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Preparation and sensor evaluation of a Pacman phthalocyanine

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Abstract—We report both the preparation and sensor evaluation of a new metal-free calixarene bridged binuclear phthalocyanine.
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The binuclear phthalocyanines have attracted much interest as potential catalysts for the four electron reduction of water.[1] However, little work has been carried out into their potential use as environmental sensors for heavy metals. In fact, we could not find any previous work involving the application of non-ionophore metal-free phthalocyanines in cation sensing applications.[2] We believe that the cofacial metal-free binuclear phthalocyanines, which possess an electron rich core of eight nitrogens, may offer a unique opportunity for the potential sensing of soft heavy metals such as silver and mercury.[3] However, cofacial binuclear phthalocyanines prepared in the past use rigid bridges which do not afford much conformational flexibility, a property which is desirable in chemoreceptor applications. We desired to create a new system using a bridge that not only places two phthalocyanine rings in a cofacial arrangement, but also allows conformational flexibility.

Outlined in Figure 1 is our proposed target, a calix[4] arene bridged binuclear phthalocyanine (**1**), the first ever Pacman phthalocyanine. We chose a calixarene bridge since the calixarene scaffold would not only allow for the cofacial placement of two phthalocyanine rings on the lower rim of the calixarene but would also act as a molecular lever, allowing for open and closed forms. Furthermore, the calixarene bridge would impart organic solubility to the system, which is a necessary requirement for immobilisation into polymer membranes.[4]

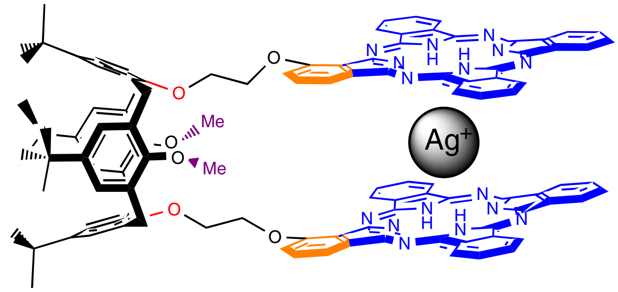

Figure 1. Target binuclear phthalocyanine **1**.

We are aware that many calixarene derivatives possess cation complexing ability, however, past studies have shown that hard oxygen calixarenes such as **4** (Scheme 1) are not only ineffective at binding hard metals such as Na^{+1}, K^{+1} and Ca^{+2}, but are also incapable of coordinating soft metals.[5] As a consequence of this, the calixarene bridge's ionophore properties are 'turned off' in **1**.

The synthetic route used to prepare **1** is outlined in Scheme 1. The preparation of **2** was achieved by treating calix[4] arene with methyl iodide, potassium carbonate base in DMF at 70 °C for 1 h. After purification, a 33% yield of **2** was obtained, it should be noted that trace quantities of the trimethoxy derivative were also formed, which could be separated by silica gel column chromatography.

The preparation of the spacer required two steps; esterification of the remaining hydroxy groups of **2** using NaH and ethyl bromoacetate in DMF at 70 °C for 2 days followed by reduction of the esters to their respective alcohols. Extra additions of base and ethyl bromoacetate were required to drive the esterification reaction to completion. After purification by column chromatography, a yield of 50% was obtained for **3**. Ester **3** was

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Keywords: Calixarene; Temperature ^{1}H NMR; Conformation; Ion selective electrode; Binuclear phthalocyanine; Pacman; Silver selective.

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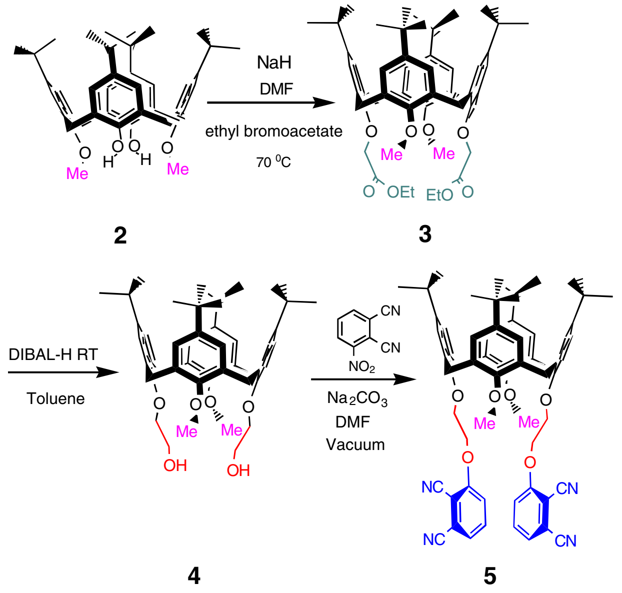


