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Metal ion-activated molecular receptors for aromatic anions with receptor cavities formed from 1- or 2-naphthyloxy moieties appended to cyclen

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Studies of two newly synthesised, isomeric metal ion-activated molecular receptors, [Cd(1,4,7,10-tetrakis{(*S*)-(−)-2-hydroxy-3-(1′-naphthyloxy)propyl}-1,4,7,10-tetraazacyclododecane)]$(ClO_4)_2 \cdot H_2O$ and [Cd(1,4,7,10-tetrakis{(*S*)-(−)-2-hydroxy-3-(2′-naphthyloxy)propyl}-1,4,7,10-tetraazacyclododecane)]$(ClO_4)_2$, show that both act as molecular receptors for the *p*-toluenesulfonate anion. The binding cavity depths for the two receptors were calculated from *ab initio* molecular modelling to be 4.81 and 7.27 Å, respectively. Despite the smaller cavity depth for the first receptor, it forms the more stable inclusion complexes, as assessed by the relative magnitude of the decrease in electrical conductivity and ^{13}C NMR spectral changes. This indicates that hydrogen bonds, from the hydroxyl hydrogen-bond donors at the base of the receptor cavity, rather than π interactions between the aromatic walls of the cavity and the included *p*-toluenesulfonate are principally responsible for its retention. Nonetheless, the hydrophobic character of the aromatic-binding cavity walls may play a major kinetic role in the formation of the inclusion complexes.

Introduction

In previous work,[1–3] we have demonstrated that it is possible to assemble or disassemble molecular receptors for aromatic anions by using pendant donor tetraaza-macrocyclic ligands whose three dimensional shape and rigidity is controlled by the presence or absence of an octa-coordinating metal ion. Pendant arms are used on the macrocycle to carry aromatic appendages and donor atoms that lock into position around the co-ordinating metal ion in such a way that a cavity is formed by the aromatic rings. An example of the outcome of this strategy for metal ion-activated molecular recognition appears in Fig. 1.

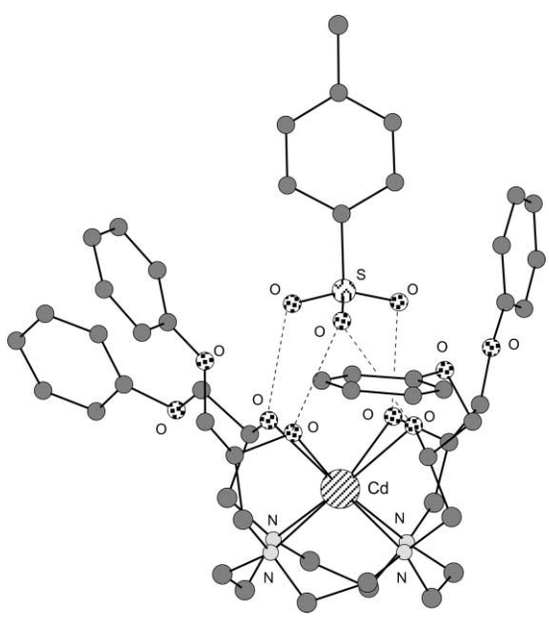
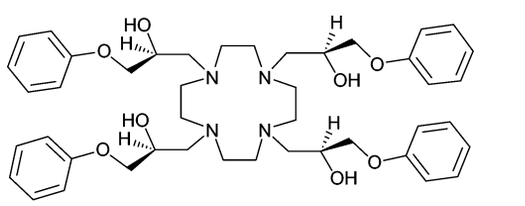
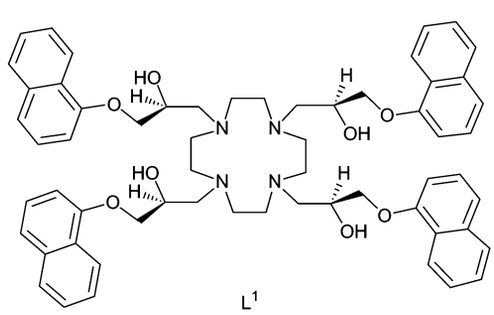


Fig. 1 Molecular structure, determined by X-ray diffraction, of a Cd(II)-activated molecular receptor holding a *p*-toluenesulfonate anion, *via* multiple hydrogen bonding, in a binding cavity formed from four juxtaposed phenoxy moieties.[1] Hydrogen atoms are omitted for clarity.

The figure shows the structure, determined by X-ray diffraction, of a receptor complex in which a *p*-toluenesulfonate anion is retained by multiple hydrogen bonding within the structure of a cyclen-based ligand (cyclen = 1,4,7,10-tetraazacyclododecane) that has been locked into the necessary *trans*-I configuration (all arms projecting in the same direction[4]) by coordination to cadmium(II). In this example, and in other previous work,[3] we utilised the ligand (*S*)-thphpc12 (Fig. 2), where the aromatic moieties defining the boundaries of the cavity are phenoxy groups, but have commented on the somewhat open nature of the cavity that results. To form a more enclosed cavity we have now undertaken comparable work in

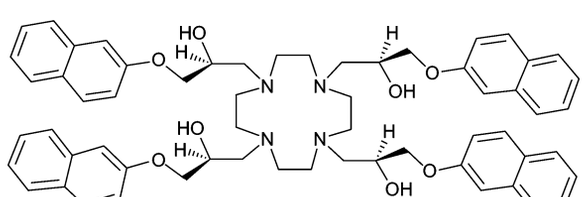


(*S*)-thphpc12



L^1

(*S*)-thn1pc12



L^2

(*S*)-thn2pc12

Fig. 2 Structures of ligands under discussion in this paper.

