in enzymatic reactions of the mitochondrial respiratory chain. Either a deficiency, or an excess of Fe^{3+} ions can cause a variety of diseases such as anemia, liver and kidney damage, diabetes, heart disease and cancer.[3] Chemosensors that can selectively detect Fe ions are rare and due to the importance of discrimination between Fe^{3+} and Fe^{2+} in the regulation of their biological function, the design of a fluorescent chemosensor capable of binding selectivity to Fe^{3+} ions is an important challenge, one that both Kim's [4a] and Rao's[4b] groups have recently tackled.

On the other hand, mercury is one of those elements that can accumulate in living tissues, thereby causing many harmful effects on human health. The toxicity of Hg^{2+} ions is related to the fact that biological ligands such as proteins, DNA, and enzymes can coordinate with these ions. Consequently, toxic levels of Hg^{2+} cause significant damage to the brain, kidney, stomach, and the Central Nervous System.[5]

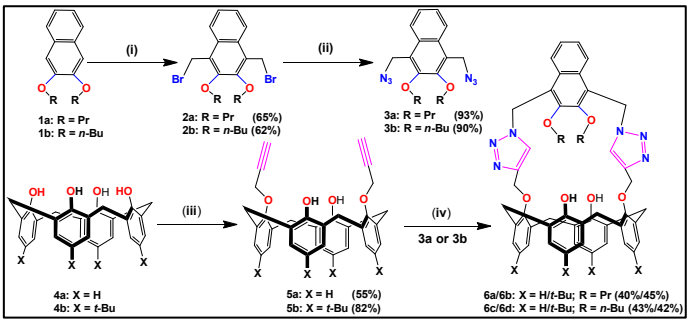
The application of the Cu(I)-catalyzed 1,3-dipolar cycloaddition of an azide and a terminal alkyne ("CuAAC" or "click" reaction) to form 1,2,3-triazole-linked derivatives has provided a straightforward molecular linking strategy which has been adopted in a wide range of applications.[1a,6] The properties of the 1,2,3-triazole moiety as a linker in multivalent derivatives can be exploited for the binding of cations, such as in the accelerated catalysis of the click reaction itself by the *in situ* formation of copper complexes. In calixarene chemistry, the 1,2,3-triazole moiety was first exploited for the functionalization of the calixarene scaffold by Ryu and Zhao in 2005.[7] More relevant to this work has been the incorporation of the 1,2,3-triazole moiety onto calixarene and related[8a-g, 9] molecular scaffolds tailored for the selective binding of various metal cations. The determination of traces of these ions in clinical, medicinal, environmental and different industrial samples has been an important topic. Over the last two decades, the need has increased for the determination of extremely low concentrations of Fe^{3+} and Hg^{2+} in various samples. Therefore, the design and development of efficient ligands that may be used to selectively complex these metal ions are turning out to be extremely important. Herein, we report the synthesis, using a CuAAC methodology, and the properties of new 1,4-naphthyl-"capped" triazoyl-bridged calix[4]arene hosts **6a-6d** as potential chemosensors for $Fe^{3+}$and Hg^{2+}ions. Santoyo-Gonzalez and co-workers had fist reported the use CuAAC reactions to form an anthracenyl- and two ferrocenyl-capped calix[4]arenes.[9]

2. Results and discussions

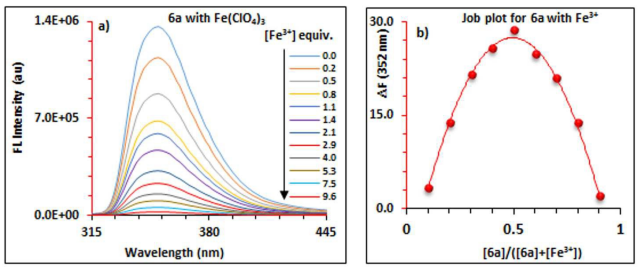
The 1,4-naphthyl-2,3-dialkoxy "capped" triazoyl-bridged hosts **6a-6d** were synthesized by using the CuAAC methodology through the Cu(I)-catalyzed linking of the corresponding 1,3-bis(propargyl)-calix[4]arene and bis-azide derivatives (Scheme

1). The starting materials *de-tert*-butylcalix[4]arene **4a**,[10a] *p-tert*-butylcalix[4]arene **4b**,[10b] *p-tert*-butyl-25,27-di(*O*-propargyl)-calix[4]arene **5b**[10c-d] were all synthesized according to the published literature procedures. A modified literature procedure, however was used to synthesize **5a**.[10e] 1,4-Bis(azidomethyl)-2,3-dialkoxynaphthalenes **3a-3b** were synthesized via the corresponding 1,4-bis(bromomethyl)-2,3-dialkoxynaphthalenes **2a-2b**.[11] Reactions of **5a** with **3a** or **3b** afforded **6a** or **6b**; and reactions of **5b** with **3a** or **3b** afforded **6c** or **6d**, respectively.

