

Metal Ion Dependent Molecular Inclusion Chemistry: Inclusion of *p*-Toluenesulfonate and *p*-Nitrophenolate within the Structure of Coordinated 1,4,7,10-Tetrakis((*S*)-2-hydroxy-3-phenoxypropyl)-1,4,7,10-tetraazacyclododecane

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The pendant donor macrocyclic ligand 1,4,7,10-tetrakis((*S*)-2-hydroxy-3-phenoxypropyl)-1,4,7,10-tetraazacyclododecane ((*S*)-thphpc12) has been synthesized in quantitative yield from cyclen (1,4,7,10-tetraazacyclododecane) and (2*S*)-(+)-3-phenoxy-1,2-epoxypropane. An X-ray diffraction study supports the result of molecular orbital calculations in showing that complexation with hydrated cadmium(II) diperchlorate produces an approximately square-antiprismatic complex in which the metal ion is located between a plane containing the four nitrogen atoms and a plane containing the four oxygen atoms. As a consequence of this the four phenoxyethyl moieties, each attached to one of the four N–O chelate rings, juxtapose to form a substantial empty cavity allowing the complex to act as a molecular receptor. Inclusion complexes have been formed from this complex in which either a *p*-toluenesulfonate or *p*-nitrophenolate anion has entered the cavity. An X-ray crystallographic study of [Cd-((*S*)-thphpc12)(*p*-toluenesulfonate)]ClO₄ shows that the guest anion is retained within the cavity by four hydrogen bonds to the group of hydroxyl moieties associated with the ligand. ¹³C NMR and conductivity studies indicate that this inclusion complex retains its integrity in DMSO or DMF solution. Parallel studies have been conducted with [Pb((*S*)-thphpc12)](ClO₄)₂ indicating that the corresponding inclusion complexes are of lower stability.

Introduction

Pendant donor macrocycles derived from cyclen (1,4,7,10-tetraazacyclododecane) almost invariably coordinate to a metal ion in such a way that all four pendant arms project in the same direction.¹ If, in addition to carrying a donor atom, the pendant arms also have an aromatic moiety attached to them, the possibility arises of using the coordination of the ligand to a metal ion as a way of assembling a molecular receptor with a substantial cavity that arises from the juxtaposition of the four aromatic groups. Recently we demonstrated the feasibility of this approach for forming molecular receptors through the synthesis and study of 1,4,7,10-tetrakis((*R*)-2-hydroxy-2-phenylethyl)-1,4,7,10-tetraazacyclododecane (*R*-thpec12).^{2,3}

Molecular orbital calculations carried out on *R*-thpec12, using Gaussian 94,⁴ predicted that in the gas phase the four phenyl groups would collectively form a saucer-shaped array, where

this positioning is determined by structural rigidity that is imposed through the formation of hydrogen bonds between adjacent pendant hydroxyl groups. On complexation by alkali metal ions the curvature of this saucer shaped array varies over an approximately 20° range in accordance with the ionic radius of the particular alkali metal that is chosen. Large metal ions such as Cs⁺ effect a relatively large separation between the nitrogen and oxygen planes, causing the curvature of the saucer to flatten to about 14°. By comparison, the smaller metal ion, Na⁺, gives a curvature of 34°. These structures (except with Li⁺) all have C₄ symmetry and one diastereomer is predicted to be of significantly greater stability than the other. When the stereocenter within each pendant arm has *R* chirality the preferred diastereomer is Δ*R* for Δ*R*-thpec12 and Δ[Na(*R*-thpec12)]⁺, and Λ*R* for Λ[M(*R*-thpec12)]⁺ where M = K⁺, Rb⁺, or Cs⁺ (Δ and Λ refer respectively to the clockwise or anticlockwise rotation of the O₄ plane with respect to the N₄ plane, when viewing the molecule from the O₄ plane in the direction of the N₄ plane and noting the direction of displacement of an oxygen atom with respect to the nitrogen atom to which it is connected). This modeling is in accord with experimental syntheses, in which only one diastereomer was observed spectroscopically or isolated, as well as with earlier observations^{5–7} and calculations^{8,9} for related ligands and their complexes. Variable temperature ¹³C NMR studies of *R*-thpec12