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which we have studied the effect on aromatic anion inclusion of substituting larger 1- or 2-naphthyloxy moieties for the smaller phenoxy group, whilst leaving other features of the receptor unchanged. Both naphthyloxy isomers have been investigated as it seemed likely that the geometry of the cavity could be quite different in each case. In this report, we describe the outcome of an *ab initio* modelling study of the cavity shape likely to be generated by each isomer, and a synthetic study in which we have synthesised the two isomeric Cd(II)-activated receptors and compared their relative abilities to include aromatic anions using *p*-toluenesulfonate as an example.

Experimental

General

$^{13}C\{^1H\}$ and ^1H NMR spectra were recorded at 75.46 and 300.08 MHz, respectively, using a Varian Gemini 300 spectrometer at 295 K. ^{13}C chemical shifts are quoted with respect to the central resonance of the solvent multiplet, for which the resonance positions were taken as δ 77.00 for $CDCl_3$ and δ 39.60 for DMSO-d_6. ^1H NMR chemical shifts are quoted with respect to the residual protonated solvent peaks, taken as 7.26 ppm for $CDCl_3$ and 2.60 ppm for DMSO-d_6. Elemental analyses were performed at the University of Otago, New Zealand. Conductivity measurements were made on 10^{-3} M solutions in dimethylformamide at 298 K using a TPS LC84 conductivity meter. Established conductivity ranges for 10^{-3} M 1 : 1 and 2 : 1 electrolytes in DMF are 65–90 and 130–170 cm^2 Ω^{-1} mol^{-1}, respectively.[5] Optical rotations were measured at ambient temperature using a PolAAr 21 automatic polarimeter. Melting points were recorded on a Reichert hot stage melting point apparatus and are uncorrected. Cyclen was prepared by the literature procedure.[6] Solvents were purified before use by established methods.[7] Reactions were carried out under an atmosphere of dry nitrogen.

Syntheses

(*S*)-(+)-3-(1′-Naphthyloxy)-1,2-epoxypropane. This was synthesised using the method of Klunder.[8] A solution of 1-naphthol (1.52 g, 10.44 mmol) in dry DMF (12 cm^3) was added dropwise over 5 min to a suspension of oil-free sodium hydride (315 mg, 13.05 mmol) in dry DMF (15 cm^3). The green suspension was stirred at room temperature for 1 h, followed by the dropwise addition of a solution of (*S*)-glycidyl tosylate (2.0 g, 8.7 mmol) in dry DMF (12 cm^3) over a 5 min period. Reaction progress was monitored by thin layer chromatography (TLC; CH_2Cl_2–hexane 3 : 1) and was found to be complete after 4 h. Stirring was discontinued and saturated aqueous NH_4Cl solution (10 cm^3) was added. The suspension was diluted with water (150 cm^3) and extracted with ether (4 × 150 cm^3). The organic extracts were washed with ice-cold sodium hydroxide solution (0.1 M, 2 × 200 cm^3), water (200 cm^3) and then brine (200 cm^3). After drying (Na_2SO_4) and filtering, the solvent was evaporated to give the crude product as a pale yellow liquid. The product was isolated as a colourless liquid (1.27 g, 72%) after flash chromatography on silica gel (CH_2Cl_2–hexane 3 : 1). ^1H NMR ($CDCl_3$): δ 8.28–8.32 (m, 1H); 7.77–7.80 (m, 1H); 7.43–7.50 (m, 3H); 7.32–7.37 (m, 1H); 6.77–6.80 (d, J = 7.4, 1H); 4.35–4.40 (dd, J = 3.0, 11.0, 1H); 4.09–4.15 (dd, J = 5.7, 11.3, 1H); 3.45–3.48 (m, 1H); 2.93–2.96 (t, J = 4.1, 1H); 2.82–2.84 (dd, J = 2.5, 4.94 Hz, 1H). ^{13}C NMR ($CDCl_3$): δ 154.32, 134.59, 127.50, 126.56, 125.75, 125.64, 125.37, 122.06, 120.89, 104.99, 68.88, 50.15, 44.63. $[a]_D^{20}$ = +13.5° (*c* 2, $CHCl_3$) {lit.[9] $[a]_D^{20}$ = +17.3° (*c* 2, $CHCl_3$)}.

(*S*)-(−)-3-(2′-Naphthyloxy)-1,2-epoxypropane. This was prepared from 2-naphthol in identical fashion to the 1-naphthyl analogue. The product was obtained as white crystals (1.27 g, 72%). M.p. 76–78 °C. ^1H NMR ($CDCl_3$): δ 7.71–7.78 (m, 3H); 7.33–7.44 (m, 2H); 7.13–7.20 (m, 2H); 4.32–4.36 (dd, J = 3.3, 11.1, 1H); 4.04–4.10 (dd, J = 5.7, 10.8, 1H); 3.40–3.46 (m, 1H); 2.93–2.96 (t, J = 4.8, 1H); 2.80–2.83 (dd, J = 2.7, 5.1, 1H). ^{13}C NMR ($CDCl_3$): δ 156.54, 134.49, 129.62, 129.25, 127.73, 126.86, 126.51, 123.91, 118.83, 106.90, 68.70, 50.04, 44.69. $[a]_D^{20}$ = −4.0° (*c* 2, $CHCl_3$).