All of the synthesized compounds were characterized by ^{1}H- and ^{13}C-NMR and mass spectrometry. The ^{1}H-NMR spectra in $CDCl_3$ of macrocycles **6a-6d** revealed new one-proton singlets at δ 7.58, 7.73, 7.52 and 7.65 ppm, respectively. These signals were assigned to the triazole protons of the macrocycles formed from the CuAAC reactions of the corresponding precursors. Two other two-proton singlets due to the two different -CH_2- bridges which link the triazole units, were observed at δ6.01 and 5.07 ppm for **6a**; at δ5.99 and 5.06 ppm for **6b**; at δ6.01 and 5.07 ppm for **6c**, and at δ5.93 and 5.04 ppm for **6d**. The ^{1}H-NMR spectra of **6a-d** indicated that the calix[4]arene units are all in *cone* conformations since the chemical shifts of the calix[4]arene bridging –CH_2– group protons, appeared as pairs of AB doublets: at δ 3.98 and 2.90 ppm (J = 13.5 Hz)for **6a**; at δ 4.02 and 3.02 ppm (J = 12.0 Hz) for **6b**; at δ 3.98 and 2.88 ppm (J = 15.0 Hz)for **6c**; and at δ 4.00 and 2.99 ppm (J = 12.9 Hz)for **6d**.



Scheme 1. Synthesis of **6a-6d**: (i) **1a** (**1b**) + HBr 33 wt. % solution in CH_3COOH, rt, 72 h; (ii) **2a** (**2b**) + NaN_3 in DMF, 90°C, 24h,; (iii) **4a** (**4b**) + propargyl bromide, K_2CO_3, acetone, reflux, 24-48 h: (iv) **5a** (**5b**) CuI/DIPEA in THF, 60°C for 24 h.



2.1. Complexation studies

Fig. 1 (a) Fluorescence spectra of **6a** from the titration of $Fe(ClO_4)_3$ (0-9.6 equivalents) to a fixed concentration (i.e. 1.50 ×10^{-5} M) of **6a**, in 9:1,v:v CH_3CN:CH_3Cl. λ_{ex} = 291nm; (b) Job plot for **6a** with Fe^{3+}.

The 1:1 complex formation between **6a** and Fe^{3+} was also confirmed by a separate continuous variation method[12] (Job) plot by fluorescence spectrometry. In the Job plot (Fig, 1b), a maximum fluorescence change was observed when the molar fraction of ionophore **6a** vs Fe^{3+} was 0.5, indicative of 1:1 complex formation. Similar fluorescence titration behaviour and 1:1 binding stoichiometry were observed for all of the "capped" receptors **6a-6d** tested with other metal ions. Fig. 2 shows a histogram comparing the K_{assoc} values for **6a** (red), **6b** (blue), **6c** (purple) and **6d** (yellow) with metal ions using a 1:1 global fit analysis of the entire fluorescence quenching spectra.[13a,b] The modified B-H method[13c,d] gave smaller values (Table S7 in the SI), but the limitations of the B-H have been well-addressed in the literature.[13a] Detailed titration data are summarized in the Supplementary Information (Tables S6- S7; Figs. SI-18 to SI-30).

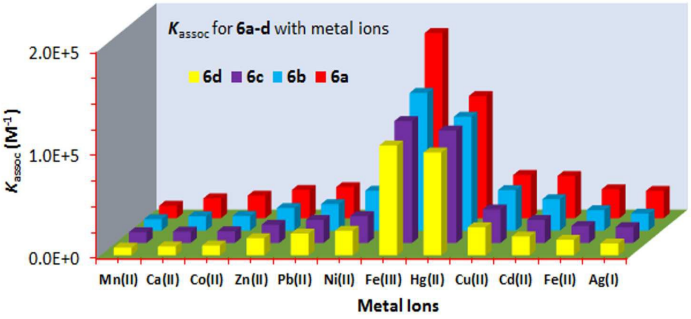


Fig. 2. Histogram showing the K_{assoc} values for **6a** (red), **6b** (blue), **6c** (purple) and **6d** (yellow) with metal ions (M^{n+}).

2.2 UV-vis and fluorescence spectral data

Spectroscopic experiments were conducted using 1-cm capped quartz fluorescence cuvettes. UV-vis spectra were recorded on an Agilent 8543 Diode Array Spectrophotometer. Data manipulations were conducted using software supplied by the manufacturer. Emission spectra were measured on a Photon Technology International (PTI) Quanta Master 6000 Spectrofluorometer equipped with a continuous xenon arc lamp as the excitation source.