Scheme 1.

converted to alcohol **4** using DIBAL-H in THF for 24 h under N_2. After purification, a 70% yield of **4** was obtained. The structure of **4** was confirmed by ESI-MS, with a $[M+Na]^+$ peak at 787 amu. Bisphthalonitrile **5** was prepared using an S_NAr substitution reaction between **4** and 3-nitrophthalonitrile, with Na_2CO_3 in DMF under vacuum for 5 days to give **5** in 25% yield after column chromatography.[6] The presence of **5** was confirmed by ESI-MS with a $[M+Na]^+$ peak at 1039 amu and a $[M+K]^+$ peak at 1055 amu.

The ^1H NMR spectra of **3**, **4** and **5** were poorly resolved at room temperature. This result was expected as lower rim intramolecular hydrogen bonding is lost. To resolve the ^1H NMR spectra of the calixarenes a series of high temperature ^1H NMR studies on **3**, **4** and **5** were undertaken. We initially used DMSO-d_6 as the NMR solvent, however, we could not dissolve **3** in DMSO-d_6.[7] We chose an alternative solvent, nitrobenzene-d_5, which offers both a superior temperature range to DMSO-d_6 and can readily solubilise less polar molecules.[8]

The results of the temperature studies on **3**, **4** and **5** are shown in Figure 2. At 150 °C, we observed a timed average spectrum for **3** resulting from rapid conformational changes. As a result, the structure resolves into a cone conformation with a pair of doublets for the bridging methylene protons at δ 3.49 ppm and 4.47 ppm; a singlet at 4.53 ppm, a quartet at 4.34 ppm and a triplet at 1.35 ppm for the ethyl acetate substituents. Calixarene **4** also gave a poorly resolved ^1H NMR spectrum at room temperature. Resolution of the ^1H NMR of **4** was partially achieved in nitrobenzene-d_5 at 150 °C (Fig. 2). Again, a time averaged spectrum for **4** was obtained with a pair of doublets at δ 3.55 ppm and 4.40 ppm. However, the pendent glycol groups could not be properly resolved even at 195 °C. We believe that the pendent alcohol groups are involved in intramolecular hydrogen bonding with the lower rim phenoxy oxygens of the calixarene, which stabilises some of the conformations present in the solution.

The high temperature ^1H NMR spectrum of **5** (Fig. 2) in nitrobenzene-d_5 at 125 °C, again showed a time resolved spectrum indicating an apparent cone conformation for the calixarene. However, unlike **4** the spacer methylene groups could be resolved at 195 °C giving two triplets at δ 4.39 ppm and 4.73 ppm (Fig. 2). The phthalonitrile protons occurred as a triplet at δ 7.73 ppm and a doublet at 7.40 ppm, however, the other expected doublet could not be seen as it overlapped with one of the solvent peaks.

We originally believed that the nitrile groups of **5** should be able to coordinate soft metal ions such as silver via the nitrogens of the nitrile groups. However, we found from ion selective electrode studies that **5** showed no selectivity for any of the metals screened.[9] This can be explained by the lack of a pre-organisation of the binding cavity on the lower rim of the calixarene as a result of the random orientation of the phthalonitrile substituents, as confirmed by the ^1H NMR spectrum of **5** at room temperature.

Calixarene **5** was reacted with an eightfold excess of phthalonitrile in Li/pentanol at 110 °C for 24 h[10] to afford **1**, which was isolated by silica gel column chromatography using chloroform then THF as eluant. A small quantity of the isolated phthalocyanine mixture from this column was dissolved in a minimum amount of THF and applied to a size exclusion column (Bio-Beads SX-3).[11] The mixture separated into two bands, the first band was the target binuclear phthalocyanine **1** followed by unsubstituted phthalocyanine. Final purification of **1** involved precipitation from THF/methanol to give **1** in an 8% yield. The presence of **1** was confirmed by MALDI-TOF MS. As expected, the calixarene bridge imparts excellent solubility for **1** in organic solvents, even in the absence of substituents on the peripheral benzo groups of the phthalocyanine rings (Scheme 2).

