Fluorescent signaling provides deeper insight into aromatic anion uptake by metal-ion activated molecular receptors†

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Received (in Durham, UK) 12th December 2007, Accepted 13th March 2008
First published as an Advance Article on the web 28th April 2008
DOI: 10.1039/b719183a

Two new, octadentate, fluorescent, macrocyclic ligands, 1-(2-(9-anthrylmethylamino)ethyl)-4,7,10-tris((2*S*)-2-hydroxy-3-phenoxypropyl)-1,4,7,10-tetraazacyclododecane (**L^1**) and 1-(2-(9-anthrylmethylamino)ethyl)-4,7,10-tris((2*S*)-2-hydroxy-3-[4′-(methyl)phenoxy]propyl)-1,4,7,10-tetraazacyclododecane (**L^2**), have been prepared with a view to using them to study aromatic anion sequestration. The eight-coordinate Cd(II) complexes of **L^1** and **L^2**, [Cd**L^1**](ClO$_4$)$_2$·2H$_2$O and [Cd**L^2**](ClO$_4$)$_2$·4H$_2$O, have both been shown capable of acting as receptors for a range of aromatic oxoanions. This has been demonstrated by perturbation of both ^{1}H NMR chemical shift values and the anthracene derived fluorescence emission intensity as the potential guest anion and the receptor are combined. Non-linear least squares regression analysis of the resulting titration curves leads to the determination of binding constants in 20% aqueous 1,4-dioxane which lie in the range $10^{2.3}$ M^{-1} (benzoate) to $10^{7.5}$ M^{-1} (2,6-dihydroxybenzoate). By reference to earlier, X-ray determined structures of related, but non-fluorescent, inclusion complexes the primary anion retention force is known to arise from hydrogen bonding between the anion and four convergent hydroxy groups that exist at the base of a cavity that develops in **L^1** and **L^2** as their aromatic groups juxtapose upon metal ion coordination. This work reveals significant stability enhancement when hydroxy groups are positioned on the anion at points where O–H···π hydrogen bonding to the aromatic rings that constitute the walls of the cavity becomes geometrically possible.

Introduction

In earlier work we have synthesised anion receptors that are derived from the macrocyclic ligand cyclen (1,4,7,10-tetraazacyclododecane) by equipping it with four pendant arms, each having a hydroxy group and an aromatic group attached at or through the 2-position.[1] On coordination to a metal ion with the potential for eight-coordination, this receptor ligand pre-assembles into a receptor complex where the four aromatic groups come together to form a partially enclosed space, or cavity. This cavity is well suited to aromatic oxoanion retention since it has at its base four convergent hydroxy groups that are activated towards hydrogen bond donation to an incoming anion by simultaneous coordination to the metal ion. A number of these receptor complexes containing bound anions have been structurally characterized by X-ray crystallography,[1a–d] with the one displayed schematically in Fig. 1(a) being typical.

Here *p*-aminobenzoate is the guest anion and Cd(II) is the eight-coordinating metal ion responsible for pre-assembling the receptor ligand **1**, Fig. 1(b), into the appropriate conical configuration with the O–H bonds directed into the anion binding cavity. Up to this point we have studied anion inclusion in this class of receptor using, principally, NMR and X-ray crystallography to probe the anion inclusion behaviour in solution and the solid state, respectively. We now turn our attention to fluorescence perturbation as a means of signaling anion inclusion,[2] in solution, within the binding cavity of these receptor complexes. Since this technique is of higher sensitivity than routine NMR spectroscopy it allows work down to lower host and guest concentrations and consequently the acquisition of binding constant data for host–guest complexes over a wider stability range. This in turn presents an opportunity to gain a fuller understanding of the principles of molecular recognition that are operative for

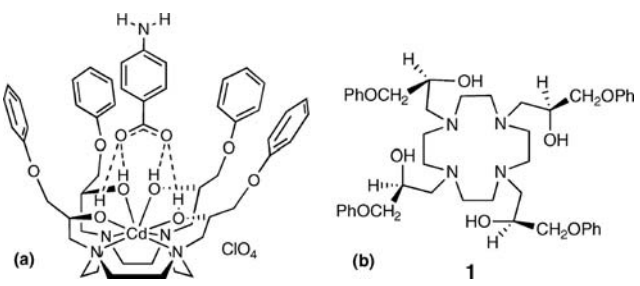

Fig. 1 (a) The structural characteristics of *p*-aminobenzoate inclusion within the host–guest complex formed from the Cd(II) complex of the receptor ligand **1**, shown in (b).

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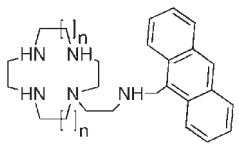
† Electronic supplementary information (ESI) available: Syntheses for the hydrohalide derivatives of compounds **5**, **6**, **L^1** and **L^2** produced for the purpose of acquiring microanalytical data relevant to the parent compounds; Table S1, giving binding constant determinations made using UV monitored titrations. See DOI: 10.1039/b719183a

these hosts and of the selectivity of the receptors over a wider range of guest molecules. The design of our receptor ligands is such that it is relatively easy to replace one of the 2-hydroxyethyl pendant arms in **1**, for example, with a similar arm containing a photoinduced electron transfer (PeT) responsive fluorophore.[3] To preserve the aromatic anion retaining capabilities of $[Cd(\mathbf{1})]^{2+}$ the replacement arm, besides being potentially fluorescent, must also contain an electron donor group that is capable of binding to the metal ion and simultaneously acting as a hydrogen bond donor for the guest. It must also have an aromatic moiety capable of forming a part of the cavity wall. A pendant group that meets these requirements is the 2-(9-anthrylmethylamino)ethyl moiety. In previous work this has been attached as a pendant arm to cyclen by Kimura *et al*. to give **2**,[4] and to cyclam (1,4,8,11-tetraazacyclotetradecane) by Fabbrizzi *et al*. to give **3**.[5] Accordingly, we describe in this report the means by which ligand **1**, and its analogue in which the phenyl groups are replaced by *p*-tolyl, can be modified to incorporate the 2-(9-anthrylmethylamino)ethyl fluorophore as one of the pendant arms. We demonstrate that the Cd(II) complexes of the modified ligands retain the anion including capabilities of $[Cd(\mathbf{1})]^{2+}$, and we report on their anion including properties together with the associated fluorescence perturbations.



2, n = 1
3, n = 2

Experimental

General information

All syntheses were performed under dry nitrogen. Solvents were purified using literature methods.[6] Microanalyses were conducted at the University of Otago, New Zealand. NMR data were collected using a Varian Gemini 300 spectrometer operating at 300.075 MHz for protons and 75.462 MHz for ^{13}C. ^{1}H NMR chemical shifts were referenced to the residual protonated solvent peak taken as 7.26 ppm for $CDCl_3$, 2.60 ppm for DMSO-d_6, 3.31 ppm for CD_3OD and 1.96 ppm for CD_3CN. For ^{13}C NMR spectra, chemical shifts were referenced to the central resonance of the solvent multiplet peak taken as 77.00 ppm for $CDCl_3$, 49.00 ppm for CD_3OD, 39.52 for DMSO-d_6, and δ 118.10 for CD_3CN (*C*N resonance). UV-Visible absorbance spectra were measured on a Varian Cary 50 SCAN UV-Visible spectrophotometer. Flash chromatography was carried out using the method of Still *et al*.,[7] with silica gel from Merck Kieselgel (particle size 230–400 mesh) as the stationary phase. (2*S*)-(+)-3-Phenoxy-1,2-epoxypropane,[1a] (2*S*)-(+)-3-[4′-(methyl)phenoxy]-1,2-epoxypropane,[8] 1-(benzyloxycarbonyl)-1,4,7,10-tetraazacyclododecane,[9] and 9-(2-bromoethyliminomethyl)anthracene[5] were prepared by literature methods.