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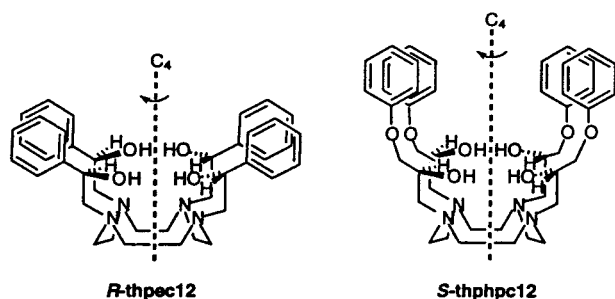
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Scheme 1



and its alkali metal complexes indicated that the structures predicted for the gas phase are, at least qualitatively, retained by the ligand and its complexes when dissolved in dimethylformamide.^{2,3}

Although not fully tested yet, it appears that the receptor area within *R*-thpcc12 and its complexes may be too shallow for many applications in the general field of host–guest chemistry. Accordingly it was of importance to explore the possibility of deepening the cavity by appending aromatic moieties to the pendant arms in such a way that they have a greater degree of freedom to do this. In complexes of *R*-thpcc12 only one bond separates the aromatic moiety from the potential chelate ring to which it is attached and since this is a relatively inflexible point of attachment the only degree of freedom open to the phenyl ring is rotation about the single bond. This has the effect of turning the plane of the ring from approximate orthogonality with the C_4 axis into a position where it is parallel to it (as shown in Scheme 1), without allowing the C_2 axes of the four phenyl groups to align parallel to the C_4 axis of the molecule. To allow this, more than one covalent bond must be involved in the linkage of the phenyl ring to the chelate ring. We have been able to establish a three-bond linkage between each of four phenyl groups in the new and related ligand 1,4,7,10-tetrakis((*S*)-2-hydroxy-3-phenoxypropyl)-1,4,7,10-tetraazacyclododecane ((*S*)-thpcc12), and it is upon the gas-phase structure, the solid-state structure, and the inclusion chemistry of this ligand and its Cd(II) and Pb(II) complexes that we now wish to report.

Experimental Section

General. Carbon-13 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 position was taken as δ 77.00 for CDCl_3 and δ 39.60 for $\text{DMSO}-d_6$. Elemental analyses were performed at the University of Otago, New Zealand. Conductivity measurements were made on 10^{-3} M solutions in dimethylformamide at 293 K using a Philips PW9504 conductivity bridge. Established conductivity ranges for 10^{-3} M 1:1 and 2:1 electrolytes in DMF are 65–90 and 130–170 $\Omega^{-1} \text{cm}^2 \text{mol}^{-1}$, respectively.¹⁰ Optical rotations were measured at ambient temperature using a PolAAR 21 automatic polarimeter. Cyclen was prepared by the literature procedure.¹¹ Solvents were purified before use by established methods.¹² Reactions were carried out under an atmosphere of dry nitrogen.

