Electrochemically and photochemically active Palladium(II) heterotopic metallacalix[3]arenes†

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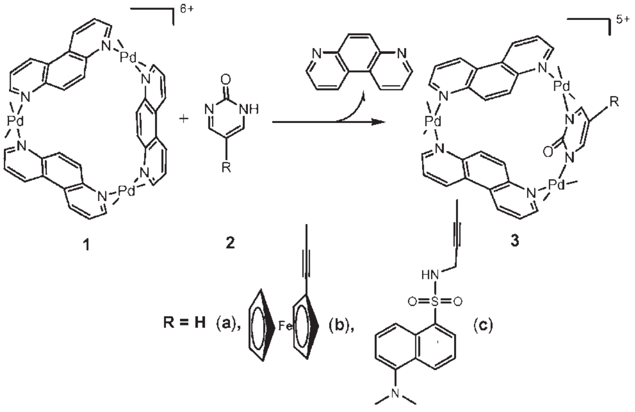
The cyclic trinuclear system, $[(en)_3Pd_3(4,7\text{-phen})_3]^{6+}$, undergoes a ligand exchange reaction with 5-R-2-hydroxypyrimidine derivatives (HRpymo; R = ethynylferrocene, 5-(dimethylamino)-*N*-(2-propynyl)-1-naphthalene sulfonamide) to give $[(en)_3Pd_3(4,7\text{-phen})_2(Rpymo)]^{5+}$, functional supramolecular receptors of mononucleotides.

Metal ions play an important role in the self-assembly processes of discrete nano-sized containers. These systems are useful as unique chemical environments for highly selective host–guest interactions, sensing and catalytic processes.[1] As far as sensing is concerned, it is also necessary to implement a function capable of transducing the molecular recognition event into a measurable signal, usually electrochemical or photochemical.[2,3] In this regard, some of the most versatile and widely used systems are the functionalised macrocycles of the calixarene family.[4,5] The formal substitution of the methylene linker and phenol ring in classical organic calixarenes by a metal fragment and a bent nitrogen heterocycle, respectively, leads to the formation of their inorganic analogues termed as metallacalix[*n*]arenes.[6,7] Although, we[6] and others[8,9] have demonstrated their suitability for supramolecular recognition, as proven by ^{1}H NMR, there are no reports on functionalised metallacalix[*n*]arenes systems acting as sensors. In contrast to classical organic calixarenes, the typical cationic charge of metallacalix[*n*]arenes makes them well suited for selective anion binding, with the recognition of mononucleotides in highly competitive, *i.e.* aqueous, media a highly desirable target.[10]

In previously reported work, we have studied the ligand exchange reactions of $[Pd_3(en)_3(4,7\text{-phen})_3]^{6+}$ (**1**) with 2-hydroxypyrimidine (Hpymo; **2a**) as a convenient strategy to produce heterotopic metallacalix[*n*]arenes of the type $[Pd_n(en)_n(4,7\text{-phen})_{n-m}(\text{pyrimidin-2-olate})_m]^{(2n-m)+}$.[11] In the present communication, we take advantage of this approach to incorporate electro- or photochemical functionality in a metallacalixarene by means of the ligand exchange reaction of **1** with 5-ethynylferrocene-2-hydroxypyrimidine (**2b**) or 5-{5′-(dimethylamino)-*N*-(2′-propynyl-1′-yl)-1-naphthalenesulfonamide}-2-hydroxypyrimidine (**2c**) derivatives to produce the functionalised derivatives $[Pd_3(en)_3(4,7\text{-phen})_2(\text{5-ethynylferrocenepyrimidin-2-olate})]^{5+}$ (**3b**) and $[Pd_3(en)_3(4,7\text{-phen})_2(5\text{-}\{5'\text{-(dimethylamino)-}N\text{-(2'-propynyl-1'-yl)-1-naphthalenesulfonamide}\}\text{pyrimidin-2-olate})]^{5+}$ (**3c**) (Scheme 1).