1,4,7,10-Tetrakis[(*S*)-(−)-2-hydroxy-3-(1′-naphthyloxy)-propyl]-1,4,7,10-tetraazacyclododecane, (*S*)-thn1pc12 (L^1). A solution of (*S*)-(+)-3-(1′-naphthyloxy)-1,2-epoxypropane (1.2 g, 6.0 mmol) in dry ethanol (10 cm^3) was added to a solution of cyclen (258 mg, 1.5 mmol) in dry ethanol (20 cm^3) and the mixture heated under reflux in the absence of light. After 1 h, the solution became cloudy and a white precipitate began to form. After 5 h, the reaction was judged complete by TLC (CH_2Cl_2–hexane 3 : 1) and the suspension was cooled to room temperature. The precipitated product was filtered off and dried under high vacuum in the absence of light. Yield 1.24 g, 86%. ^{13}C NMR ($CDCl_3$): δ 154.54, 134.51, 127.49, 126.33, 126.01, 125.64, 125.13, 121.98, 120.36, 104.92, 70.07, 66.00, 59.19, 51.34. (Found: C, 73.83; H, 7.32; N, 5.85; $C_{60}H_{68}N_4O_8$ requires C, 74.05; H, 7.04; N, 5.76%). $[a]_D^{20}$ = −109.5° (*c* 2, $CHCl_3$).

1,4,7,10-Tetrakis[(*S*)-(−)-2-hydroxy-3-(2′-naphthyloxy)-propyl]-1,4,7,10-tetraazacyclododecane, (*S*)-thn2pc12 (L^2). (*S*)-(−)-3-(2′-naphthyloxy)-1,2-epoxypropane (1.245 g, 6.2 mmol) was added to a solution of cyclen (268 mg, 1.55 mmol) in dry ethanol (40 cm^3) and the mixture was heated under reflux in the absence of light. The solution became cloudy after 1 h and the product began to precipitate from solution. After 6 h, the reaction was judged complete by TLC (CH_2Cl_2–hexane 3 : 1) and the suspension was cooled to room temperature. The precipitated product was filtered off and dried under high vacuum in the absence of light. Yield 1.32 g, 87%. ^{13}C NMR ($CDCl_3$): δ 156.79, 134.59, 129.37, 129.05, 127.62, 126.90, 126.37, 123.66, 118.88, 106.93, 69.87, 65.76, 58.55, 51.18. (Found: C, 73.37; H, 7.08; N, 5.70; $C_{60}H_{68}N_4O_8\cdot0.5H_2O$ requires C, 73.15; H, 7.01; N, 5.72%). $[a]_D^{20}$ = −91.2° (*c* 0.91, $CHCl_3$).

[Cd{(*S*)-thn1pc12}]$(ClO_4)_2\cdot H_2O$, [CdL^1]$(ClO_4)_2$. A solution of cadmium(II) perchlorate hexahydrate (115 mg, 0.27 mmol) in dry DMF (7 cm^3) was added to a solution of (*S*)-thn1pc12 (222 mg, 0.23 mmol) in dry DMF (15 cm^3). The clear solution was heated at 100 °C for 1 h, then cooled to room temperature. The solvent was removed *in vacuo* and the residue triturated with ethanol (20 cm^3). A white solid formed and the suspension was stirred for 24 h. The fine white powder was filtered off and dried under vacuum. Yield 245 mg, 84%. ^{13}C NMR (DMSO-d_6): δ 153.78, 134.13, 127.58, 126.60, 126.26, 125.32, 124.83, 121.69, 120.53, 105.32, 70.21, 64.78, 55.17, 50.05, 48.19. (Found: C, 55.29; H, 5.21; N, 4.42; $C_{60}H_{70}CdCl_2N_4O_{17}$ requires C, 55.33; H, 5.42; N, 4.30%). Λ_M 133 cm^2 Ω^{-1} mol^{-1} (1×10^{-3} M, DMF) (2 : 1).

[Cd{(*S*)-thn2pc12}]$(ClO_4)_2$, [CdL^2]$(ClO_4)_2$. This was prepared in analogous fashion to the 1-naphthyl analogue from ligand (*S*)-thn2pc12. The product was obtained as a white powder. Yield 83%. ^{13}C NMR (DMSO-d_6): δ 156.21, 134.24, 129.51, 128.70, 127.64, 126.79, 126.64, 123.92, 118.59, 107.04, 69.94, 64.57, 54.69, 49.90, 48.08. (Found: C, 55.94; H, 5.51; N, 4.54; $C_{60}H_{68}CdCl_2N_4O_{16}$ requires C, 56.10; H, 5.34; N, 4.36%). Λ_M 137 cm^2 Ω^{-1} mol^{-1} (1×10^{-3} M, DMF) (2 : 1).