2.3 Fluorescence complexation studies for 6a-d with metal ions

To record the fluorescence spectra of **6a-d**, stock solutions of **6a-d** (~1.50 × 10^{-5} M to ~4.00 × 10^{-5} M), and the metal perchlorate salts (~1.5 × 10^{-2} M) were prepared in 9:1(v:v) CH_3CN:$CHCl_3$ solvent mixture. The receptors **6a-d** displayed monomer emission at 331 nm at the 291 nm excitation wavelength. The fluorescence emissions were quenched upon the addition, in each case, of Mn^{2+}, Ca^{2+}, Co^{2+}, Zn^{2+}, Pb^{2+}, Ni^{2+}, Fe^{3+}, Hg^{2+}, Cu^{2+}, Cd^{2+}, Fe^{2+} or Ag^{+}. The highest K_{assoc} values with the all of the receptors were obtained with $Fe^{3+}$and Hg^{2+}. Fig. 2 shows the histogram for the K_{assoc} values determined for all of the complexes and it is clearly evident that the largest K_{assoc} values of 1.79 × 10^5 M^{-1}, 1.33 × 10^5 M^{-1}, 1.18 × 10^5 M^{-1} and 1.06 × 10^5 M^{-1} which were observed were for the binding between **6a-d** and Fe^{3+}, respectively.

2.4 Metal competitive experiments

To confirm the selectivity of **6a** towards Fe^{3+} over the other metal ions (M^{n+}) competitive fluorescence experiments[4b] were carried out with **6a** which were conducted by adding up to a molar equiv. of Fe^{3+} (Fig. SI-17) to each respective solution in which

the mole ratio of the various metal ions (M^{n+} = 1.50 × 10^{-4} M) were kept constant at a 1:10 ratio with respect to **6a** (1.50 × 10^{-5} M). The histogram in Fig. 3 shows the quenching by the addition of the Fe^{3+} indicating that **6a** is more selective for Fe^{3+} over the other metal ions tested, with the exception of Hg^{2+} which showed very little change.

During the same period that the present work was being completed we became aware of a study by W.-S. Chung and coworkers[8g] on the behaviour of $Fe(ClO_4)_3$ with a related calixarene-based ionic receptor. These authors demonstrated that Fe^{3+} was capable of oxidizing both the appended anthracenyl groups and *also* one or both of the free phenolic groups in their particular calixarene system. The oxidation resulted in the concomitant removal of the *tert*-butyl groups to form the corresponding mono- or bisquinonoidal calixarene derivatives, and also oxidation of their anthracenyl groups. It is therefore possible that reactions of $Fe(ClO_4)_3$with **6a-d,** based on Chung's work, that a similar occurrence could be involved with our system during the fluorescence study. Although this is a possibility in our case, the 1:1 Job plot behaviour shown in Fig. 1b makes this unlikely. At the very least, if oxidation was occurring instead of quenching involving a typical photoinduced electron transfer (PET) or heavy-metal effect,[14] then the 1:1 stoichiometry would imply that **6a**-**d** can act instead as sensitive chemodosimeters for Fe^{3+} (*see references cited in Reference. 8g*).

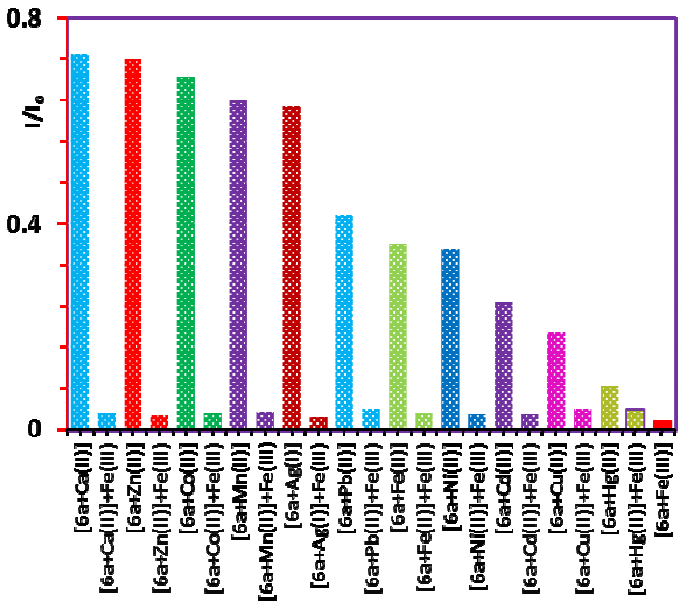


Fig. 3. Histogram showing the metal competitive fluorescence quenching of **6a** with Fe^{3+} in the presence of various metals ions (M^{n+}) in CH_3CN:$CHCl_3$ (9:1). I_o = Fluorescence intensity of free **6a**; I = Fluorescence intensity of complex **6a** with M^{n+} ions; [**6a**] = 1.50×10^{-5} M; M^{n+} = 1.5×10^{-4} M and Fe^{3+} = 1.50×10^{-4} M.

2.5 ^{1}H-NMR complexation study of 6a with $Hg(ClO_4)_2$.