Syntheses

1-(Benzyloxycarbonyl)-4, 7,10-tris((2*S*)-2-hydroxy-3-phenoxypropyl)-1,4,7,10-tetraazacyclododecane (5, R = phenyl). A solution of (2*S*)-(+)-3-phenoxy-1,2-epoxypropane (623 mg, 4.15 mmol) in dry EtOH (30 cm^3) was added to a refluxing solution of 1-(benzyloxycarbonyl)-1,4,7,10-tetraazacyclododecane (424 mg, 1.38 mmol) in dry ethanol (10 cm^3). The reaction was monitored by TLC on silica (hexane–CH_2Cl_2, 9 : 1) and upon complete disappearance of the epoxide, which occurred after 10 days, the reaction mixture was cooled and the solvent was evaporated under vacuum to give the pure product as a viscous yellow oil (1.05 g, quantitative), $\delta_H(CDCl_3)$ 7.29 (10 H, br m, Ar*H*), 6.94 (10 H, br m, Ar*H*), 5.13 (2 H, s, BnCH_2), 4.3–2.0 (34 H, br m, C*H*, CH_2 and O*H*); $\delta_C(CDCl_3)$ 158.57 (3 C, PhO, *ipso*), 156.20 (1 C, C=O), 136.61 (1 C, Bn, *ipso*), 129.28 (6 C PhO), 128.52 (1 C, Bn), 128.37 (2 C, Bn), 127.90 (2 C,Bn), 120.72 (3 C, PhO), 114.43 (6 C, PhO), 69.74 (2 C, O*C*H_2) , 69.62 (1 C, O*C*H_2), 67.04 (1 C, *C*H_2Bn), 66.02 (2 C, *C*HOH), 65.34 (1 C *C*HOH) 59.46 (2 C, *exo*-*C*H_2N), 58.00 (1 C, *exo*-*C*H_2N), 55.06 (2 C, cyclen*C*H_2), 52.76 (2 C, cyclen*C*H_2), 49.77 (2 C, cyclen*C*H_2), 47.60 (2 C, cyclen*C*H_2).

1, 4, 7-Tris((2*S*)-2-hydroxy-3-phenoxypropyl)-1, 4, 7,10-tetraazacyclododecane (6, R = phenyl). Cyclohexene (300 mg, 3.65 mmol) was added to a stirred solution of 1-(benzyloxycarbonyl)-4,7,10-tetraazacyclododecane (523 mg, 0.69 mmol) dissolved in absolute ethanol (10 cm^3). 10% Palladium-on-carbon catalyst (500 mg) was then added. The reaction mixture was refluxed at 80 °C for 5 h, filtered through Celite and the filtrate concentrated *in vacuo* to give the free base as a brown oil (507 mg, 97%); $\delta_H(CDCl_3)$ 7.27 (6 H, m, Ph*H*); 6.92 (9 H, m, Ph*H*); 4.8–2.0 (35 H, br m, C*H*, CH_2, O*H*, N*H*); $\delta_C(CDCl_3)$ 158.67 (2 C, Ph, *ipso*), 158.60 (1 C, Ph, *ipso*), 129.29 (2 C, Ph), 129.23 (4 C, Ph), 120.72 (1 C, Ph), 120.60 (2 C, Ph), 114.45 (4 C, Ph), 114.40 (2 C, Ph), 69.91 (2 C, *C*H_2O), 69.28 (1 C, *C*H_2O), 66.44 (1 C, *C*HOH), 65.46 (2 C, *C*HOH), 60.20 (3 C, *exo*-*C*H_2N), 51.41 (4 C, cyclen*C*H_2), 44.36 (4 C, cyclen-*C*H_2).

1-(2-(9-Anthrylmethylamino)ethyl)-4, 7, 10-tris((2*S*)-2-hydroxy-3-phenoxypropyl)-1,4,7,10-tetraazacyclododecane (L^1). 1,4,7-Tris((2*S*)-2-hydroxy-3-phenoxypropyl)-1, 4, 7,10-tetraazacyclododecane (2.71 g, 4.35 mmol) was dissolved in dry MeCN (200 cm^3) and 9-(2-bromoethyliminomethyl)anthracene (1.36 g, 4.35 mmol) was added as a solid, along with $NaHCO_3$ (540 mg) and molecular sieves. The reaction was wrapped in foil to keep out light and then refluxed for 10 days before cooling it to room temperature, filtering it and removing the solvent under reduced pressure. This gave the intermediate imine as a red oil (3.23 g, 87%). The imine was redissolved in EtOH (40 cm^3) and $NaBH_4$ (216 mg, 5.71 mmol) was added. The reaction mixture was stirred overnight, and then diluted with water (40 cm^3), and extracted with CH_2Cl_2 (4 × 30 cm^3). The combined organic layers were dried over Na_2SO_4, then filtered and evaporated to yield the crude product as a red oil (1.82 g, 76%). Purification was achieved either by column chromatography on basic alumina with 1% MeOH–CH_2Cl_2 as eluent (yield 1.0 g, 41%) or by converting it to its pentahydrobromide salt, (1.09 g, 45%), as described in the ESI.† The free ligand

was recovered from the HBr salt by dissolving the salt in 1 : 1 water–ethanol and basifying to pH 13. Extraction with CH_2Cl_2, drying with Na_2SO_4, filtration and evaporation of the solvent under reduced pressure gave the free base as a reddish brown oil (quantitative), λ_{max}/nm (20% aqueous 1,4-dioxane) 388.5 nm (ε/dm^3 mol^{-1} cm^{-1} 6896), 368.4 (7347), 350.6 (4647), 334.4 (2170), 321.1 (sh) (805); δ_H(DMSO-d_6) 8.6 (3 H, m Anth*H*), 8.1 (2 H, m, Anth*H*), 7.6 (4 H, m, Anth*H*), 7.30 (6 H, m, Ph*H*), 6.95 (9 H, m, Ph*H*), 5.3–2.0 (41 H, br m, -C*H*, -CH_2-, O*H*, N*H*); δ_C($CDCl_3$) 158.0 (3 C, Ph, *ipso*), 132.4 (2 C, Anth), 132.2 (2 C, Anth), 130.4 (6 C, Ph), 130.0 (1 C, Anth), 126.9 (2 C, Anth), 126.1 (1 C, Anth), 126.0 (2 C, Anth), 121.6 (2 C, Anth), 121.3 (2 C, Anth), 120.3 (3 C, Ph), 115.2 (6 C, Ph), 71.4 (1 C, *C*H_2O), 71.1 (1 C, *C*H_2O), 68.7 (1 C, *C*H_2O), 68.4 (1 C, *C*HOH), 67.5 (1 C, *C*HOH), 67.1 (1 C, *C*HOH), 61.4 (1 C, *exo*-*C*H_2N), 58.9 (1 C, *exo*-*C*H_2N), 58.3 (1 C, *exo*-*C*H_2N), 57.4 (1 C, *exo*-*C*H_2N), 56.4 (1 C, *C*H_2NH), 53.1 (2 C, cyclen*C*H_2), 52.5 (2 C, cyclen*C*H_2), 51.4 (2 C, cyclen*C*H_2), 50.4 (2 C, cyclen*C*H_2), 46.0 (1 C, Anth*C*H_2).