[Cd{(*S*)-thn1pc12}(*p*-$CH_3C_6H_4SO_3$)]ClO_4. Sodium *p*-toluenesulfonate (29 mg, 0.15 mmol) was added to a solution of [Cd{(*S*)-thn1pc12}]$(ClO_4)_2\cdot H_2O$ (193 mg, 0.15 mmol) in dry acetonitrile (15 cm^3). The suspension was heated under reflux for 2 h, by which time the sodium *p*-toluenesulfonate had completely dissolved. After cooling to room temperature, the solution was filtered and the solvent removed under reduced

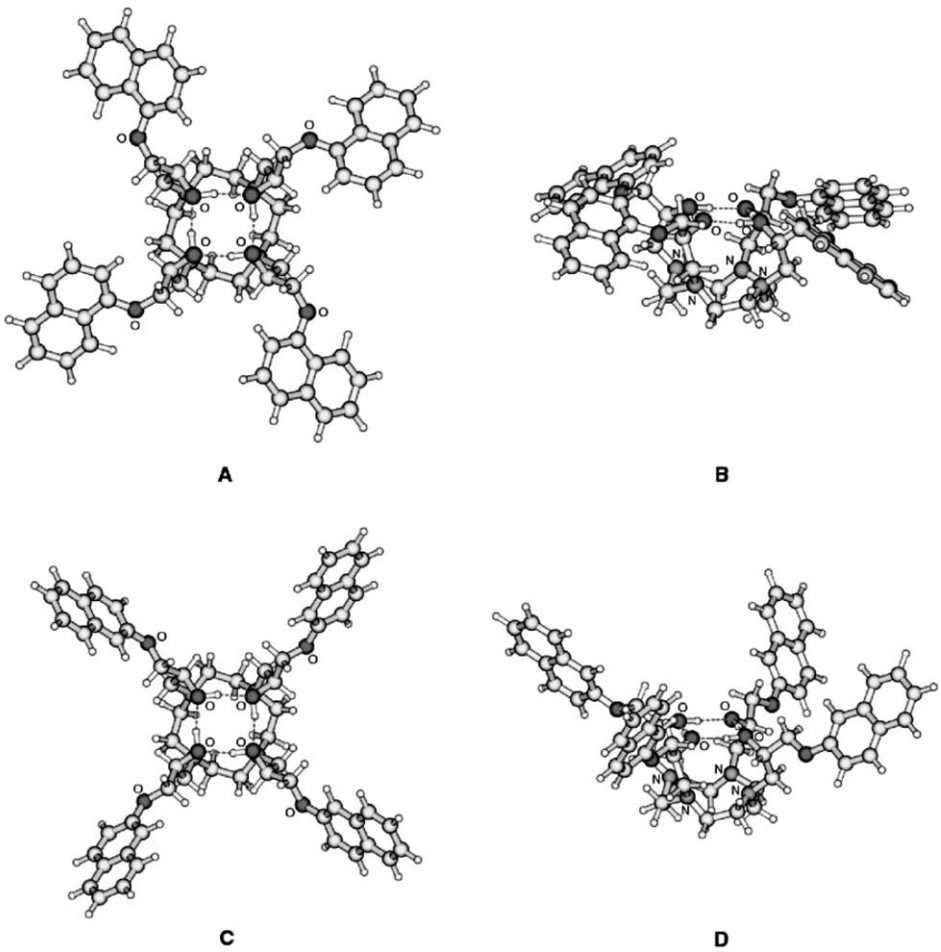

Fig. 3 *Ab initio* modelled global energy minimum structures for L^1 (A and B) and L^2 (C and D); plan views on the left and elevations on the right. Hydrogen bonds are shown as dotted lines.

pressure. Ethanol (10 cm^3) was added to the residue, which then solidified. The suspension was heated to boiling point and acetonitrile was added until dissolution occurred. Very fine needle-like crystals formed on cooling of the solution. These were filtered off and dried under vacuum. Yield 121 mg, 61%. ^{13}C NMR (DMSO-d_6): δ 153.78, 145.02, 138.07, 134.10, 128.19, 127.50, 126.54, 126.22, 125.60, 125.28, 124.84, 121.73, 120.45, 105.28, 70.14, 64.76, 55.27, 50.15, 48.21, 20.82. (Found: C, 59.35; H, 5.27; N, 4.36; $C_{67}H_{75}CdClN_4O_{15}S$ requires C, 59.33; H, 5.57; N, 4.13%). Λ_M 98 $cm^2\ \Omega^{-1}\ mol^{-1}$ (1×10^{-3} M, DMF) (1 : 1–2 : 1).

[Cd{(*S*)-thn2pc12}(*p*-$CH_3C_6H_4SO_3$)]ClO_4·$2H_2O$. The title compound was synthesised in the same manner as for the (*S*)-thn1pc12 complex, in 86% yield starting from [Cd((*S*)-thn2pc12)]$(ClO_4)_2$. This compound could not be recrystallised as it precipitated as an oil from all the hot solvents that were investigated, therefore, stirring the solid residue from the evaporated reaction mixture in ethanol overnight (to remove the sodium perchlorate by dissolution), washing the residual solid with clean ethanol, and then drying it under vacuum was the only method of purification used. ^{13}C NMR (DMSO-d_6): δ 156.23, 145.28, 138.01, 134.26, 129.51, 128.70, 128.24, 127.66, 126.81, 126.64, 125.61, 123.92, 118.64, 107.03, 69.92, 64.57, 54.77, 49.97, 48.10, 20.83. (Found: C, 57.64; H, 5.73; N, 4.24; $C_{67}H_{79}CdClN_4O_{17}S$ requires C, 57.80; H, 5.72; N, 4.23%). Λ_M 107 $cm^2\ \Omega^{-1}\ mol^{-1}$ (1×10^{-3} M, DMF) (1 : 1–2 : 1).