Since ^{1}H NMR spectra can potentially provide evidence for the site of binding of the metal ions and the receptors, titration experiments were conducted. To a solution of **6a** for example, in 3:1 v/v CD_2Cl_2/CD_3CN (1.98 × 10^{-3} M) in an NMR tube were added aliquots of 4.00 ×10^{-2} M $Hg(ClO_4)_2$ and in the same solvent. The ^{1}H NMR spectra were recorded after each addition. The NMR probe temperature was maintained at 27 °C and the added [Hg^{2+}] mole ratio was varied up to 2.0 equivalents (Fig. 4). The signals of the protons of **6a** corresponding to the triazole-*H* (Hj, +Δδ = 0.15 ppm) and calix−*OH* (Hi, +Δδ = 0.09 ppm) protons were all found to shift downfield with Hg^{2+}. The paramagnetism of Fe^{3+} prohibited an equivalent determination by ^{1}H NMR. Furthermore, solubility and other considerations neccessitated a change of the solvent system used for the NMR study compared with that used for the fluorescence studies.

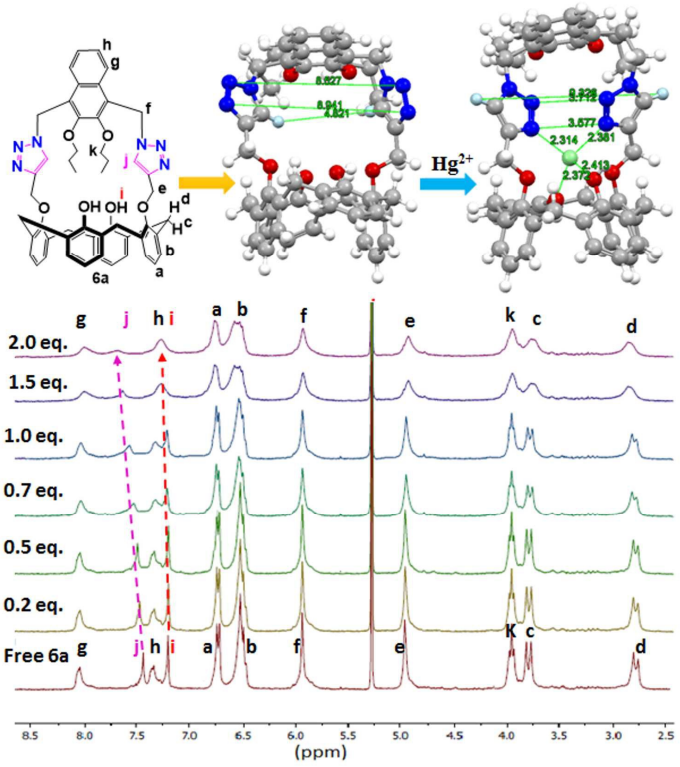


Fig. 4. *Top: Left*: ChemDraw structure of **6a**. The geometry-optimized (ball-and-stick) structure of **6a** (top centre) and complex **6a**⊃Hg^{2+}(top right) using B3LYP/lanl2dz basis set. Colour code: Hg^{2+} = light green, triazole nitrogen = dark blue, triazole hydrogen = light blue and oxygen atom = red. *Bottom*: Partial ^{1}H NMR (300 MHz) spectra of **6a** (1.98×10^{-3} M) with $Hg(ClO_4)_2$ (0–2.0 eqiv.) upon addition of 3:1, v/v CD_2Cl_2:CD_3CN at 298K.

2.6 Computational studies

A computation study was carried out for each of the complexes formed from receptors **6a-6d** with Fe^{3+} and Hg^{2+}. The individual structures for all structures in the gas-phase were fully geometry-optimized using *Gaussian 09 Revision D.01*[15] at the B3LYP level[16] of DFT and the lanl2dz basis set.[17] Significant distance changes were observed for the two triazole moieties in all of the receptors **6a-6d** as their respective metal ion complexes, as can be seen for example, in Fig. 4 (*top centre* and *right*) for **6a** with Hg^{2+} and in Table 1 for **6a** with Fe^{3+} and Hg^{2+}. The detailed computational results for **6a-d** with $Fe^{3+}$and Hg^{2+} ions are summarized in the Supplementary Information (Tables S1 to S5 and Figures SI-1 to SI-16).

The DFT B3LYP/lanl2dz basis set-calculated binding or interaction energies (BE) of the metal cation complexes of the receptors **6a-d**

formed between the metal cation (M^{n+}) and the free receptors **6a-d** in the gas phase at 298 K are based on equation (1). The results are summarized in Table S1 in the Supplementary Information. For this system, the binding energy (***BE***) (where **L** = **6a-d**, and M^{n+}= metal ion) can be expressed as follows:

$$\boldsymbol{BE} = \{(\mathbf{L}{:}M^{n+})_{complex} - E(L_{free}) - E(M^{n+})\} \quad (1)$$

Table 1. The calculated distances (Å) for selected parameters for the receptor **6a** and complex with metal cations.