Synthesis of (2*S*)-(+)-3-Phenoxy-1,2-epoxypropane. The title compound was prepared using the modified procedure of Klunder and co-workers.¹³ A solution of phenol (1.48 g, 16 mmol) in dry DMF (10 mL) was added to a stirred suspension of oil-free sodium hydride (473 mg, 20 mmol) in dry DMF (15 mL). The solution was stirred at room temperature for 1 h. (2*S*)-Glycidyl tosylate (3.0 g, 13 mmol) in dry DMF (12 mL) was then added dropwise, and the reaction mixture was stirred at room temperature. A further 10 mL of DMF was added after 1 h, as the mixture became viscous. The reaction was monitored by TLC ($\text{CH}_2\text{Cl}_2/\text{hexane}$ 9:1, silica gel) and upon disappearance of the starting material (ca. 18 h), saturated NH_4Cl solution (10 mL) was added. After diluting with water (150 mL), the aqueous solution was extracted with ether (4×150 mL). The ether extract was washed with ice-cold NaOH solution (0.1 M, 4×100 mL), water (200 mL) then brine (100 mL). After drying and solvent evaporation a pale yellow oil remained that was purified by flash chromatography (silica gel, $\text{CH}_2\text{Cl}_2/\text{hexane}$ 9:1) to give a colorless oil; yield 1.3 g, 66%. ^1H NMR (CDCl_3): δ 7.25–7.30, (m, 2H); 6.90–6.98, (m, 3H); 4.19, (dd, $J = 3.3, 11.1$, 1H); 3.93, (dd, $J = 5.4, 10.8$, 1H); 3.33, (m, 1H); 2.87, (t, $J = 4.2$, 1H); 2.73, (dd, $J = 2.4, 5.1$, 1H). ^{13}C NMR (CDCl_3): δ 158.53 (1 C), 129.50 (2 C), 121.18 (1 C), 114.58 (2 C), 68.54 (1 C), 49.98 (1 C), 44.51 (1 C). $[\alpha]_D^{25} +11.3$ (c 2.57 g/100 mL, MeOH) [lit.¹³ $[\alpha]_D^{25} +14.1$ (c 2.36 g/100 mL, MeOH)].

Synthesis of 1,4,7,10-Tetrakis((*S*)-(-)-2-hydroxy-3-phenoxypropyl)-1,4,7,10-tetraazacyclododecane ((*S*)-thpcc12). A solution of the above epoxide (953 mg, 6.3 mmol) in dry ethanol (8 mL) was added dropwise over 5 min to a stirring refluxing solution of cyclen (273 mg, 1.6 mmol) in dry ethanol (10 mL). The resulting solution was heated under reflux and the progress of the reaction monitored by TLC (silica gel, $\text{CH}_2\text{Cl}_2/\text{hexane}$ 9:1). After disappearance of the starting material (ca. 24 h) the solvent was removed in vacuo to give a viscous yellow oil; yield 1.3 g, quantitative. ^{13}C NMR (CDCl_3), 295 K: δ 158.86 (4 C), 129.41 (8 C), 120.75 (4 C), 114.57 (8 C), 69.71 (4 C), 65.78 (4 C), 58.72 (4 C), 51.23 (8 C). ^{13}C NMR (CDCl_3) 223 K: δ 158.40 (4 C), 129.48 (8 C), 120.55 (4 C), 114.03 (8 C), 68.86 (4 C), 65.21 (4 C), 58.18 (4 C), 51.45 (4 C), 49.45 (4 C). $[\alpha]_D^{25} -68.8$ (c 2.6 g/100 mL, MeOH).

Synthesis of (*S*)-thpcc12-4HBr. 48% Aqueous HBr (180 μL , 1.56 mmol) was added dropwise to a stirring solution of (*S*)-thpcc12 (201 mg, 0.26 mmol) in dry ethanol (5 mL) at 0 °C. The majority of the solvent was then removed in vacuo and the residue triturated with ether. A fine white precipitate formed that was filtered off under nitrogen and washed with ether (5 mL). The solid was dried under high vacuum; yield 214 mg, 75%. ^{13}C NMR ($\text{DMSO}-d_6$): δ 158.64 (4 C), 129.82 (8 C), 121.12 (4 C), 114.78 (8 C), 70.13 (4 C), 64.17 (4 C), 55.75 (4 C), 49.75 (4 C), 47.79 (4 C). Anal. Calcd for $\text{C}_{44}\text{H}_{64}\text{Br}_4\text{N}_4\text{O}_8$: C, 48.19; H, 5.88; N, 5.16. Found: C, 48.1; H, 5.6; N, 5.2.