1-(2-(9-Anthrylmethylamino)ethyl)-4, 7,10-tris((2*S*)-2-hydroxy-3-phenoxypropyl)-1,4,7,10-tetraazacyclododecanecadmium(II) diperchlorate dihydrate ([CdL^1](ClO_4)$_2$·2H_2O). [Note: Perchlorate salts are potentially explosive. Although no problems were encountered, precautions **MUST** be taken when handling these substances.] A solution of cadmium(II) perchlorate hexahydrate (0.117 g, 0.29 mmol) in EtOH (2.3 cm^3) was added dropwise over 5 min to a refluxing solution of 1-(2-(9-anthrylmethylamino)ethyl)-4,7,10-tris((2*S*)-2-hydroxy-3-phenoxypropyl)-1,4,7,10-tetraazacyclododecane (0.214 g, 0.25 mmol) in EtOH (7 cm^3). A white precipitate formed instantly. The suspension was maintained at reflux temperature for 1 h before cooling it to room temperature and evaporating the solvent. Trituration of the residue with diethyl ether produced a cream colored powder. This was collected by filtration, washed with ice-cold water (1 cm^3), and dried under vacuum to give the pure product. Yield: 0.203 g, 70%. (Found C, 51.9; H, 6.0; N, 5.6. $C_{52}H_{69}CdCl_2N_5O_{16}$ requires C, 51.9; H, 5.8; N, 5.9%); λ_{max}/nm (20% aqueous 1,4-dioxane) 387.7 (ε/dm^3 mol^{-1} cm^{-1} 6733), 367.7 (7202), 349.8 (4700), 333.3 (2619), 318.3 (sh) (1190); δ_H(DMSO-d_6) 8.79–8.20 (3 H, br, m, Anth*H*), 8.14 (2 H, br d, Anth*H*), 7.58 (4 H, br m, Anth*H*), 7.30 (6 H, br s, Ph*H*), 6.95 (9 H, br s, Ph*H*), 5.05 (3 H, br m, -O*H*), 4.60–2.00 (38 H, br m, C*H*, CH_2, N*H*); δ_C(CD_3CN) 159.4 (3 C, Ph, *ipso*), 132.4 (1 C, Anth, *ipso*), 130.6 (6 C, Ph), 130.3 (2 C, Anth, *ipso*), 129.6 (2 C, Anth, *ipso*), 127.7 (2 C, Anth), 126.7 (1 C, Anth), 126.3 (2 C, Anth), 124.9 (2 C, Anth), 124.4 (2 C, Anth), 122.4 (1 C, Ph), 122.3 (2 C, Ph), 115.8 (2 C, Ph), 115.6 (4 C, Ph), 70.6 (1 C, O*C*H_2), 70.2 (1 C, *C*H_2O), 69.6 (1 C, *C*H_2O), 66.1 (1 C, *C*HOH), 65.6 (1 C, *C*HOH), 64.8 (1 C, *C*HOH), 60.0 (1 C, *exo*-*C*H_2N), 57.0 (1 C, *C*H_2NH), 55.3 (2 C, *exo*-*C*H_2N), 54.7 (1 C, *exo*-*C*H_2N), 53.3 (1 C, cyclen*C*H_2), 52.7 (1 C, cyclen*C*H_2), 51.2 (1 C, cyclen*C*H_2), 51.0 (1 C, cyclen*C*H_2), 50.4 (1 C, cyclen*C*H_2), 50.2 (1 C, cyclen*C*H_2), 49.8 (1 C, cyclen*C*H_2), 49.1 (1 C, cyclen*C*H_2), 45.8 (1 C, Anth-*C*H_2).

1-(Benzyloxycarbonyl)-4,7,10-tris((2*S*)-2-hydroxy-3-[4′-(methyl)-phenoxy]propyl)-1,4,7,10-tetraazacyclododecane (5, R = *p*-tolyl). A solution of (2*S*)-(+)-3-[4′-(methyl)phenoxy]-1,2-epoxypropane (2.05 g, 12.5 mmol) in dry EtOH (30 cm^3) was added to a refluxing solution of 1-(benzyloxycarbonyl)-1,4,7,10-tetraazacyclododecane (1.28 g, 4.17 mmol) in dry ethanol (30 cm^3). The reaction was monitored by TLC on silica (hexane–CH_2Cl_2, 9 : 1) and upon complete disappearance of the epoxide, which occurred after ten days, the reaction mixture was cooled to room temperature and the solvent was evaporated to give the product as a viscous yellow oil (3.33 g, quantitative). δ_H($CDCl_3$) 7.37 (5 H, m, Bn), 7.09 (6 H, m, Ph), 6.86 (6 H, m, Ph), 5.32 (2 H, br s, BnCH_2), 5.12 (3 H, br s, -O*H*), 4.6–2.2 (31 H, br m, C*H*, CH_2), 2.26 (9 H, s, CH_3); δ_C($CDCl_3$) 156.9 (2 C, Ph, *ipso*), 156.6 (1 C, Ph, *ipso*), 155.9 (1 C, *C*=O), 136.4 (1 C, Bn, *ipso*), 131.7 (3 C, Ph), 131.6 (6 C, Ph), 128.8 (2 C, Bn), 128.2 (3 C, Bn), 115.6 (6 C, Ph), 70.1 (1 C, *C*H_2O), 69.6 (2 C, *C*H_2O), 67.0 (1 C, Bn*C*H_2-), 66.2 (1 C, *C*HOH), 65.9 (2 C, *C*HOH), 60.9 (1 C, *exo*-*C*H_2N), 59.9 (1 C, *exo*-*C*H_2N), 58.1 (1 C, *exo*-*C*H_2N), 53.8 (2 C, cyclen*C*H_2), 51.3 (2 C, cyclen*C*H_2), 48.0 (2 C, cyclen*C*H_2), 46.0 (2 C, cyclen-*C*H_2), 20.5 (3 C, *C*H_3).

1,4,7-Tris((2*S*)-2-hydroxy-3-[4′-(methyl)phenoxy]propyl)-1,4, 7,10-tetraazacyclododecane (6, R = *p*-tolyl). Cyclohexene (1.91g, 23.3 mmol) was added to a stirred solution of 1-(benzyloxycarbonyl)-4, 7, 10-tris((2*S*)-2-hydroxy-3-[4′-(methyl)-phenoxy]propyl)-1,4,7,10-tetraazacyclododecane (3.33 g, 4.17 mmol) dissolved in absolute ethanol (65 cm^3). 10% Palladium-on-carbon catalyst (3.2 g) was then added. The reaction mixture was refluxed at 80 °C for 5 h, and filtered through Celite. The filtrate was concentrated *in vacuo* to give the free base (1.66 g, 60%). δ_H($CDCl_3$) 7.35 (4 H, br s, Ph*H*), 7.05 (4 H, d, *J* 7.2 Hz, Ph*H*); 6.79 (4 H, d, *J* 7.2 Hz, Ph*H*); 4.3–2.0 (35 H, br, m, O*H*, N*H*, C*H*, CH_2); 2.27 (9 H, s, CH_3); δ_C($CDCl_3$) 156.6 (3 C, Ph, *ipso*), 130.0 (3 C, Ph), 129.5 (6 C, Ph), 114.4 (6 C, Ph), 70.3 (2 C, *C*H_2O), 70.0 (1 C, *C*H_2O), 67.1 (1 C, *C*HOH), 66.0 (2 C, *C*HOH), 61.1 (2 C, *exo*-*C*H_2N), 60.4 (1 C, *exo*-*C*H_2N), 59.7 (1 C, cyclen*C*H_2), 55.8 (1 C, cyclen-*C*H_2), 54.6 (1 C, cyclen*C*H_2), 54.2 (1 C, cyclen*C*H_2), 52.9 (1 C, cyclen*C*H_2), 49.6 (1 C, cyclen*C*H_2), 47.8 (1 C, cyclen*C*H_2), 46.0 (1 C, cyclen*C*H_2), 20.4 (3 C, *C*H_3).