Parameter	6a	6a⊃Fe^{3+}	6a⊃Hg^{2+}
	Distance (Å)	Distance (Å)	Distance (Å)
N_3–N_{24}	8.941	3.024	3.577
N_4–N_{23}	8.527	3.517	3.712
H_{84}–H_{112}	4.821	8.548	9.326
N_3–O_{61}	5.713	3.41	3.818
N_3–O_{74}	6.39	3.901	4.2
N_{24}–O_{61}	6.118	4.244	4.476
N_{24}–O_{74}	4.829	2.898	3.307
M^{n+}–N_3	–	2.149	2.314
M^{n+}–N_{24}	–	2.272	2.381
M^{n+}– O_{61}	–	2.104	2.372
M^{n+}–O_{74}	–	2.126	2.413

3. Experimental section

All reagents used for the syntheses of the calixarenes **3**-**6** and reagents used in the complexation studies were purchased from Sigma-Aldrich or AlfaAesar. ^{1}H-NMR spectra were recorded at either 300 or 500 MHz as noted and for the ^{13}C-NMR spectra at 75 MHz as noted.

Reagents. All the metal ion salts were received from Sigma Aldrich in >99 % purity. High-purity spectral grade $CHCl_3$ and CH_3CN was supplied by Sigma Aldrich or Cambridge Isotope Labs and were used as received.

25,27-Dihydroxy-26,28-bis(*O*-propargyl)calix[4]arene 5a

25,27-Dihydroxy-bis(propargyl)-calix[4]arene **5a** was synthesized by a modified literature procedure.[10e]A mixture of potassium carbonate (885 mg, 5.89 mmol) and calix[4]arene **4** (1.00 g, 2.35 mmol) in dry acetone (25 mL) was stirred at room temperature for 1 h. A solution of propargyl bromide (980 mg, 8.24 mmol) in dry acetone (5 mL) was added dropwise into the above stirred mixture over a period of 5 min. The reaction mixture was refluxed for 2 days and was then allowed to cool to room temperature. The reaction mixture was filtered over Celite® to remove insoluble particles, and the filtrate was concentrated on a rotavap. The residue was dissolved in dichloromethane (20 mL) and acidified with $HCl_{(aq)}$ (1N, 50 mL), and the product was extracted with dichloromethane (3×50 mL). The combined organic extract was successively washed with water and brine (50 mL), dried over anhydrous Na_2SO_4, filtered, and the solvent was removed on a rotavap. The residue was purified by crystallization from CH_2Cl_2/ CH_3OH to afford **5a** as a light yellow solid (660 mg, 55% yield). ^{1}H NMR (300 MHz, $CDCl_3$): δ= 7.07 (d, *J* = 9.0 Hz, 4H, ArH), 7.03 (s, 2H, Ar-OH), 6.84 (d, *J* = 9.0 Hz, 4H, ArH), 6.72 (m, 4H, ArH), 4.79 (d, *J* = 3.0 Hz, 4H, ArOC*H*$_2$C≡CH), 4.41 (d, *J* = 12.0 Hz, 4H, ArC*H*$_2$Ar AB), 3.41 (d, *J* = 12.0 Hz, 4H, ArC*H*$_2$Ar AB), 2.57 (t, *J* = 3.0 Hz, 2H, ArOCH$_2$C≡C*H*); ^{13}C-NMR ($CDCl_3$, 75.46 MHz): δ=, 152.0; 151.4, 133.4, 129.0, 128.5, 125.7, 119.2, 76.6, 63.4, 31.8; APCI(+) MS (*m/z*, relative intensity) 500 (M^+, 100).

5,11,17,23-Tetra-*tert*-butyl-25,27-dihydroxy-26,28-bis(*O*-propargyl)calix[4]arene 5b[10c-d]**.** A mixture of potassium carbonate (5.10 g, 36.7 mmol) and *p-tert*-butylcalix[4]arene (10.0 g, 15.4 mmol) in dry acetone (200 mL) was stirred at room temperature for 1 h. A solution of propargyl bromide (6.49 g, 30.8 mmol) in dry acetone (50 mL) was added dropwise into the above stirred mixture over a period of 30 min. The reaction mixture was heated at reflux for 24 h and was then allowed to cool to room temperature. The reaction mixture was filtered over Celite® to remove insoluble particles, and the filtrate was concentrated on a rotavap. Aqueous HCl (2 M, 100 mL) was added to the concentrated reaction mixture, and the product was extracted with dichloromethane (3 × 100 mL). The combined organic extract was successively washed with water and brine (100 mL), dried over anhydrous Na_2SO_4, filtered, and evaporated to dryness on a rotavap and with a vacuum pump. The crude product was crystallized from CH_2Cl_2/CH_3OH to afford **5b** as a white solid (9.10g, 82% yield). ^{1}H NMR ($CDCl_3$, 300 MHz,): δ= 7.07 (s, 4H, ArH), 6.72 (s, 4H, ArH), 6.47 (s, 2H, Ar-OH), 4.74 (d, *J* = 2.4 Hz, 4H, ArOC*H*$_2$C≡CH), 4.37 (d, *J* = 13.4 Hz, 4H, ArC*H*$_2$Ar AB), 3.33 (d, *J* = 13.4 Hz, 4H, ArC*H*$_2$Ar AB), 2.54 (t, *J* = 2.4 Hz, 2H, ArOCH$_2$C≡C*H*), 1.30 (s, 18H, *t*Bu), 0.90 (s, 18H, *t*Bu). ^{13}C-NMR ($CDCl_3$, 75.46 MHz): δ= 30.9, 31.7, 32.0, 33.88, 63.3, 76.3, 78.8, 125.0, 125.5, 128.0, 132.6, 141.6, 147.2, 149.5, 150.4. APCI(+) MS (*m/z*, relative intensity) 725.45 (M^+, 100).