The first step has been to prepare the functionalised ligands. We have used a Sonogashira-type coupling reaction[12] between 5-iodo-2-hydroxypyrimidine[13] and either ethynylferrocene or 5-(dimethylamino)-*N*-(2-propynyl)-1-naphthalenesulfonamide[14] to afford the novel electrochemically active 5-ethynylferrocene-2-hydroxypyrimidine (**2b**) system and the fluorescent 5-{5′-(dimethylamino)-1-naphthalenesulfonamide-*N*-(2′-propynyl-1′-yl)}-2-hydroxypyrimidine (**2c**) derivative. ^{1}H NMR, ESI-MS for **2b** and **2c** and X-ray crystallographic studies for **2b**‡ confirm the attachment of the ethynyl groups to the C5 position of the pyrimidine ring (Fig. 1).

Cyclic voltammetry of **2b** in acetonitrile solution exhibits the expected reversible one-electron wave with a formal potential $E_{1/2}^{\circ}$ lying at +0.105 V *vs.* ferrocene/ferrocinium and −0.195 V *vs.* ethynylferrocene/ethynylferrocinium. The electronic spectrum of **2c** reveals an absorption band centred at 413 nm and an emission band at 547 nm. In addition, DFT calculations at the B3LYP/3-21G(*) level on **2b** show that the ethynylferrocene substituent is responsible for only slight



Scheme 1 Ligand exchange reaction between $[Pd_3(en)_3(4,7\text{-phen})_3]^{6+}$ (**1**) and 2-hydroxypyrimidine derivatives (**2**) yields metallacalix[3]arenes of $[Pd_3(en)_3(4,7\text{-phen})_2(\text{5-R-pyrimidin-2-olate})]^{5+}$ type with R = H (**3a**)[11]; ethynylferrocene (**3b**); and 5-(dimethylamino)-*N*-(2-propynyl)-1-naphthalene sulfonamide (**3c**).

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† Electronic supplementary information (ESI) available: Experimental details, ESI-MS, cyclic voltametry, electronic spectra and crystallographic data (CCDC 677962) in CIF format. See DOI: 10.1039/b805705b

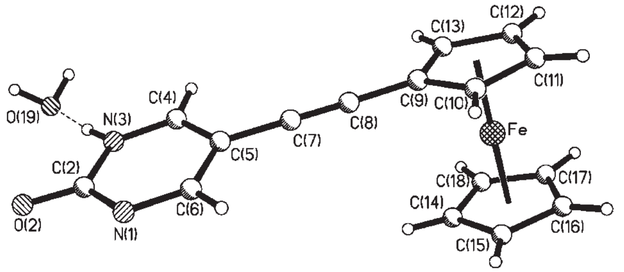


Fig. 1 The molecular structure of 5-ethynylferrocene-2-hydroxypyrimidine (**2b**), including the hydrogen-bonded water molecule.

charge withdrawal from the pyrimidine ring, which is not expected to significantly change the coordinative properties of the heterocycle.

The reaction between metallacalix[3]arene **1** and **2b** at 50 °C for 4 h gives rise to exchange of one of the 4,7-phenanthroline bridging ligands with **2b**, yielding the functionalised heterotopic [Pd$_3$(en)$_3$(4,7-phen)$_2$(5-ethynylferrocenepyrimidin-2-olate)]$^{5+}$ (**3b**) species (Scheme 1). This reaction was followed by ^{1}H NMR, ESI-MS and cyclic voltammetry. The ^{1}H NMR studies are indicative of the quantitative formation of **3b**. The phenanthroline resonances split and shift as a consequence of the lowering of the original C_{2v} symmetry of the phenanthroline ligands in **1** (Fig. 2). In addition, we also observe resonances corresponding to free 4,7-phen. Coordination of **2b** to Pd in **3b** is responsible for a significant high-field shift (0.17 pmm) of the pyrimidine H4,H4′ resonances and the manteinance of the its orginal C_{2v} symmetry agrees with a *N*1,*N*3-bridging coordination mode.

The formation of **3b** was also confirmed by ESI-MS, with the observation of peaks at *m*/*z* = 1472.01 corresponding to [Pd$_3$(en)$_3$(4,7-phen)$_2$(5-ethynylferrocenepyrimidin-2-olate)(NO$_3$)$_5$]$^+$ with one deprotonated ethylenediamine. Smaller fragments of this assembly include [Pd$_3$(en)$_3$(4,7-phen)(5-ethynylferrocenepyrimidin-2-olate)(NO$_3$)$_5$]$^+$ (*m*/*z* = 1291.9), [Pd$_2$(en)$_2$(5-ethynylferrocenepyrimidin-2-olate)(NO$_3$)$_2$]$^+$ (*m*/*z* = 760.9) and [Pd(en)(5-ethynylferrocenepyrimidin-2-olate)]$^+$ (*m*/*z* 468.9) (Fig. 3).