1-(2-(9-Anthrylmethylamino)ethyl)-4, 7, 10-tris((2*S*)-2-hydroxy-3-[4′-(methyl) phenoxy]propyl)-1, 4, 7, 10-tetraazacyclododecane (L^2). 1,4,7-Tris((2*S*)-2-hydroxy-3-[4′-(methyl)phenoxy]propyl)-1,4,7,10-tetraazacyclododecane (0.87 g, 1.23 mmol) was dissolved in dry MeCN (60 cm^3). 9-(2-Bromoethyliminomethyl)anthracene (0.39 g, 1.23 mmol) was added as a solid, along with $NaHCO_3$ (0.13 g) and molecular sieves. The reaction was wrapped in foil to keep out light and refluxed for 10 d before cooling it to room temperature, filtering it and removing the solvent under reduced pressure. This gave the intermediate imine as a red oil. The imine was redissolved in EtOH (25 cm^3) and $NaBH_4$ (100 mg, 2.64 mmol) was added as a solid. The reaction mixture was stirred overnight then diluted with water (30 cm^3) and extracted with CH_2Cl_2 (4 × 30 cm^3). The combined organic layers were dried over Na_2SO_4, then filtered and evaporated to yield the crude

product as a red oil (0.74 g, 67%). Purification was achieved by formation of the pentahydrobromide salt as described in the ESI.† The free ligand was recovered by dissolving the salt in water–ethanol 1 : 1 and basifying to pH 13 with 1 M NaOH. Extraction with CH_2Cl_2, drying with Na_2SO_4, filtration and evaporation of the solvent under reduced pressure gave the pure product as a reddish brown oil (quantitative); λ_{max}/nm (20% aqueous 1,4-dioxane) 386.4 (ε/dm^3 mol^{-1} cm^{-1} 6226), 366.5 (6673), 348.8 (4345), 332.6 (2141), 320.1 (sh) (920); δ_H($CDCl_3$) 8.44 (1 H, s, Anth*H*), 8.02 (2 H, d, J = 8.0 Hz, Anth*H*), 7.46 (2 H, d, J = 9.0 Hz, Anth*H*), 7.33 (4 H, m, Anth*H*), 7.07 (6 H, m, Ph*H*), 6.80 (6 H, br s, Ph*H*), 5.3–2.5 (41 H, br m, N*H*, O*H*, C*H* and CH_2), 2.23 (9 H, s, CH_3); δ_C($CDCl_3$) 156.5 (1 C, Ph, *ipso*), 156.3 (2 C, Ph, *ipso*), 131.4 (2 C, Anth), 130.0 (6 C, Ph), 129.2 (3 C, Ph), 129.0 (1 C, Anth), 128.7 (2 C, Anth), 128.4 (1 C, Anth), 128.15 (2 C, Anth), 128.05 (2 C, Anth), 126.3 (2 C, Anth), 125.3 (2 C, Anth), 115.3 (2 C, Ph), 114.3 (4 C, Ph), 70.3 (2 C, *C*H$_2$O), 69.2 (1 C, *C*H$_2$O), 66.4 (1 C, *C*HOH), 65.6 (2 C, *C*HOH), 62.9 (1 C, *exo*-*C*H$_2$N), 60.4 (2 C, *exo*-*C*H$_2$N), 59.7 (1 C, *exo*-*C*H$_2$N), 57.2 (1 C, *C*H$_2$N*H*), 53.0–50.0 (8 C, m, cyclen*C*H$_2$), 45.5 (1 C, Anth-*C*H$_2$), 20.4 (3 C, *C*H$_3$).

1-(2-(9-Anthrylmethylamino)ethyl)-4, 7, 10-tris((2*S*)-2-hydroxy-3-[4′- (methyl) phenoxy]propyl)- 1, 4, 7, 10- tetraazacyclododecane-cadmium(II) diperchlorate tetrahydrate ([CdL^2](ClO$_4$)$_2$·4H$_2$O). [Note: Perchlorate salts are potentially explosive. Although no problems were encountered, precautions **MUST** be taken when handling these substances.] A solution of cadmium(II) perchlorate hexahydrate (0.183 g, 0.43 mmol) in EtOH (3.5 cm^3) was added dropwise over 5 min to a refluxing solution of 1-(2-(9-anthrylmethylamino)ethyl)-4,7,10-tris((2*S*)-2-hydroxy-3-[4′- (methyl)phenoxy]propyl)- 1, 4, 7, 10-tetraazacyclododecane (0.302 g, 0.39 mmol) in EtOH (10 cm^3). A white precipitate formed instantly. The suspension was maintained at reflux temperature for 1 h before cooling it to room temperature and evaporating the solvent. Trituration of the residue with diethyl ether produced a cream colored powder. This was collected by filtration, washed with ice-cold water (1 cm^3), and dried under vacuum to give the pure product. Yield: 0.261 g, 50%. (Found: C, 51.9; H, 6.5; N, 5.6. $C_{55}H_{79}CdCl_2N_5O_{18}$ requires C, 51.6; H, 6.2; N, 5.5%); λ_{max}/nm (20% aqueous 1,4-dioxane) 386.4 (ε/dm^3 mol^{-1} cm^{-1} 6464), 366.4 (6960), 348.6 (4564), 332.6 (2274), 319.5 (sh) (1008); δ_H(DMSO-d$_6$) 8.78–8.30 (3 H, br m, Anth*H*), 8.10 (2 H, br d, Anth*H*), 7.53 (4 H, br m, Anth*H*), 7.26 (6 H, br s, Ph*H*), 6.90 (6 H, br s, Ph*H*), 5.00 (3 H, br m, -O*H*), 4.70–2.10 (38 H, br, m, N*H*, C*H* and CH_2), 2.00 (9 H, CH_3); δ_C(DMSO-d$_6$) 156.4 (3 C, Ph, *ipso*), 131.4 (2 C, Anth, *ipso*), 130.7 (2 C, Anth, *ipso*), 130.0 (6 C, Ph), 129.5 (3 C, Ph, *ipso*), 129.2 (1 C, Anth, *ipso*), 127.6 (1 C, Anth), 127.2 (2 C, Anth), 125.9 (2 C, Anth), 125.2 (2 C, Anth), 121.8 (2 C, Anth), 115.3 (6 C, Ph), 71.3 (3 C, *C*H$_2$O), 68.0 (1 C, *C*HOH), 67.0 (1 C, *C*HOH), 66.0 (1 C, *C*HOH), 61.8 (1 C, *exo*-*C*H$_2$N), 59.8 (1 C, *C*H$_2$NH), 58.3 (1 C, *exo*-*C*H$_2$N), 57.0 (1 C, *exo*-*C*H$_2$N), 56.0 (1 C, *exo*-*C*H$_2$N), 53.9 (2 C, cyclen*C*H$_2$), 54.0 (2 C, cyclen*C*H$_2$), 52.8 (2 C, cyclen*C*H$_2$), 51.3 (2 C, cyclen*C*H$_2$), 45.9 (1 C, Anth*C*H$_2$), 20.2 (3 C, *C*H$_3$).

Binding constant measurements using ^{1}H NMR

Binding constants for host–guest associations were determined by monitoring changes in the chemical shift of a convenient guest ^{1}H NMR resonance whilst known aliquots of the host complex, in DMSO-d$_6$, were added to 1 × 10^{-3} mol dm^{-3} samples of the sodium salt of the guest in DMSO-d$_6$. A series of ^{1}H NMR spectra were recorded at 294 ± 0.5 K for each host–guest combination from a host : guest ratio of 0 : 1 to 10 : 1. Approximately fifteen different host : guest ratios were used to construct each titration curve which was then fitted using a non-linear curve fitting procedure to yield the value of the binding constant.

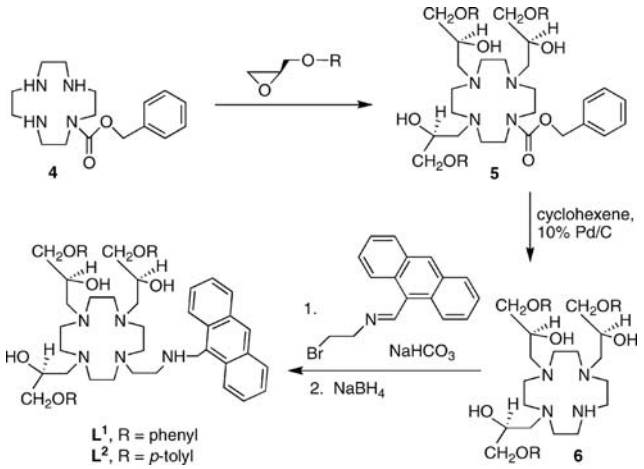
Binding constant measurements using fluorescence emission

In a similar way to the ^{1}H NMR method, titration of the host complex with the sodium salt of the various different guest anions, during which the fluorescence emission intensity of the host at 416 nm was monitored, gave a titration curve that was analysed by non-linear least squares regression to yield the host–guest binding constants and the molar fluorescence (ε'_{HG}) of the host–guest complexes. These titrations were conducted in 20% aqueous 1,4-dioxane (I = 0.1 M Et$_4$NClO$_4$) at pH 7.00 (0.02 M lutidine). The fluorescence emission spectra at 298 ± 0.1 K were recorded on a Varian Cary Eclipse fluorescence spectrophotometer, using stoppered 10 mm quartz cells, over a wavelength range of 370–550 nm at 0.15 nm intervals, with a scan rate of 40 nm min^{-1}. Both the excitation and emission monochromator slit widths were set at 5 nm, and due to the highly fluorescent nature of the compounds, a 1.5 absorbance attenuator was used for 10^{-3} and 10^{-4} mol dm^{-3} solutions, while 10^{-6} mol dm^{-3} solutions required no attenuation. All samples were purged with N_2 prior to use. Quantum yields were calculated with respect to quinine in 0.5 mol dm^{-3} H_2SO_4 according to the method of Demas and Crosby,[10] and are corrected for solvent refractive index.