A UV–vis analysis of **1** (Fig. 3) revealed a typical broadening and blue shift of the phthalocyanine Q-band. Further analysis of the spectrum indicated that **1** existed as a conformational mixture of cofacial and open forms. The peak observed at 630 nm was assigned to the coupled cofacial or 'clamshell' conformation, whereas the peaks at 700 and 650 nm are due to the uncoupled absorption of the open form.[12]

To evaluate the cation complexing ability of **1**, the ligand was incorporated into a PVC membrane based ion selective electrode (ISE). A blank membrane was also prepared, which was identical in composition to the membrane containing **1**, except that no ionophore was present (ion-exchange salt only).[13] A comparison of the two membranes served as a rapid means to ascertain the selectivity induced by **1**. The potentiometric response of ISEs to each of a series of cations is shown in Figure 4. The blank membrane, containing no element of cavity pre-organisation, resulted in a

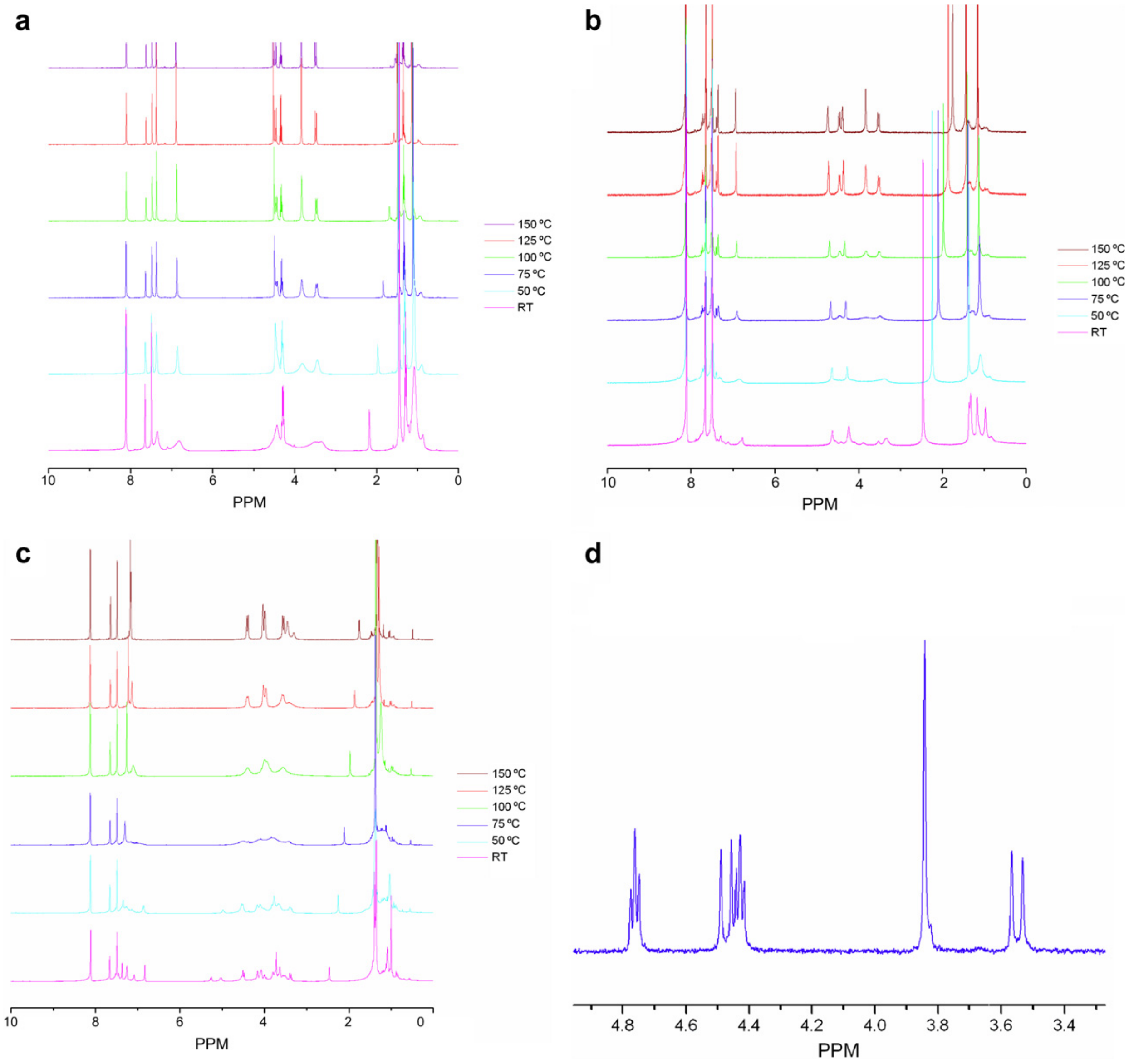
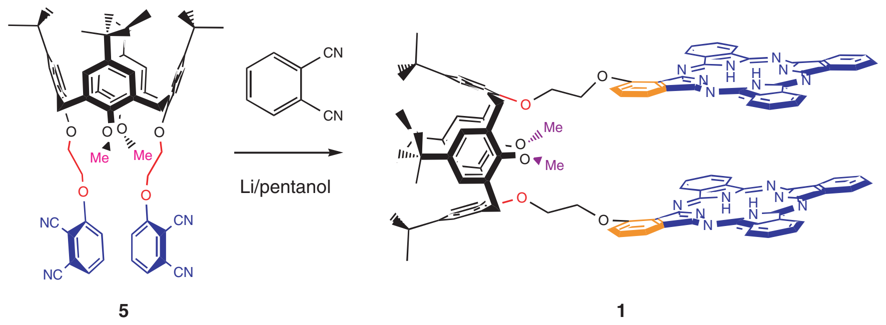