Ab initio modelling

Ab initio modelling was performed using Gamess-US[10] at the restricted Hartree–Fock level of theory with the in-built effective core potential-containing basis set of Stevens, Basch, Krauss, Jasien and Cundari (the SBKJC basis set).[11–13] All electrons for H, C, N and O were incorporated, but only the valence shell electrons for Cd^{2+}, together with its effective core potential. To ensure that the predicted structures shown in Fig. 3 and 4 and detailed in Table 1 represent the structure having the true global energy minimum, trial structures with

Table 1 Bond lengths (Å) and angles (°) for L^1, L^2 and their Cd(II) complexes, derived from Hartree–Fock *ab initio* calculations using Gamess-US with the SBKJC basis set[a]

	L^1	L^2	$[CdL^1]^{2+}$	$[CdL^2]^{2+}$
HO ··· OH	2.70	2.71	2.92	2.93
OH ··· OH	1.73	1.73	—	—
O–H ··· OH	170.4	169.9	—	—
O–C–C–O	172.0	173.8	42.1	52.3
Cd–O(H)	—	—	2.44	2.43
Cd–N	—	—	2.63	2.58
Twist angle,[b] φ	−3.7	−3.7	−11.9	+7.1
Cd ··· $(OH)_4$ plane	—	—	1.29	1.27
Cd ··· N_4 plane	—	—	1.46	1.41
HO ··· $OC_{10}H_7$	3.68	3.63	2.59	2.66
OH ··· $OC_{10}H_7$	—	—	2.04	2.21
O–H ··· $OC_{10}H_7$	—	—	113.6	107.1
Depth of cavity[c]	3.59	6.81	4.81	7.27

[a] The global minimum energies for L^1, L^2, $[CdL^1]^{2+}$ and $[CdL^2]^{2+}$ are −531.53208, −531.54633, −697.26177 and −697.27480 E_h, respectively, where E_h = 2622.99 kJ mol^{-1}. [b] The twist angle, φ, is the clockwise (+) or anticlockwise (−) angle of rotation of the O_4 plane with respect to the N_4 plane, denoting the direction and angle of displacement of an oxygen atom with respect to the nitrogen atom to which it is connected. [c] The depth of the cavity is defined by the distance between the plane formed by the hydroxy oxygens and that containing the uppermost H atoms.