Results and discussion

Synthesis of the receptor ligands and complexes

The receptor ligands **L^1** (R = phenyl) and **L^2** (R = *p*-tolyl), which are analogues of **1** where one of the pendant arms is the fluorophore 2-(9-anthrylmethylamino)ethyl, were synthesised in three steps from the known compound 1-(benzyloxycarbonyl)cyclen, **4**,[9] using the procedure shown in Scheme 1. The use of an enantiomerically pure epoxide in the first step, which proceeds quantitatively, is necessary to ensure that only the homochiral diastereomer of the monoprotected product, **5**, is formed. For removal of the benzyloxycarbonyl protecting group, in the second step, both the catalytic transfer hydrogenation method,[11] using cyclohexene with palladium-on-charcoal catalyst, and acid hydrolysis, using HBr in acetic acid,[12] were investigated. The former method proved to be the superior of the two, giving the pure product, **6**, directly and in near quantitative yield. The final step proceeds in *ca.* 40% yield, over 10 days in acetonitrile, during which time precautions must be taken to avoid photodegradation of the anthracene sub-unit.[13]



Scheme 1

Cd(II) complexes of $\mathbf{L^1}$ and $\mathbf{L^2}$ were readily formed as their diperchlorate salts by the addition of cadmium(II) perchlorate to a solution of the ligand in hot ethanol and were characterised by NMR spectroscopy, microanalysis and their fluorescence behaviour. The structure of these complexes is expected to be similar to many other Cd(II) complexes which have been formed from cyclen derived ligands that have four appended 2-hydroxyethyl, carboxymethyl, or carbomoylmethyl moieties where the structures have been determined using X-ray diffraction and found to be as shown in Fig. 1(a).[1b] In the case of $\mathbf{L^1}$ and $\mathbf{L^2}$ the fluorescence data that follow confirm that the fluorescent arm is coordinated through the anthrylamine under the conditions used for anion inclusion experiments. Thus, it seemed reasonable to initiate anion inclusion experiments on the basis that the anthryl moiety has the potential to juxtapose with the other three aromatic moieties to form a cavity suitable for anion retention, but this first needed to be verified.

Study of the anion binding ability of $[CdL^1]^{2+}$ and $[CdL^2]^{2+}$ compared to $[Cd(1)]^{2+}$, using ^{1}H NMR monitoring

We set out to verify that $[Cd\mathbf{L^1}]^{2+}$ and $[Cd\mathbf{L^2}]^{2+}$ show similar anion including behaviour that seen with $[Cd(\mathbf{1})]^{2+}$ by using them in the same type of ^{1}H NMR monitored titrations, with the same set of aromatic anions, as we used previously to measure anion binding constants with $[Cd(\mathbf{1})]^{2+}$ in DMSO-d_6.[1c] In this way any commonality in the binding constant values, subject to known differences in the structure of the receptor, could be taken as evidence of similar anion retaining behaviour. The binding constants obtained are shown in Table 1. Those recorded for $[Cd\mathbf{L^1}]^{2+}$ and $[Cd\mathbf{L^2}]^{2+}$ were found to be of similar, but smaller, magnitude to those recorded with $[Cd(\mathbf{1})]^{2+}$, which is consistent with the new anion receptors presenting three convergent O–H groups plus one weaker N–H hydrogen bond donor group,[14] compared to $[Cd(\mathbf{1})]^{2+}$, which presents four convergent O–H groups. These data were taken as confirmation of the anion binding properties previously discovered with $[Cd(\mathbf{1})]^{2+}$ being substantially retained by $[Cd\mathbf{L^1}]^{2+}$ and $[Cd\mathbf{L^2}]^{2+}$.

Table 1 Binding constants[a] in DMSO-d_6, expressed as $\log(K/M^{-1})$, for the inclusion of guest anions within the receptor complexes, determined by ^{1}H NMR monitored titrations

	Receptor complex		
Guest anion	$[Cd(\mathbf{1})]^{2+}$[b]	$[Cd\mathbf{L^1}]^{2+}$[c]	$[Cd\mathbf{L^2}]^{2+}$[c]
p-Nitrophenolate	4.2 ± 0.1	3.5 ± 0.1	3.3 ± 0.1
p-Formylphenolate	>4.5[c]	>4.5	>4.5
p-Nitrobenzoate	4.5 ± 0.4	4.4 ± 0.1	4.0 ± 0.1
Phenoxyacetate	>5	4.8 ± 0.1	4.4 ± 0.1
(D)-Histidinate[d]	4.2 ± 0.2	4.5 ± 0.2	3.6 ± 0.1
(L)-Histidinate[d]	4.2 ± 0.4	>4.5	4.1 ± 0.2

[a] Measured at 294 ± 0.5 K with [guest anion] = 10^{-3} M. Uncertainties are one SD. [b] Taken from ref. 1*c*. [c] This work. [d] At 313 K in 10% (v/v) D_2O in DMSO-d_6.

pH Dependence of the UV absorption and fluorescence emission of $\mathbf{L^1}$ and $\mathbf{L^2}$

Since the fluorescence emission intensity of the 2-(9-anthrylmethylamino)ethyl moiety is known to be modulated by the extent of protonation of the anthrylamine, through the PeT effect,[4] it was important at the outset of the fluorescence investigations to establish the pH dependence of both the UV and fluorescence emission spectra of $\mathbf{L^1}$ and $\mathbf{L^2}$. This and all subsequent work was performed in 20% aqueous 1,4-dioxane since the ligands and complexes under discussion were insufficiently soluble in water. As the pH of a 10^{-4} M solution of the respective ligand was increased from 1.7 to 10.1 the three major UV spectral bands shown by $\mathbf{L^1}$ (Fig. 2) and $\mathbf{L^2}$ underwent a hypsochromic shift of 0.4 nm and the minor band a bathochromic shift of 0.4 nm. This behaviour produced an isosbestic point at 350 nm which would subsequently be used as the excitation wavelength for the fluorescence emission experiments. The intensity of the four well defined UV bands increased by up to *ca.* 10% as the pH was increased, which is consistent with an increase in electron delocalisation brought about by deprotonation of the anthrylamine.[15]

The intensity of the fluorescence emission spectra of $\mathbf{L^1}$ (Fig. 3) and $\mathbf{L^2}$ initially increased slightly as the pH was raised

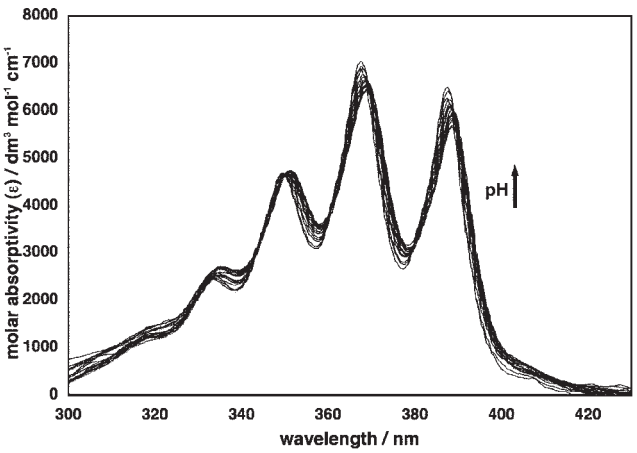


Fig. 2 Changes in the UV spectrum of protonated $\mathbf{L^1}$, 10^{-4} mol dm^{-3} in 20% aqueous 1,4-dioxane (I = 0.1 mol dm^{-3}, Et_4NClO_4), as the pH is raised from 1.7 to 10.1 by the addition of aliquots of NEt_4OH, at 298 K. The pH interval between spectra is *ca.* 0.5 pH units.