1,4-Bis(azidomethyl)-2,3-dipropoxynaphthalene 3a. To a mixture of 1,4-bis(bromomethyl)-2,3-dipropoxy-naphthalene **2a**[11] (0.86 g, 2.0 mmol) and sodium azide (2.00 mg, 30.8 mmol), was added 20 mL of dimethylformamide. The mixture was stirred at 90^{o}C under N_2 for 48 h. After cooling to room temperature, the reaction mixture was poured into water (100 mL) and extracted with ethyl acetate (2×100 mL). The combined organic layer was washed with brine solution (50 mL). The organic layer was dried over anhydrous $MgSO_4$ and the solvent was removed using a rotavap. The residue was purified by column chromatography (silica gel, eluting with 80:20 hexane:ethyl acetate) to give a colourless oil (0.56 g, 80%, m.p. 123.2 °C). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.98 (m, 2H, naphthyl-*H*), 7.53 (m, 2H, naphthyl-*H*), 4.86 (s, 4H, naphthyl-*H*), 4.05 (t, *J* = 6.6 Hz, 4H, –OC*H*$_2$CH$_2$CH$_3$), 1.89 (m, 4H, –OCH$_2$C*H*$_2$CH$_3$), 1.10 (t, *J* = 7.5 Hz, 6H, -O(CH$_2$)$_2$C*H*$_3$). ^{13}C-NMR ($CDCl_3$, 75.46 MHz): δ = 150.4, 129.9, 126.1, 124.41, 124.2, 76.3, 45.2, 23.6, 10.6. APCI (+) MS (*m/z*, relative intensity) 353.4 [(M-2*N*)$^+$, 80).

1,4-Bis(azidomethyl)-2,3-dibutoxynaphthalene 3b. To a mixture of 1,4-bis(bromomethyl)-2,3-dibutoxy-naphthalene **2b**[10] (0.912 g, 2.00 mmol) and sodium azide (2.00 mg, 30.8 mmol), was added 20 mL of dimethylformamide. The mixture was stirred

at 90 °C under N_2 for 48 h. After cooling to room temperature, the reaction mixture was poured into water (100 mL) and extracted with ethyl acetate (2×100 mL). The combined organic layer was washed with brine solution (50 mL). The organic layer was dried over anhydrous $MgSO_4$ and the solvent was removed using a rotavap. The residue was purified by column chromatography (silica gel, eluting with 80:20 hexane:ethyl acetate) to give a colourless oil (0.64 g, 83%, m.p. 115.6°C). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.98 (m, 2H, naphthyl-*H*), 7.54 (m, 2H, naphthyl-*H*), 4.86 (s, 4H, naphthyl-*H*), 4.09 (t, *J* = 6.6 Hz, 4H, –$OCH_2(CH_2)_2CH_3$), 1.89 (m, 4H, $OCH_2CH_2C_2H_5$), 1.55 (m, 4H, –$O(CH_2)_2CH_2CH_3$), 1.02 (t, *J* = 7.5 Hz, 6H, $O(CH_2)_3CH_3$); ^{13}C-NMR ($CDCl_3$, 75.5 MHz): δ= 151.4, 129.9, 126.1, 124.4, 124.2, 74.6, 45.2, 32.4, 19.4, 14.0. APCI (+) MS (*m/z*, relative intensity) 353.4 [(M-2*N*)$^+$], 100).