Synthesis of (*S*)-thpcc12-2TsOH-2H₂O. 4-Toluenesulfonic acid monohydrate (85 mg, 0.44 mmol) was added with stirring to a solution of (*S*)-thpcc12 (172 mg, 0.22 mmol) in ethanol (5 mL). The solution was stirred at ambient temperature for 2 h and the solvent was removed under reduced pressure. Ether (ca. 20 mL) was added, and the oily residue scraped with a spatula. This residue solidified and was stirred in the ethereal solution for 1 h. The fine white powder was collected by filtration and dried under vacuum. Yield: 194 mg, 76%. ^{13}C NMR ($\text{DMSO}-d_6$): δ 158.61 (4 C), 145.75 (2 C), 138.11 (2 C), 129.80 (8 C), 128.41 (4 C), 125.78 (4 C), 121.11 (4 C), 114.70 (8 C), 70.02 (4 C), 64.01 (4 C), 55.45 (4 C), 50.49 (4 C), 47.24 (4 C), 20.85 (4 C). Anal. Calcd for $\text{C}_{58}\text{H}_{80}\text{N}_4\text{O}_{16}\text{S}_2$: C, 60.40; H, 6.99; N, 4.86. Found: C, 60.7; H, 7.0; N, 5.0. Λ_M (1×10^{-3} M, DMF): 95 $\Omega^{-1} \text{cm}^2 \text{mol}^{-1}$ (1:1 to 1:2).

Synthesis of [Cd((*S*)-thpcc12)](ClO₄)₂. CAUTION: Perchlorate salts of metal complexes are potentially explosive. Although we have had no outward incidents with this or other perchlorates described in this work, suitable precautions should be taken. Cadmium perchlorate hexahydrate (530 mg, 1.3 mmol) was dissolved in dry ethanol (10 mL), and the solution was added dropwise over 5 min to a refluxing solution of (*S*)-thpcc12 (878 mg, 1.14 mmol) in dry ethanol (30 mL). The

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solution went cloudy during the addition, and a fine white solid precipitated. The suspension was heated under reflux for 1 h, and then cooled to room temperature. The fine white solid was filtered off and washed with cold ethanol (5 mL). Yield 1.08 g, 88%. ^{13}C NMR (DMSO- d_6): δ 158.52 (4 C), 129.87 (8 C), 121.27 (4 C), 114.76 (8 C), 69.78 (4 C), 64.55 (4 C), 54.70 (4 C), 49.86 (4 C), 48.04 (4 C). Anal. Calcd for $\text{C}_{44}\text{H}_{60}\text{Cl}_2\text{CdN}_4\text{O}_{16}$: C, 48.73; H, 5.54; N, 5.17. Found: C, 48.9; H, 5.3; N, 5.0. Λ_{M} (1×10^{-3} M, DMF): $132 \Omega^{-1} \text{cm}^2 \text{mol}^{-1}$ (1:2).

Synthesis of [Pb((S)-thphpc12)](ClO₄)₂·H₂O. A solution of lead perchlorate trihydrate (274 mg, 0.59 mmol) in dry ethanol (7 mL) was added dropwise over 5 min to a refluxing solution of (S)-thphpc12 (307 mg, 0.4 mmol) in dry ethanol (12 mL). The solution went cloudy over time, and an oily layer formed. After heating under reflux for 1 h, the solution was cooled in ice and the oil solidified. The resulting solid material was scraped out and washed with cold ethanol (5 mL). Recrystallization from ethanol gave fine white needles; yield 355 mg, 75%. ^{13}C NMR (DMSO- d_6): δ 158.60 (4 C), 129.91 (8 C), 121.26 (4 C), 114.79 (8 C), 70.43 (4 C), 65.62 (4 C), 56.45 (4 C), 51.96 (4 C), 50.03 (4 C). Anal. Calcd for $\text{C}_{44}\text{H}_{60}\text{Cl}_2\text{N}_4\text{O}_{17}\text{Pb}$: C, 44.15; H, 5.22; N, 4.68. Found: C, 43.9; H, 5.4; N, 4.5. Λ_{M} (1×10^{-3} M, DMF): $127 \Omega^{-1} \text{cm}^2 \text{mol}^{-1}$ (1:2).