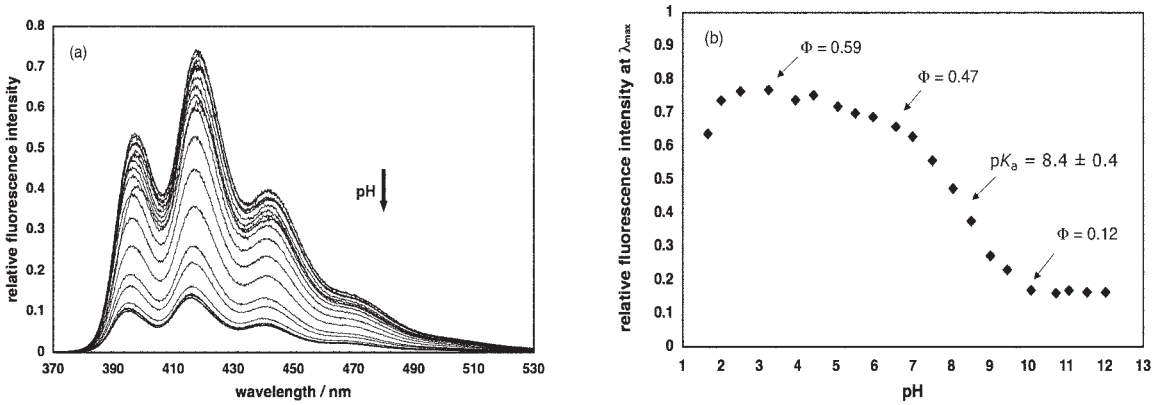


Fig. 3 (a) Changes in the fluorescence emission spectra (λ_{ex} = 350 nm) of protonated $\mathbf{L^1}$, 10^{-6} mol dm^{-3} in 20% aqueous 1,4-dioxane (I = 0.1 mol dm^{-3}, Et_4NClO_4) during titration with Et_4NOH at 298 K. Emission maxima are at 398.1, 418.8 and 442.6 nm at pH 3 and 396.0, 416.7 and 441.2 nm at pH 10. Maximum fluorescence emission intensity decreases from pH 3.0 to pH 12.0; (b) fluorescence emission intensity and quantum yields (Φ) of $\mathbf{L^1}$ at λ_{max} plotted against pH, values derived from (a).

from pH 1.7 to 3.0 using Et_4NOH. This behaviour with anthracene derivatives has been noted previously by Czarnik *et al*. and attributed to deprotonation of the aromatic ring.[2a] Beyond pH 3 and up to the limit of the titration at pH 12 the fluorescence decreased significantly. The sigmoidal shape of this region of the associated titration curve (Fig. 3(b)) clearly indicated a connection between the fluorescence decrease and a deprotonation occurring with a pK_a of 8.4 ± 0.4 in $\mathbf{L^1}$ and 8.2 ± 0.4 in $\mathbf{L^2}$ in a similar way to that which was seen with ligand **2**, where the corresponding pK_a was measured as 7.2 in water.[4] In that work ^{1}H NMR experiments were used to associate the deprotonation responsible for the fluorescence decrease with the anthrylamine and hence to establish PeT originating from the anthrylamine lone pair electrons as the reason for the fluorescence quenching. The same explanation appears to hold for $\mathbf{L^1}$ and $\mathbf{L^2}$ since the measured pK_a values in 20% aqueous dioxane are slightly higher than the value obtained in water, as would be expected in a solvent of lower dielectric constant, and quite similar to the value of 8.91 measured for propyl(9-anthrylmethyl)amine by Fabbrizzi *et al*. in 20% aqueous acetonitrile.[5] The quantum yield values recorded at pH 12 for $\mathbf{L^1}$ and $\mathbf{L^2}$ are 0.117 and 0.047, respectively. Both of these values are in excess of the value of 0.02 recorded for **2** in water by Kimura *et al*.[4] and of 0.028 measured by ourselves for **2** in 20% aqueous 1,4-dioxane. The most likely explanation for the higher baseline fluorescence of $\mathbf{L^1}$ and $\mathbf{L^2}$ lies with the presence of the hydroxy group on the pendant arms adjacent to the anthrylamine. If one or more of these should act as a hydrogen bond donor towards it, the result would be a withdrawal of lone pair electron density from the anthrylamine thereby diminishing the effectiveness of the PeT quenching.[3]

The effect of metal ion complexation on the fluorescence of $\mathbf{L^1}$ and $\mathbf{L^2}$

Metal complexes of $\mathbf{L^1}$ and $\mathbf{L^2}$ formed with Cd(II) ion were of principal interest in this study because of the observations made in earlier work that had demonstrated their superiority in anion sequestration over those of other potentially eight-coordinating metal ions, such as Pb(II) and Hg(II), or the potentially six-coordinating Zn(II) ion.[1] It was necessary, therefore, to characterise fully the fluorescence emission behaviour of $[Cd\mathbf{L^1}]^{2+}$ and $[Cd\mathbf{L^2}]^{2+}$ before investigations of its perturbation upon anion uptake could begin. For comparative purposes the fluorescence emission of the Pb(II), Hg(II) and Zn(II) complexes of $\mathbf{L^1}$ was also investigated.

Titration of a micromolar solution of $\mathbf{L^1}$ or $\mathbf{L^2}$ in 20% aqueous dioxane at pH 7.0 (1 mM HEPES, I = 0.1 M (Et_4NClO_4)) with $Cd(ClO_4)_2$ produced only very slight increases to the molar absorptivity of the UV spectral bands, but very significant increases in the intensity of the fluorescence emission bands. This is shown for $\mathbf{L^1}$ in Fig. 4. With both $\mathbf{L^1}$ and $\mathbf{L^2}$ these increases terminate once one equivalent of Cd(II) has been added. Well established stability constant data leave no doubt that the cyclen component of each ligand molecule will be fully bound to the metal ion, under these conditions, once one equivalent of Cd(II) has been added;[16] the fact that the

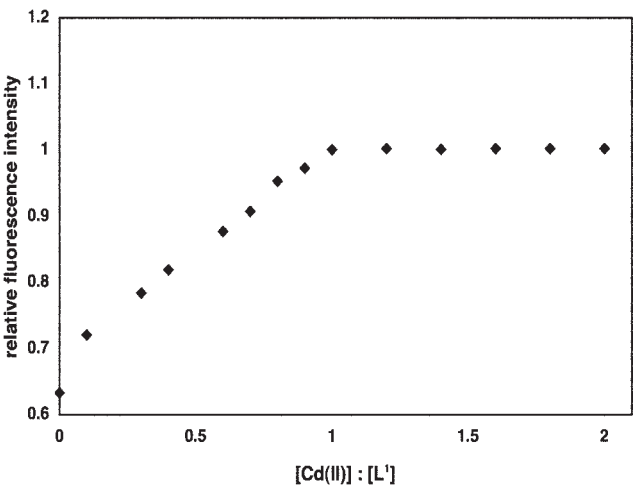


Fig. 4 The relative fluorescence emission intensity at λ_{max} for $\mathbf{L^1}$, 10^{-6} mol dm^{-3} in 20% aqueous 1,4-dioxane, I = 0.1 mol dm^{-3} (Et_4NClO_4), at pH 7.0 (0.01 mol dm^{-3} HEPES) as it is titrated with $Cd(ClO_4)_2{\cdot}6H_2O$.