25,27-Dihydroxy-26,28-bridge[1′,4′-bis(1″,2″,3″-triazoly-methyl)-2′,3′dipropoxynaphthalene)]calix[4]arene 6a. A solution of dialkyne **5a** (188 mg, 0.376 mmol), diazide **3a** (150 mg, 0.342 mmol), DIPEA (160 μL, 0.90 mmol), and CuI (35 mg, 0.18 mmol) in toluene (40 mL) was heated at reflux for 24 h under N_2. After evaporation of the solvent on a rotavap, the resulting crude product was dissolved in chloroform (100 mL) and washed with water (50 mL). The organic layer was separated and dried over anhydrous $MgSO_4$ and the solvent was removed using a rotavap. The residue was purified by column chromatography (silica gel, eluting with 90:10 dichloromethane: methanol) giving **6a** (128 mg, 40%) as a colourless solid: mp. 129.1 °C (*dec*); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.11 (m, 2H, naphthyl-*H*), 7.58 (s, 2H, triazoly-*H*), 7.398 (m, 2H, naphthyl-*H*), 7.15 (s, 4H, Ar-*OH*), 6.81 (d, *J*=7.2 Hz, 4H, Ar*H*), 6.01 (m, 8H, Ar*H*), 6.01 (s, 4H, naphthyl-CH_2-triazole), 5.07 (s, 4H, ArOCH_2-triazole), 3.92 (m, 8H, ArCH_2Ar AB system and –$OCH_2C_2H_5$), 2.90 (d, *J*=13.5 Hz, 4H, ArCH_2Ar AB system), 1.83 (m, 4H, –$OCH_2CH_2CH_3$), 1.02 (t, *J*=7.2 Hz, 6H, –$O(CH_2)_2CH_3$). ^{13}C-NMR ($CDCl_3$, 75.46 MHz): δ= 152.8, 151.1, 150.4, 143.3, 133.1, 129.6, 128.7, 128.3, 127.9, 126.8, 125.3, 124.3, 124, 123.7, 119.0, 76.1, 69.2, 44.8, 31.2, 23.6, 10.6; HRMS APPI (+) calcd. for $C_{52}H_{50}N_6O_6$:854.3792, found: 854.3794.

5,11,17,23-Tetra-*tert*-butyl-25,27-dihydroxy-26,28-bridge-[1′,4′-bis(1″,2″,3″-triazolymethyl)-2′,3′dipropoxy-naphthalene)]calix-[4]arene (6b). A solution of dialkyne **5b** ((218 mg, 0.301 mmol), diazide **3a** (150 mg, 0.342 mmol), DIPEA (160 μL, 0.90 mmol), and the CuI (35 mg, 0.18 mmol) in toluene (40 mL) was heated at reflux for 24 h under N_2. After evaporation of the solvent, the resulting crude product was dissolved in chloroform (100 mL) and washed with water (50 mL). The organic layer was separated and dried over anhydrous $MgSO_4$ and the solvent was removed on a rotavap. The residue was purified by column chromatography (silica gel, eluting with 90:10 dichloromethane: methanol) to give a colourless solid (140 mg, 45%, m.p. 145.5 °C). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.06 (m, 2H, naphthyl-*H*); 7.73 (s, 2H, triazole-*H*); 7.38 (m, 2H, naphthyl-*H*), 6.92 (s, 4H, Ar*H*), 6.83 (s, 2H, Ar-O*H*), 6.63 (s, 4H, Ar*H*), 5.99 (s, 4H, naphthyl-CH_2-triazole), 5.06 (s, 4H, ArOCH_2-triazole), 4.02 (d, *J*=12.0 Hz, 4H, ArCH_2Ar, AB system), 4.02 (t, *J*=6.0 Hz, naphthyl-O$CH_2C_2H_5$), 3.02 (d, *J*= 12.0 Hz, 4H, ArCH_2Ar, AB system), 1.82 (m, 4H, -$OCH_2CH_2CH_3$), 1.27 (s, 18H, *t*Bu) 1.02 (t, *J*=9.0 Hz, 6H, , -$O(CH_2)_2CH_3$), 0.89 (s, 18H, *t*Bu); ^{13}C-NMR ($CDCl_3$, 75.46 MHz): δ= 150.5, 150.3, 149.4, 147.0, 143.8, 141.5, 132.4, 129.6, 127.8, 125.5, 125.0, 124.1, 124.0, 123.6, 76.04, 69.3, 53.4, 44.9, 33.8, 31.7, 30.9, 24.0, 10.7; HRMS APPI (+) calcd. for $C_{68}H_{82}N_6O_6$: 1078.6296, found: 1078.6236.