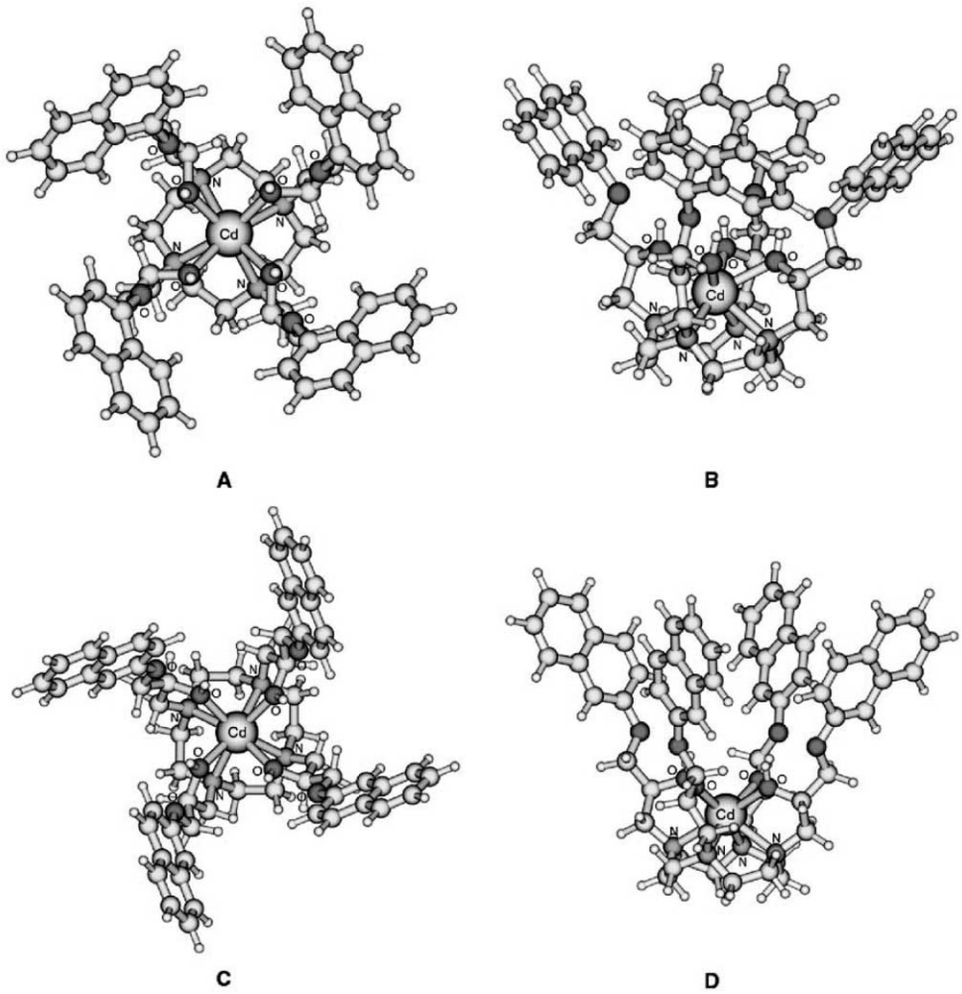

Fig. 4 *Ab initio* modelled global energy minimum structures for $[CdL^1]^{2+}$ (A and B) and $[CdL^2]^{2+}$ (C and D); plan views on the left and elevations on the right. For the sake of clarity, the four hydrogen bonds, from each hydroxyl group to the phenoxy oxygen atom on the same arm, are omitted.

pendant arms either all on the same side of the nitrogen atom plane or on differing sides were used as starting points for the minimisation. A range of pendant arm conformations were superimposed on these structures to give a broad selection of starting points.

Results and discussion

Synthesis of the receptors

The light-sensitive macrocyclic ligands (*S*)-thn1pc12 and (*S*)-thn2pc12 (see Fig. 2), hereafter referred to as L^1 and L^2, were formed in good yield by the reaction of cyclen with (*S*)-(+)-3-(1′-naphthyloxy)-1,2-epoxypropane or (*S*)-(−)-3-(2′-naphthyloxy)-1,2-epoxypropane, respectively, in ethanol. Use of an optically pure form of each epoxide is necessary to ensure that only the homochiral diastereomer of each ligand is formed. The epoxides were synthesised from commercially available (*S*)-glycidyl tosylate and the appropriate sodium naphthoxide, following the method of Klunder.[8] The two Cd(II) complexes, $[CdL^1](ClO_4)_2{\cdot}H_2O$ and $[CdL^2](ClO_4)_2$, which act as molecular receptors, were prepared by combining the ligand with cadmium perchlorate hexahydrate in refluxing DMF. Neither of these complexes appear to be particularly light sensitive.

Molecular modelling of the receptor cavity

To assess the geometrical characteristics of each molecular receptor cavity, ligands L^1 and L^2, and both Cd(II) complexes were modelled using the *ab initio* approach and the Gamess-US program[10] at the restricted Hartree–Fock level of theory with the in-built effective core potential-containing basis set of Stevens, Basch, Krauss, Jasien and Cundari (the SBKJC basis set).[11–13]

For L^1 and L^2, the modelling predicts the global minimum energy conformations to be those shown in Fig. 3. The associated structural parameters are tabulated in Table 1. The dominant feature of these structures is the adoption of the *trans*-I conformation, which has C_4 symmetry. This conformation is stabilised by a cyclic array of hydrogen bonds that link the pendant hydroxyl groups, as has been noted previously for (*S*)-thphpc12 and other related ligands.[1,14–16] In the two cases here, the hydrogen bonds are similarly characterised by O ⋯ O separations of *ca*. 2.7 Å, H ⋯ O separations of 1.73 Å and O–H ⋯ O angles of *ca*. 170°, which, on the basis of all three attributes, ranks them as moderately strong.[17] Although in the *trans*-I conformation, Fig. 3 shows that, in the absence of a coordinating metal ion, the binding cavity in L^1 and L^2 is not well developed. This arises because the O–C–C–O torsion angle in each arm (around the first bond) stabilises at *ca*. 173°, positioning the electronegative oxygen atoms remotely from one another, as might be expected on electrostatic grounds. In turn, this distances the naphthyl groups, preventing formation of a confined cavity, and, particularly in the case of L^1, the optimised rotation around the $C_{10}H_7$–O bond results in the naphthyl rings drooping markedly. In the case of L^2, a local energy minimum conformation was found that is basically the same as the global minimum shown, except that it had O–C–C–O torsion angles of 78.6°. This resulted in the naphthyl rings coming together to produce a cavity geometrically similar to those

formed on Cd(II) complexation (Fig. 4). This local minimum, however, is 39.0 kJ mol^{-1} higher in energy than the global minimum energy conformation.