Synthesis of [Cd((S)-thphpc12)(p-toluenesulfonate)]ClO₄. Sodium *p*-toluenesulfonate (40 mg, 0.21 mmol) was added to a refluxing solution of [Cd((S)-thphpc12)](ClO₄)₂ (224 mg, 0.21 mmol) in dry CH₃-CN (15 mL) under a nitrogen atmosphere. The solution was heated under reflux for 2 h, after which the majority of the solvent was removed in vacuo. Ether (ca. 10 mL) was added to precipitate the product. The resulting off-white solid was suspended in absolute ethanol (20 mL) and boiled for 30 min to remove occluded sodium perchlorate. After filtering off the solid (186 mg, 78%) it was recrystallized from methanol (ca. 40 mL) to give large pale pink prisms suitable for structural analysis. ^{13}C NMR (DMSO- d_6): δ 158.52 (4 C), 145.58 (1 C), 138.17 (1 C), 129.83 (8 C), 128.40 (2 C), 125.78 (2 C), 121.22 (4 C), 114.76 (8 C), 69.74 (4 C), 64.53 (4 C), 54.77 (4 C), 49.93 (4 C), 48.05 (4 C), 20.84 (1 C). Anal. Calcd for $\text{C}_{51}\text{H}_{67}\text{CdClN}_4\text{O}_{15}\text{S}$: C, 52.99; H, 5.84; N, 4.85. Found: C, 53.0; H, 6.0; N, 4.9. Λ_{M} (1×10^{-3} M, DMF): $84 \Omega^{-1} \text{cm}^2 \text{mol}^{-1}$ (1:1).

Synthesis of [Pb((S)-thphpc12)(p-toluenesulfonate)]ClO₄·H₂O. Sodium *p*-toluenesulfonate (19 mg, 0.09 mmol) was added to a solution of [Pb((S)-thphpc12)](ClO₄)₂·H₂O (115 mg, 0.09 mmol) in dry CH₃-CN (15 mL) under a nitrogen atmosphere. The resulting suspension was heated under reflux for 2.5 h, during which time the sodium salt dissolved. The majority of the solvent was then removed in vacuo, and ether (20 mL) was added to precipitate a white powder. The white powder was collected by filtration and recrystallized from ethanol (ca. 7.5 mL) to give fine white needles of the pure product; 76 mg, 62%. ^{13}C NMR (DMSO- d_6): δ 158.58 (4 C), 145.79 (1 C), 138.05 (1 C), 129.86 (8 C), 128.37 (2 C), 125.77 (2 C), 121.20 (4 C), 114.76 (8 C), 70.38 (4 C), 65.58 (4 C), 56.47 (4 C), 51.93 (4 C), 50.02 (4 C), 20.83 (1 C). Anal. Calcd for $\text{C}_{51}\text{H}_{69}\text{ClN}_4\text{O}_{16}\text{PbS}$: C, 48.28; H, 5.48; N, 4.42. Found: C, 48.2; H, 5.3; N, 4.4. Λ_{M} (1×10^{-3} M, DMF): $122 \Omega^{-1} \text{cm}^2 \text{mol}^{-1}$ (1:2).