5,11,17,23-Tetra-*tert*-butyl-25,27-dihydroxy-26,28-bridge[1′,4′-bis(1″,2″,3″-triazolmethyl)-2′,3′dibutoxynaphthalene)]calix[4]-arene (6c). A solution of dialkyne **5a** (188 mg, 0.376 mmol), diazide **3b** (120 mg, 0.237 mmol), DIPEA (160 μL, 0.90 mmol), and CuI (35 mg, 0.18 mmol) in toluene (40 mL) was heated at reflux for 24 h under N_2. After evaporation of the solvent, the resulting crude product was dissolved in chloroform (100 mL) and washed with water (50 mL). The organic layer was separated and dried over anhydrous $MgSO_4$ and the solvent was removed using a rotavap. The residue was purified by column chromatography (silica gel, eluting with 90:10 dichloromethane: methanol) to give a colourless solid (130 mg, 43%, m.p. 153.4°C). ^{1}H NMR (300 MHz, $CDCl_3$): δ= 8.09 (m, 2H, naphthyl-*H*), 7.52 (s, 2H, triazole-*H*), 7.38 (m, 2H, naphthyl-*H*), 7.10 (s, 2H, ArO*H*), 6.80 (d, *J* = 6.0 Hz, 4H, Ar*H*), 6.55 (m, 8H, Ar*H*), 6.01 (s, 4H, naph-CH_2-triazole), 5.07 (s, 4H, ArOCH_2-triazole), 4.04 (t, *J* = 6.0 Hz, 4H, -$OCH_2CH_2CH_2CH_3$), 3.94 (d, *J* = 15.0 Hz, 4H, ArCH_2, AB system), 2.94 (d, *J* = 15.0 Hz, 4H, ArCH_2, AB system), 1.76 (m, 4H, -$O(CH_2)_2CH_2CH_3$), 1.49 (m, 4H), 0.96 (t, *J*=6.0 Hz, 6H, -$O(CH_2)_3CH_3$). ^{13}C-NMR ($CDCl_3$, 75.46 MHz): δ = 152.8, 151.0, 143.2, 133.2, 129.6, 128.7, 128.3, 127.9, 126.9, 125.3, 124.3, 124.0, 123.8, 119.0, 74.5, 69.1, 44.9, 32.4, 31.2, 19.4, 14.0; HRMS APPI (+) calcd. for $C_{54}H_{54}N_6O_6$: 882.4105, found: 882.4070.

25,27-Dihydroxy-26,28-bridge[1′,4′-bis(1″,2″,3″-triazoly-methyl)-2′,3′dibutoxynaphthalene)]calix[4]arene (6d). A solution of dialkyne **5b** (218 mg, 0.301mmol), diazide **3b** (120mg, 0.237 mmol), DIPEA (160 μL, 0.90 mmol), and the copper Iodide (35 mg, 0.18 mmol) in toluene (40 mL) was refluxed for 24 h under N_2. After evaporation of the solvent, the resulting crude product was dissolved in chloroform (100 mL) and washed with water (50 mL). The organic layer was separated and dried over anhydrous $MgSO_4$ and the solvent was removed using a rotavap. The residue was purified by column chromatography (silica gel, eluting with 90:10 dichloromethane: methanol) to give a colourless solid (140 mg, 42%, m.p. 171.6 °C). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.02 (m, 2H, naphthyl-H), 7.65 (s, 2H, triazole-H), 7.36 (m, 2H, naphthyl-H), 6.91 (s, 4H, ArH), 6.74 (s, 2H, ArOH), 5.98 (s, 4H, ArH), 5.93 (s, 4H, naphthyl-CH_2-triazole), 5.05 (s, 4H, ArOCH_2-), 4.05 (m, 4H, $OCH_2CH_2CH_2CH_3$), 4.00 (d, *J* = 12.9 Hz, 4H, ArCH_2, AB system), 2.99 (d, *J* = 12.9 Hz, 4H, ArCH_2Ar, AB system), 1.77 (m, 4H, -$OCH_2CH_2CH_2CH_3$), 1.49 (m, 4H, $OCH_2CH_2CH_2CH_3$), 1.27 (s, 18H, *t*Bu), 0.95 (t, *J*=14.4 Hz, 6H, -$OCH_2CH_2CH_2CH_3$), 0.86 (s, 18H, *t*Bu); ^{13}C-NMR ($CDCl_3$, 75.46 MHz): δ=150.6, 150.2, 149.4, 146.9, 143.7, 141.5, 132.4, 129.6, 127.8, 126.6, 125.4, 124.9, 124.1, 124.0, 123.6, 74.4, 69.2, 44.8, 33.8, 32.4, 31.7, 30.9, 29.7, 19.4, 14.0; HRMS APPI (+) calcd. for $C_{70}H_{86}N_6O_6$: 1106.6609, found: 1106.6584.

Conclusions

Four new substituted-naphthyl ring "capped" 1,2,3-triazole-linked calix[4]arenes have been synthesized and characterized. Binding

studies conducted by fluorescence quenching with twelve different metal ions showed that these new macrocyclic receptors were sensitive chemosensors for Fe^{3+} and Hg^{2+}, in particular, for Fe^{3+} ions. The association, or binding constants, were determined using a 1:1 non-linear global analytical program developed by Thordarson and were compared with the values obtained with the classical Benesi-Hildebrand method. The site of the binding of the metal ions to the macrocyclic receptors was shown by a ^{1}H NMR spectroscopic analysis and was confirmed by a detailed DFT computational analysis.

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Naphthyl "capped" triazole-linked calix[4]arene hosts as fluorescent chemosensors towards Fe^{3+} and Hg^{2+}: an experimental and computational study

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