The modelling studies predict that C_4 symmetry is retained upon coordination of Cd(II). Both ligands accommodate the metal ion between the N_4 and O_4 donor atom planes, as an octa-coordinate species, with a cubic geometry slightly distorted towards that of a square anti-prism by a small twist angle (φ) that is slightly higher than in the free ligands. These, and the associated structural parameters shown in Table 1, are broadly in accord with findings from several related crystallographic studies, including that illustrated in Fig. 1.[1,3] As coordination occurs, and as a consequence of each hydroxyl oxygen atom directing a lone pair of electrons towards the Cd(II), both L^1 and L^2 rotate their O–H bonds outwards from the O_4 plane into the guest-binding cavity. This is shown schematically in Fig. 5. This breaks the cyclic, inter-arm hydrogen bonding, but allows the formation of new intra-arm hydrogen bonds between each O–H group and the adjacent phenoxy oxygen atom once an O–C–C–O torsion angle change from *ca*. 173 to 42 (L^1) or 52° (L^2) has occurred. The reduction in torsion angle brings the naphthyl groups together such that they form the four sides of a reasonably confined cavity, irrespective of rotation around the $C_{10}H_7$–O bonds. Thus, each of the cavity walls is tethered in place by an intra-arm hydrogen bond whose existence is dependent on the presence of the metal ion. The strength of each of these hydrogen bonds can be gauged qualitatively from the O ··· O and H ··· O separations, and the O–H ··· O angles, which are *ca*. 2.6 and *ca*. 2.1 Å, and *ca*. 110°, respectively. On the basis of the atom separations, these hydrogen bonds would be described as moderately strong, but are compromised by an O–H ··· O angle more commonly associated with weak hydrogen bonding.[17] A semi-quantitative assessment of the hydrogen-bond strength was obtained from the fact that during the modelling procedure we observed a local minimum energy structure for $[CdL^2]^{2+}$ having O–C–C–O torsion angles of 177.5°, but no intra-arm hydrogen bonding. This conformation is 62.8 kJ mol^{-1} higher in energy than the global minimum. Taken with the 39.0 kJ mol^{-1} reduction in energy seen in L^2 when the torsion angle increases from 78.6 to 173° without loss of hydrogen bonding (see above), this indicates, all other things being equal, a hydrogen-bond strength in $[CdL^2]^{2+}$ of *ca*. 25.4 kJ mol^{-1} per hydrogen bond, which is moderately strong.[17]

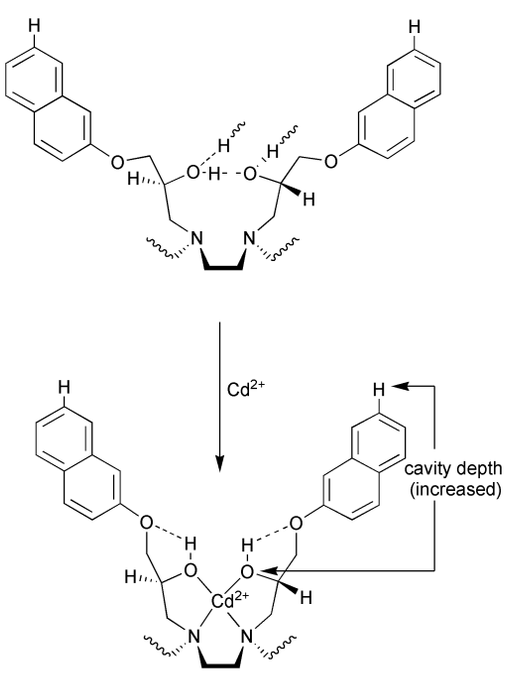

Fig. 5 Schematic diagram, using partial structures, showing how the cyclic inter-arm hydrogen bonding converts to intra-arm hydrogen bonding upon coordination of the hydroxyl groups, which tethers the naphthyl walls of the binding cavity in place.

The predicted depth of the cavities formed within the structure of $[CdL^1]^{2+}$ and $[CdL^2]^{2+}$, measured from the O_4 plane to the plane defined by the four uppermost hydrogen atoms (as shown in Fig. 5), differs markedly, being 4.81 and 7.27 Å, respectively, for the two complexes. By comparison, the predicted cavity depths in L^1 and L^2 are 3.59 and 6.81 Å, but, particularly in the case of L^2, this depth is very much an upper limit since, unlike the situation with the complexes, rotations around the $C_{10}H_7$–O bonds, which would require little energy, can reduce the depth of the cavity markedly.

On the basis of the modelling studies, it appears that $[CdL^2]^{2+}$ may be the better receptor molecule for aromatic molecules as it has the deeper cavity and also the more stable structure, with a steric energy 34.2 kJ mol^{-1} below that of isomeric $[CdL^1]^{2+}$. To investigate this further, we undertook the synthesis of an inclusion complex of each receptor using the *p*-toluenesulfonate anion as the guest species.

Synthesis of the inclusion complexes and their characterisation in solution

In previous work, *p*-toluenesulfonate has been found to be a useful guest molecule with which to probe the aromatic anion-including capabilities of these metal ion-activated molecular receptors.[1] This is particularly true when working in acetonitrile, since the receptor is soluble in this solvent but sodium *p*-toluenesulfonate is not, and so the progress of the uptake experiment can be monitored by observing its dissolution. Accordingly, we refluxed suspensions of sodium *p*-toluenesulfonate in acetonitrile solutions of each receptor, in equimolar proportions, until dissolution of the guest salt was complete. Following separation of the sodium perchlorate byproduct, we were, in each case, able to isolate compounds that analysed as $[CdL(p\text{-}CH_3C_6H_4SO_3)]ClO_4$.