Figure 2. High temperature ^{1}H NMR study in nitrobenzene-d_5: (a) **3**, (b) **4**, (c) **5** and (d) expanded region showing the methylene spacer protons of **5**.



Scheme 2.

Hofmeister order of selectivity, showing a preference for Hg^{2+} and Ag^{+}, which are the most lipophilic cations tested. ISEs containing **1** appeared to suppress the Hg^{2+} response resulting in overall Ag^{+} selectivity as dictated by the complexing properties of **1**.

We believe that the binding occurs through interaction of the phthalocyanine rings with the silver cation. This conclusion is based on the fact that **5** did not possess any silver selectivity, therefore eliminating the possibility of the ether oxygens of the calixarene bridge coordinating

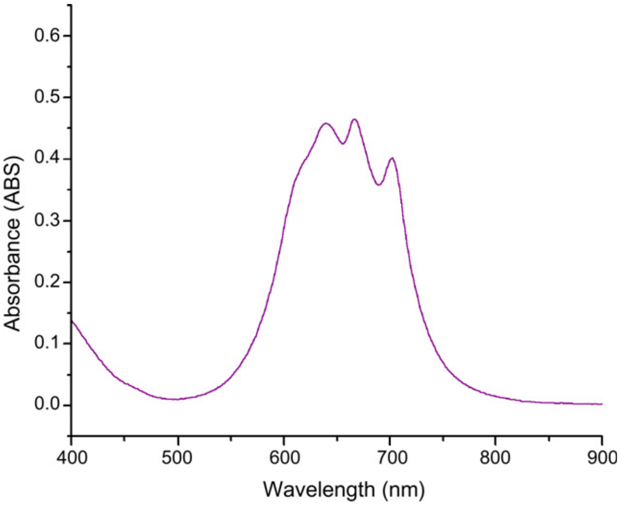


Figure 3. The electronic spectrum of **1** at 10^{-6} M in $CHCl_3$.

silver.[9] Also fluorimetric experiments were carried out on **1** in the presence of Ag^+. We found that the fluorescence of **1** decreased upon the addition of silver cations demonstrating that the two phthalocyanine rings of **1** are 'sandwiching' the silver ions.

In conclusion, we have reported the first example of the application of a metal-free binuclear phthalocyanine for the sensing of a heavy metal. A study of the broader sensor characteristics such as concentration response ranges, slopes and formal selectivity coefficients, as calculated by Nernstian equations of **1** are underway.

Acknowledgement

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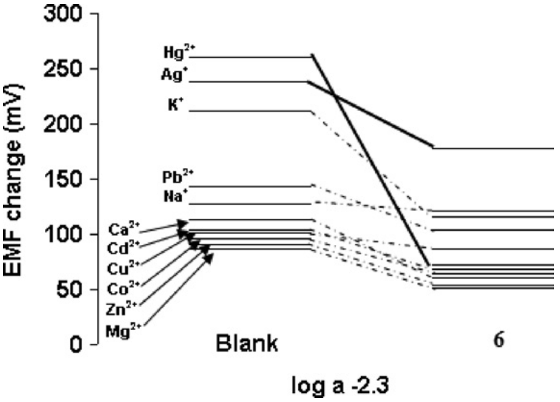
6. Preparation of 5,11,17,23-tetra-*tert*-butyl-25,27-diethyleneoxyphthalonitrile-26,28-dimethoxycalix[4]arene **5**: 3-Nitrophthalonitrile (0.95 g, 5.5 mmol), **4** (1.05 g,



Host	1
Hg^{2+}	-2.70±0.01
Ag^+	0
Pb^{2+}	-2.06±0.18
Cu^{2+}	-2.34±0.19
Co^{2+}	-2.99±0.15
Cd^{2+}	-2.85±0.16
Zn^{2+}	-3.05±0.16
H^+	-1.02±0.10
Mg^{2+}	-3.03±0.18
Ca^{2+}	-3.00±0.18
Li^+	-1.91±0.18
K^+	-0.75±0.13
Na^+	-1.04±0.08

Figure 4. ISE results for **1**. Reproducibility based on three ISE's. *Note*: I is the primary ion Ag^+ and J is the interferant specified. The Separate Solutions Method (SSM) was used where $\log a_I = \log a_J = -2.3$.