Table 2 Binding constants determined from fluorescence intensity monitored titrations,[a] expressed as log (K/M^{-1}), and fluorescence intensity perturbations at 416 nm (ΔI)[b] for the inclusion of guest anions within the receptor complexes $[CdL^1]^{2+}$ and $[CdL^2]^{2+}$

	Receptor complex			
	$[CdL^1]^{2+}$		$[CdL^2]^{2+}$	
Guest anion	log K	ΔI	log K	ΔI
Benzoate	2.3 ± 0.1[d]	117%		
p-Hydroxybenzoate	4.5 ± 0.1	27%	3.0 ± 0.1	47%
m-Hydroxybenzoate	5.3 ± 0.2[c]	21%		
o-Hydroxybenzoate	7.1 ± 0.2[c]	20%		
3,5-Dihydroxybenzoate	6.1 ± 0.1[c]	−8%		
2,6-Dihydroxybenzoate	7.5 ± 0.4[c]	−4%		
Gallate (3,4,5-trihydroxybenzoate)	7.1 ± 0.2[c]	10%		
p-Nitrobenzoate	4.9 ± 0.2[c]	−13%	4.7 ± 0.4	−6%
p-Aminobenzoate	6.5 ± 0.1[c]	59%	4.3 ± 0.4[c]	12%
p-Dimethylaminobenzoate	4.1 ± 0.4	−30%	—	0%
Phenoxyacetate	5.5 ± 0.1[c]	2%	—	0%
(D)-Histidinate	—	0%	—	0%
(L)-Histidinate	6.9 ± 0.6[c]	8%	—	0%
p-Toluenesulfonate	4.6 ± 0.3	8%	4.6 ± 0.2	−11%
Benzenesulfonate	3.4 ± 0.1	39%	3.2 ± 0.3	20%

[a] [Receptor complex] = 10^{-4} mol dm^{-3}, measured at pH 7.0 (0.02 mol dm^{-3} lutidine) in 20% aqueous 1,4-dioxane, at 298 K, I = 0.1 mol dm^{-3} (Et_4NClO_4). Uncertainties are taken as one SD. [b] Values calculated as $(I_{HG} - I_H)/I_H) \times 100$ where I_{HG} is calculated together with K from non-linear least squares regression analysis of the titration curve. [c] [Receptor complex] = 10^{-6} mol dm^{-3}. [d] [Receptor complex] = 10^{-3} mol dm^{-3}.

fluorescence enhancement also terminates at this point indicates that the PeT induced quenching is fully eliminated and therefore that the anthrylamine component of each ligand molecule is also strongly bound. The enhanced fluorescence corresponds to a 45% gain in quantum yield for **L**^{1} (from 0.471 to 0.684 for $[CdL^1]^{2+}$, both at pH 7.0), and to a 34% gain for **L**^{2} (from 0.406 to 0.546 for $[CdL^2]^{2+}$, both at pH 7.0). Similar titrations using Pb(II), Hg(II), and Zn(II) with **L**^{1} also demonstrated termination of the fluorescence change once the metal ion concentration became equimolar with that of the ligand; the quantum yields, with changes compared to **L**^{1} at pH 7.0 given in brackets, for the fully formed complexes were found to be 0.518 (+10%), 0.358 (−24%) and 0.518 (+10%), respectively. It is interesting to note that **L**^{1} shows a reversal in the relative magnitude of the fluorescence enhancement induced by Zn(II) and Cd(II) compared to that which was seen with ligand **2**,[4] which gave a higher fluorescence with Zn(II). This is likely to be due to the inability of Zn(II) to exceed a coordination number of six with the types of ligand under consideration here,[1d,17] which prevents it from binding the four pendant arms of **L**^{1} simultaneously. On a time-averaged basis, therefore, the anthrylamine is likely to be partially non-coordinated in the Zn(II) complex of **L**^{1}, allowing some PeT quenching to occur, but fully coordinated in the five-coordinate Zn(II) complex of **2**, where there is no competition from other chelating pendant donor atoms. Cd(II) on the other hand will form eight-coordinate complexes with **L**^{1} thereby fully coordinating the anthrylamine. A similar, but less marked, effect was seen with another cyclen derivative carrying four pendant arms one of which was the dansyl fluorophore.[18]

Fluorescence emission and UV absorbance perturbation in $[CdL^1]^{2+}$ and $[CdL^2]^{2+}$ due to anion sequestration

When $[CdL^1]^{2+}$ and $[CdL^2]^{2+}$ at 10^{-4} or 10^{-6} M in 20% aqueous dioxane at pH 7.0 (0.02 M lutidine, I = 0.1 M (Et_4NClO_4)), were titrated with the aromatic anions shown in Table 2 perturbations of the fluorescence emission intensity at 416 nm were seen. The maximum extent of these for each anion (ΔI) is shown in Table 2. In most cases there was also a change in the molar absorbance of the UV band at λ_{max} (350 nm) ranging from −7% (for (L)-histidinate with $[CdL^2]^{2+}$) to +52% (for benzoate with $[CdL^1]^{2+}$). Since blank titrations using the uncomplexed receptor ligands **L**^{1} and **L**^{2} failed to produce any perceptible changes at the monitored absorption and emission wavelengths under these conditions, both UV absorption and fluorescence emission perturbations induced by a potential guest anion on $[CdL^1]^{2+}$ and $[CdL^2]^{2+}$ were taken as indicators of its inclusion within the binding cavity and thus the resulting titration curves could be used to determine the guest binding constants. However, it should be noted that since the fluorescence and UV perturbations (as well as ^{1}H NMR perturbations) embrace both positive and negative displacements of the monitored signal, the observation of zero perturbation does not necessarily exclude the possibility of anion inclusion.

Recording the UV spectral perturbations was necessary to verify that there were no inner filter effects affecting the fluorescence spectra and also to acquire the absorption data necessary for the computation of the quantum yields. Also it enabled measurements of the guest binding constants to be made that are supplementary to those reported in Table 2. These are reported in the ESI,† but show no significant variance from those obtained using fluorescence data.

The fluorescence emission intensity of $[CdL^1]^{2+}$ and $[CdL^2]^{2+}$ is sufficiently high that perturbations to it can easily be recorded at 10^{-6} M, compared to 10^{-4} M for UV and 10^{-3} M for ^{1}H NMR perturbations. Because of the greater level of host–guest dissociation at the lower concentration this widens the range of anion binding constants that can be measured to an upper limit of *ca.* $10^{7.5}$, compared to $10^{4.5}$ in studies using ^{1}H NMR monitoring. A typical titration curve

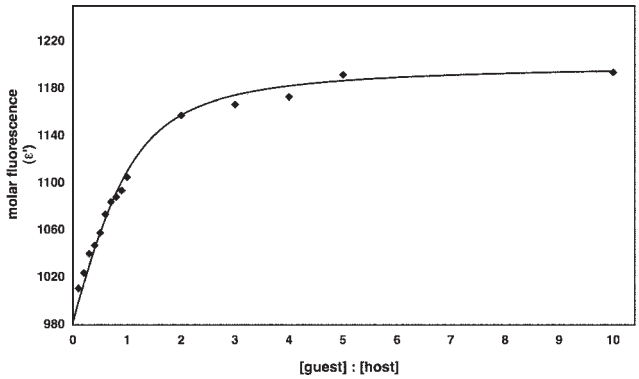


Fig. 5 Molar fluorescence changes (ε') at 416 nm for 10^{-6} mol dm^{-3} [Cd**L**^{1}](ClO$_4$)$_2$ in 20% aqueous 1,4-dioxane at pH 7.0 (0.02 mol dm^{-3} lutidine, I = 0.1 M (Et_4NClO_4)), as it is titrated with sodium *p*-hydroxybenzoate. Squares indicate the experimental data points and the curve indicates the theoretical ε' values for the calculated values of K and ε'_{HG}.

monitored by fluorescence emission at a [receptor] = 10^{-6} M, that of *p*-hydroxybenzoate with [Cd**L**^{1}]$^{2+}$, is shown as Fig. 5.