Unfortunately, it was neither possible to grow crystals of these inclusion compounds that were suitable for X-ray diffraction, nor to determine the binding constants for the guest molecule in these cases. However, information concerning the inclusion of the guest and a qualitative estimate of its binding constant can be elicited from the electrical conductivity and ^{13}C NMR spectra of the inclusion complexes. The diperchlorate salts of $[CdL^1]^{2+}$ and $[CdL^2]^{2+}$ both have conductivities in DMF that fall within the range characteristic of 1 : 2 electrolytes, as detailed in the Experimental section, but on substitution of one perchlorate ion by *p*-toluenesulfonate, the conductivity drops well below this range to the values shown in Table 2, indicating substantial immobilisation of *p*-toluenesulfonate within the receptor. The conductivity decrease is slightly greater in the case of $[CdL^1]^{2+}$, suggesting that the *p*-toluenesulfonate binding constant is greater in $[CdL^1]^{2+}$ than in $[CdL^2]^{2+}$. This is broadly supported by the relative magnitude of the changes in the chemical shifts of resonances attributable to *p*-toluenesulfonate seen in the ^{13}C NMR spectrum of the inclusion complex and compared with the corresponding value in the spectrum of sodium *p*-toluenesulfonate. (Separate resonances are not observed in the spectra of $[CdL^1]^{2+}$ and $[CdL^2]^{2+}$ for free and included *p*-toluenesulfonate, indicating that they must be in fast exchange, and thus an inclusion-modified resonance frequency reflects the ratio of included to free *p*-toluenesulfonate. Assuming that the spectrum of included *p*-toluenesulfonate is similar for both receptors, then the relative magnitudes of the chemical shift changes track the relative magnitudes of the binding constants). These chemical shift values were obtained from spectra recorded in DMSO-d_6 at identical concentration and temperature, and are tabulated in Table 2. From these values, it may be seen that all five *p*-toluenesulfonate resonances shift to a greater

Table 2 $^{13}C\{^{1}H\}$ NMR chemical shifts for free and included *p*-toluenesulfonate,[a] and molar conductivities

Compound	*p*-$CH_3C_6H_4SO_3$ resonances,[b] δ (ppm)					Molar conductivity[c]/$cm^2\ \Omega^{-1}\ mol^{-1}$
	C^1	$C^{2/6}$	$C^{3/5}$	C^4	C^7	
p-$CH_3C_6H_4SO_3Na$	145.91	125.79	128.36	138.00	20.86	55
$[CdL^1(p\text{-}CH_3C_6H_4SO_3)]ClO_4$	145.02	125.60	128.19	138.07	20.82	98
$[CdL^2(p\text{-}CH_3C_6H_4SO_3)]ClO_4$	145.28	125.61	128.24	138.01	20.83	107
$[Cd\{(S)\text{-thphpc12}\}(p\text{-}CH_3C_6H_4SO_3)]ClO_4$[d]	145.58	125.77	128.39	138.16	20.84	84
$[Pb\{(S)\text{-thphpc12}\}(p\text{-}CH_3C_6H_4SO_3)]ClO_4$[d]	145.79	125.77	128.37	138.05	20.83	122

[a] 0.05 M in DMSO-d_6 at 295 K. [b] Carbon atoms are numbered such that C^1 is *ipso* to sulfur. [c] 0.001 M in DMF at 293 K. Established conductivity ranges for 10^{-3} M 1 : 1 and 2 : 1 electrolytes in DMF are 65–90 and 130–170 $cm^2\ \Omega^{-1}\ mol^{-1}$, respectively.[5] [d] Data from ref. 1.

extent in the spectrum of the $[CdL^1]^{2+}$ inclusion complex than in that of the $[CdL^2]^{2+}$ inclusion complex.

Conclusions

The finding that *p*-toluenesulfonate is more tightly bound within the structure of $[CdL^1]^{2+}$ than within $[CdL^2]^{2+}$, despite the greater cavity depth in $[CdL^2]^{2+}$, points to the hydrogen bonding of *p*-toluenesulfonate to the receptor as being the dominant factor controlling the thermodynamic stability of the inclusion complex. Some slight evidence of non-covalent π interaction between and the aromatic walls of $[CdL^1]^{2+}$ and $[CdL^2]^{2+}$ may be seen by comparing the changes in the *p*-toluenesulfonate ^{13}C NMR resonances in the spectra of the naphthyloxy-based inclusion complexes (with respect to free sodium *p*-toluenesulfonate) with those observed for the inclusion complexes formed from (*S*)-thphpc12 (Table 2), which has cavity walls derived from less extensive phenoxy groups. For the latter, these changes are only significant for the two resonances from the *ipso*-carbon atoms C^1 and C^4, whereas for the former, all the resonances, with the exception of C^4 (and the reason for this is not clear to us) are shifted. Nonetheless, the aromatic rings forming the walls of the cavity certainly exert a considerable kinetic effect, since when they are substituted by methyl groups, no reaction with sodium *p*-toluenesulfonate in acetonitrile can be induced.[1] Thus, the principal role of the cavity wall aromatic rings appears to be one of funnelling the aromatic guest, using weak, non-covalent π interactions, into a position from which it can lock into the receptor *via* multiple hydrogen bonds to the four hydroxyl groups, which, having their hydrogen atoms rotated into the guest-binding cavity as a consequence of the metal ion co-ordination, are well positioned to act as hydrogen-bond donors. In cases where the aromatic rings in these receptors have been completely replaced by hydrogen atoms, and where it has also has been possible to measure aromatic guest-binding constant values, it has been shown that the presence of the aromatic rings enhances the binding constant by about one order of magnitude, typically from *ca*. $10^{3.5}$ to *ca*. $10^{4.5}$ in DMSO at 298 K,[18] but this is a considerably more significant alteration than the changes in cavity structure discussed here.

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