1.37 mmol) and K_2CO_3 (0.76 g, 5.5 mmol) were stirred under vacuum in anhydrous DMF (15 cm^3) for five days. Each day Na_2CO_3 (0.19 g, 1.37 mmol) and 3-nitrophthalonitrile (0.23 g, 1.37 mmol) were added to force the reaction to completion. On day six, the reaction mixture was then poured onto ice water (50 ml), filtered and the solid was washed with hot water (2 × 25 ml). The crude brown solid was purified by column chromatography using 70:30 hexane/ethyl acetate, to give a light green solid (0.34 g, 0.34 mmol, 25% yield) ^{1}H NMR: ($CDCl_3$) δ (ppm) (195 °C); 1.7, (m, 18H, *t*-Bu); 1.9, (m, 18H, *t*-Bu); 3.55, (d, 4H, $J = 13.0$ Hz, Ar-CH_2-Ar); 3.84, (s, 6H, 2Me); 4.43, (t, 4H, $J = 5.0$ Hz, CH_2 spacer); 4.47, (d, 4H, $J = 13.0$ Hz, Ar-CH_2-Ar); 4.76, (t, 4H, $J = 5.0$ Hz, CH_2 spacer); 6.67, (s, 4H, ArH); 7.36, (s, 4H, ArH); 7.40, (d, 2H, $J = 7.6$ Hz, ArH); 7.72, (t, 2H, $J = 7.6$ Hz, ArH). ESI *m*/*z*: 1039 ($M+Na^+$), 1055 ($M+K^+$) IR: (KBr [cm^{-1}]): 3500 $cm^{-1}\nu$(O–H), 3000 $cm^{-1}\nu(Bu_t)$.

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10. Preparation of 5,11,17,23-tetra-*tert*-butyl-26,28-dimethoxycalix[4]arene(diethyleneoxy) binuclear phthalocyanine **1**: Lithium (0.03 g, 4.28 mmol) was added to 3 ml of pentanol in a 10 ml round-bottom flask and heated to 60 °C for 30 min under nitrogen to form the lithium alkoxide. To this reaction flask, **5** (0.1 g, 0.122 mmol) and phthalonitrile (0.14 g, 1.10 mmol) were added to the reaction mixture and this was then heated at 110 °C under nitrogen for 24 h. The reaction mixture was cooled to room temperature and poured into 1 N HCl. A blue precipitate was formed and collected by centrifugation and was further washed, first with water and then methanol. Chromatography was carried out on a silica gel column using chloroform as eluant, followed by THF. Then a second silica gel column was carried out on all bands collected from the first column using THF as the mobile phase. The phthalocyanine crude (0.03 g) was then dissolved in THF and applied to a size exclusion column (Bio-Beads SX-3, it should be noted that 0.03 g is the optimum loading for the size exclusion column) using THF as mobile phase. Two bands were collected, the first band was **5**, followed by unsubstituted phthalocyanine. The binuclear band was then rerun on the size exclusion column. This binuclear was then columned again on a silica gel column using THF as eluant. A blue compound was obtained in 0.017 g, 0.01 mmol, 8% yield. MALDI-TOF *m*/*z*: 1790.28 (M+1).
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13. The preparation and the use of ion selective electrodes (ISEs): Potentiometric membranes were prepared using 250 mg of 2-nitrophenyl octyl ether, 125 mg PVC, 6.5 mmol ligand **5** and 2.7 mmol of potassium tetrakis(4-chlorophenyl) borate dissolved in dry THF and evaporated slowly. The ISEs referred to as the blank were prepared in an identical fashion but contained no ligand **5**. The electrochemical cell used consisted of a double junction reference electrode and a PVC membrane working electrode in the following arrangement: Ag|AgCl|3 M KCl||0.1 M LiOAc||sample solution|PVC membrane|0.01 M NaCl|AgCl|Ag. Membranes were conditioned in 0.01 M sodium chloride for 12 h and deionised water for half an hour prior to ISE titrations. The potentiometric cell was interfaced to a PC using a National Instruments SCB-68 4-channel interface. All ISE measurements were performed in triplicate.