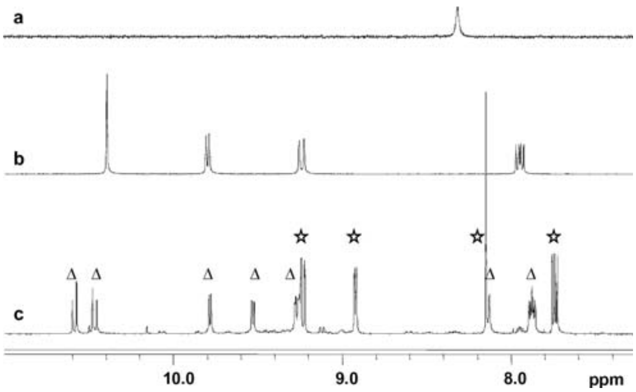


Fig. 2 Aromatic region of ^{1}H NMR (MeOD·D$_2$O, 293 K, 400 MHz). (a) 5-ethynylferrocene-2-hydroxypyrimidine (**2b**); (b) [Pd$_3$(en)$_3$(4,7-phen)$_3$]$^{6+}$ (**1**); (c) 1 : 1 reaction mixture of **1** and **2b** after 4 h at 50 °C. [Pd$_3$(en)$_3$(4,7-phen)$_2$(5-ethynylferrocenepyrimidin-2-olate)(NO$_3$)$_5$]$^{5+}$ (**3b**) (triangles), free 4,7-phen (stars).

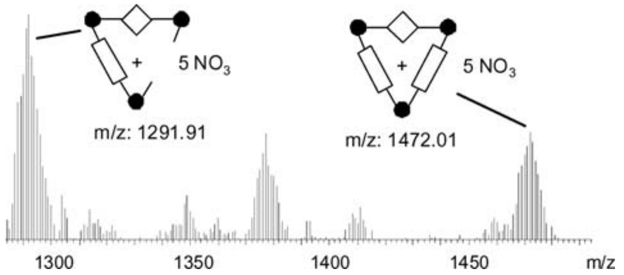
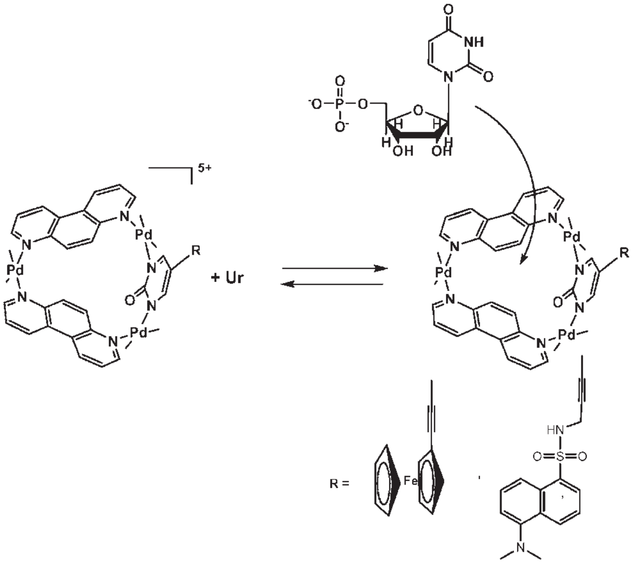


Fig. 3 Selected region of ESI-MS of compound **3b** (5-ethynylferrocenepyrimin-2-olate, diamonds; 4,7-phenanthroline, rectangles; (en)Pd, circles.

3b has also been characterised by cyclic voltammetry in a water–methanol solution and shows an unique reversible wave which is shifted −0.064 V compared to free **2b** and +0.041 V *versus* ferrocene-ferrocinium. This behaviour is attributed to the quantitative formation of complex **3b** with no residual free **2b**, as indicated by ^{1}H NMR.