The wider range of binding constants quantified through the fluorescence emission studies allows a much better insight into the manner of anion inclusion than was hitherto possible. The first seven entries in Table 2 are particularly interesting. These constitute a set of benzoate anions substituted by hydroxy groups at one or more additional sites on the aromatic ring. Acquisition of binding constant data up to $10^{7.5}$ reveals that whilst the binding of the unsubstituted benzoate anion is quite weak (log K = 2.3), the strength of the binding can be augmented, incrementally, by the presence of additional hydroxy groups in a manner dependent on their number and positioning. Thus, a *p*-hydroxy group enhances log K to 4.5, a *m*-hydroxy to 5.3, and an *o*-hydroxy to 7.1. The effect is correspondingly heightened if two *m*- or *o*-hydroxy groups are present. The enhanced stability of the *p*-hydroxybenzoate interaction, compared to benzoate, is expected on the grounds of its greater basicity (pK_a = 4.58 compared to 4.20), which causes it to hydrogen bond at the base of the cavity more strongly. However, this argument cannot be applied to the even greater binding strength of *m*-hydroxybenzoate (pK_a = 4.08) or *o*-hydroxybenzoate (pK_a = 2.98) since they are less basic than benzoate; so there must be another reason. The clue to this appears to lie with the observed fluorescence emission intensity perturbations: The interaction of benzoate with [Cd**L**^{1}]$^{2+}$ brings about a 117% increase in its fluorescence emission intensity. This most likely arises from the elimination of quenching effects due to solvent water molecules initially hydrogen bonded in the binding cavity (it was seen earlier that the quantum yield for **2** is depressed in water and this appears to be a general effect for PeT perturbed anthracene fluorescence[19]) together with some enhancement of PeT quenching due to hydrogen bond acceptance by the benzoate carboxy moiety from the anthrylamine, which will weaken the N–H bond and release electron density for PeT. This 117% enhancement diminishes to 27% when the *p*-hydroxybenzoate is introduced. Since the water elimination effect is common to all entering guest molecules the diminished enhancement must be attributable to its higher basicity, which leads to a greater weakening of the anthrylamine N–H bond and consequently greater PeT quenching than occurred in response to benzoate inclusion. With *m*- and *o*-hydroxybenzoate the level of fluorescence enhancement compared to [Cd**L**^{1}]$^{2+}$ is similar to that of *p*-hydroxybenzoate (21% and 20%, respectively) yet this cannot be due to similarly strong hydrogen bond acceptance from the anthrylamine since both are of lower basicity than *p*-hydroxybenzoate. The stronger binding, that gives rise to similar fluorescence enhancement, must, therefore, arise from another cause associated with *o*- and *m*-positioning of the hydroxy group, but not *p*-positioning. We suggest that this cause may be O–H$\cdots\pi$ hydrogen bonding to the aromatic rings that form the walls of the cavity, including the anthracene moiety.[20] As shown in Fig. 6, which is based on our knowledge of the crystal structure of *p*-aminobenzoate included in [Cd(**1**)]$^{2+}$,[1c] and of salicylate hydrogen bonded to the analogue of [Cd(**1**)]$^{2+}$ that has methyl moieties in place of the phenoxymethylene groups,[21] the O–H group is only geometrically positioned to do this when located *ortho* or, to a lesser extent, *meta* to the carboxy group. Such an interaction would not only strengthen the binding of the anion, but would also be likely to quench the fluorescence of the anthracene either through de-excitation of the anthracene through energy transfer to the O–H oscillator,[22] if the oscillator is directed towards it rather than toward one of the other three aromatic

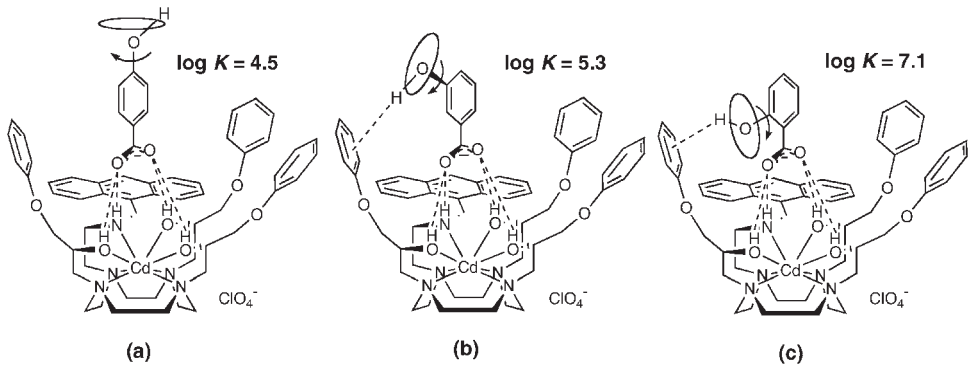


Fig. 6 Showing the potential for –O–H$\cdots\pi$ hydrogen bonding as the positioning of the hydroxy substituent on the guest molecule changes. The ellipse in each case is the approximate locus of points accessible to the hydroxy H atom in response to rotation around the O–H bond. Only in structure (c) is the hydroxy group constantly in range for –O–H$\cdots\pi$ hydrogen bonding to be possible.

groups, or alternatively by through space PeT if π-stacking with the anthracene occurs.[3] In none of the five X-ray determined structures of this class of host–guest complex that exist has π-stacking between a guest and an aromatic ring been seen.[1a,c,d] In favor of the former suggestion we note that the binding of 3,5-dihydroxybenzoate (pK_a = 4.04) and 2,6-dihydroxybenzoate (pK_a = 1.05) is stronger than for their mono-substituted counterparts, even though the basicity is still diminishing, and that the fluorescence is quenched to a greater extent, which is consistent with two appropriately positioned O–H groups doubling the probability of the anthracene being involved in an O–H···π hydrogen bond whilst the probability of π-stacking with it remains unchanged. The binding of 3,4,5-trihydroxybenzoate (gallate, pK_a = 4.41) on the grounds of basicity should be stronger than that of 3,5-dihydroxybenzoate, which it is, but its fluorescence is not diminished to the same extent, this may in some way be related to intramolecular hydrogen bonding between the *p*-hydroxy group and one or other of the *m*-hydroxy groups, which diminishes the level of O–H···π hydrogen bonding. Intramolecular O–H···π hydrogen bonding between two gallate moieties in *p-tert*-butylcalix[4]arene-1,3-digallate has been observed where the hydroxy oxygen atom of one gallate sits 3.247 Å above the facing gallate.[23] In this work preliminary *ab initio* molecular modelling of the structure in Fig. 6(c) using B3LYP/LanL2MB calculations suggests that the hydrogen atom in the O–H···π hydrogen bond proposed for that structure is positioned 4.73 Å above the nearest carbon atom of the aromatic ring.[24] This initially appeared somewhat distant for a strong interaction, but a referee has pointed out that since our binding constant and fluorescence measurements are conducted in partially aqueous solution it is quite possible that a bridging water molecule could interpose between the hydroxy group and the ring, and that the observed phenomena could be accounted for in that way.

The remaining binding constants reported in Table 2 are broadly in line with those determined by the ^{1}H NMR method and reported either in Table 1 or elsewhere.[1c] The fluorescence diminishments seen with aromatic anions that have electron withdrawing or donating groups in the *para* position: *p*-nitrobenzoate, *p*-dimethylaminobenzoate and *p*-toluenesulfonate, compared to their non-substituted parent anion, follow the pattern seen by Fabbrizzi *et al*. and are believed to be associated with through space PeT processes involving the anthracene moiety.[3d]

Acknowledgements

We are grateful to Prof. S. Salehzadeh of Bu-Ali-Sina University, Hamadan, Iran for undertaking the preliminary *ab initio* calculations. Funding of this work by the Australian Research Council is gratefully acknowledged.

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