When the same reaction was carried out between complex **1** and **2c** the formation of the related [Pd$_3$(en)$_3$(4,7-phen)$_2$-(5-{5′-(dimethylamino)-1-naphthalenesulfonamide-*N*-(2′-propynyl-1′-yl)}pyrimidin-2-olate)]$^{5+}$ (**3c**) was observed; however, in this case the reaction was not quantitative. Thus, ^{1}H NMR reveals the formation of the new species **3c** along with free phenanthroline ligand and the unreacted complex **1** (see ESI†). Increasing the time and temperature of the reaction did not improve the result. The formation of **3c** was also followed by ESI-MS, showing the formation of different fragmented species of **3c** which included [Pd$_2$(en)$_2$(4,7-phen)(5-{5′-(dimethylamino)-1-naphthalenesulfonamide-*N*-(2′-propynyl-1′-yl)}pyrimidin-2-olate)(NO$_3$)$_2$(H$_2$O)]$^+$ (*m*/*z* = 1037.1) (ESI†). These results suggest that the bulk of the dansyl residue in **2c** makes the formation of **3c** less favourable compared to **3b** and **3a**. The electronic spectra of **3c** reveals absorption and emission bands centred at 394 and 532 nm, respectively.



Scheme 2 Supramolecular recognition of uridine-5′-monophosphate by **3b** and **3c**.

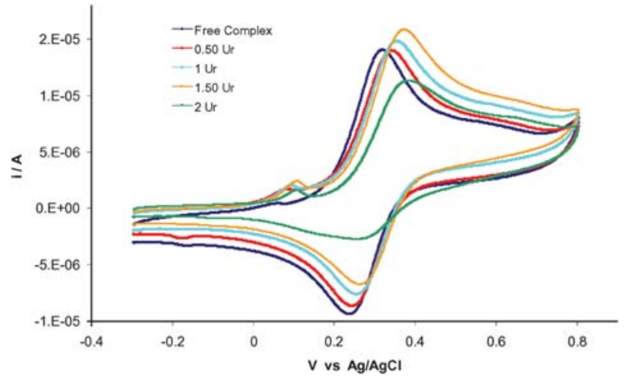


Fig. 4 Cyclic voltammograms of a titration of 1 mM **3b** with uridine-5′-monophosphate disodium salt in the 0.25–2 mM range.

The presence of functional groups in **3b** and **3c** prompted us to study the possible use of these systems as sensors for biologically relevant anions (Scheme 2). In this regard, a cyclic voltammetry titration was undertaken by adding Ur (uridine-5′-monophosphate disodium salt) to a methanol–water solution of **3b** with **3b** : Ur ratios ranging from 1 : 0 to 1 : 2. The results agree with a recognition process taking place, with potential shifts to more positive potentials being observed upon addition of Ur (Fig. 4).

The shape of the redox wave was unaltered throughout all the experiments, showing reversible voltammograms for all concentrations and therefore proving the suitability of **3b** as a potential molecular-based sensor. The K_{ass} value of 35(15) M^{-1} is comparable to those obtained by ^1H NMR methods on the related **1** system.[15] In addition, the ^1H NMR studies also reveal the preferential interaction of the aromatic residue of Ur with the cavity of **3b**, which agrees with a synergistic effect of electrostatic and stacking interactions taking place in the molecular recognition process. Likewise, the addition of mononucleotides (AMP, Ur) to a solution of **3c** gives rise to slight shifts of the emission band to higher wavelengths in the fluorescence spectra of **3c**; however, in this case the formation of a precipitate hampers reliable determination of a K_{ass}.

In summary, we report a simple strategy for the preparation of electro- and photochemically active metallacalixarenes by means of a ligand exchange reaction. This method may also be applicable to other types of inorganic macrocycles. We also show that these systems are able to transduce molecular recognition processes taking place inside the cavity of these complexes into measurable signals thus offer new potential applications for metallacalixarenes and related systems in the sensing of biorelevant anions.

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Notes and references

‡ *Crystal Data* for **2b**: [$FeC_{16}H_{12}N_2O \cdot CH_3O \cdot H_2O$], M = 354.18, triclinic, space group $P\bar{1}$, a = 6.022(4), b = 9.912(6), c = 12.964(8) Å, α = 78.772(7), β = 77.213(6), γ = 77.793(6)°, V = 728.6(8) $Å^3$, Z = 2, D_{calc} = 1.614 g cm^{-3}, T = 120 K, λ (synchrotron) = 0.6751 Å, R_{int} = 0.045, $R(F, F^2 > 2\sigma)$ = 0.075, $R_w(F^2$, all data) = 0.208) for 2205 unique reflections, goodness-of-fit = 1.07. CCDC 677962.†

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