Synthesis of [Cd((S)-thphpc12)(p-nitrophenolate)]ClO₄. A solution of sodium *p*-nitrophenolate (33 mg, 0.20 mmol) in dry methanol (4 mL) was added dropwise to a refluxing solution of [Cd((S)-thphpc12)](ClO₄)₂ (224 mg, 0.20 mmol) in dry methanol (10 mL). The solution was then heated under reflux for 2.5 h. After it had cooled to ambient temperature overnight, the solution deposited large yellow needles that were filtered off and dried in vacuo. Yield 150 mg, 67%. ^{13}C NMR (DMSO- d_6): δ 173.95 (1 C), 158.64 (4 C), 133.97 (1 C), 129.77 (8 C), 126.84 (2 C), 121.08 (4 C), 118.21 (2 C), 114.72 (8 C), 70.17 (4 C), 64.55 (4 C), 55.92 (4 C), 50.08 (4 C), 48.40 (4 C). Anal. Calcd for $\text{C}_{50}\text{H}_{64}\text{ClN}_5\text{O}_{15}\text{Cd}$: C, 53.48; H, 5.74; N, 6.24. Found: C, 53.4; H, 6.1; N, 6.4. Λ_{M} (1×10^{-3} M, DMF): $76 \Omega^{-1} \text{cm}^2 \text{mol}^{-1}$ (1:1).

Synthesis of [Pb((S)-thphpc12)(p-nitrophenolate)]ClO₄. To a refluxing solution of [Pb((S)-thphpc12)](ClO₄)₂·H₂O (174 mg, 0.15 mmol) in dry CH₃CN (15 mL) under a nitrogen atmosphere was added solid sodium *p*-nitrophenolate (24 mg, 0.15 mmol). The resulting yellow solution was heated under reflux for 1.5 h. After the solution had cooled to room temperature, the majority of the solvent was removed in vacuo,

and ether (ca. 20 mL) was added. A bright yellow precipitate formed and was filtered off. The occluded sodium perchlorate was removed by recrystallizing the product from aqueous acetone to give fine yellow needles; yield 133 mg, 75%. ^{13}C NMR (DMSO- d_6): δ 177.50 (1 C), 158.60 (4 C), 131.58 (1 C), 129.80 (8 C), 127.12 (2 C), 121.12 (4 C), 118.99 (2 C), 114.70 (8 C), 70.47 (4 C), 65.58 (4 C), 56.89 (4 C), 51.89 (4 C), 50.04 (4 C). Anal. Calcd for $\text{C}_{50}\text{H}_{64}\text{ClN}_5\text{O}_{15}\text{Pb}$: C, 49.32; H, 5.30; N, 5.75. Found: C, 49.2; H, 5.2; N, 5.6. Λ_{M} (1×10^{-3} M, DMF): $77 \Omega^{-1} \text{cm}^2 \text{mol}^{-1}$ (1:1).

Molecular Orbital Calculations. Molecular orbital calculations on (S)-thphpc12 and [Cd((S)-thphpc12)](ClO₄)₂ were carried out using Gaussian 94 with the LanL2DZ basis set⁴ on a Silicon Graphics Indigo² workstation. These calculations incorporated all electrons for H, C, N, and O and the valence electrons for the Cd(II) ion together with its core potential.^{14,15}

Crystal Structure Determinations. Unit-cell and intensity data for [Cd((S)-thphpc12)](ClO₄)₂ were measured on a Siemens SMART¹⁶ diffractometer using graphite-monochromated Mo K α X-radiation and corrected for absorption using SADABS¹⁷ by Prof. W. T. Robinson at the University of Canterbury, Christchurch, New Zealand. Unit-cell and intensity data for [Cd((S)-thphpc12)(p-toluenesulfonate)]ClO₄ were collected on a CAD-4/PC diffractometer using graphite-monochromated Mo K α X-radiation and corrected for absorption by Gaussian integration from the crystal shape. Parameters associated with unit cell dimensions, intensity data collection, and refinement for both structures are given in Table 1.

The structures were solved by using SIR92,¹⁸ otherwise computer programs of the XTAL system¹⁹ were used for all calculations. Non-hydrogen atomic coordinates and anisotropic displacement parameters for all atoms were refined by full-matrix least-squares on F^2 minimizing $\sum(|F_o|^2 - |F_c|^2)|^2/\sigma^2(F_o^2)$. Values of $\sigma^2(F_o^2)$ for [Cd((S)-thphpc12)(p-toluenesulfonate)]ClO₄ were obtained from the sum of the number of counts and a term $0.003 \times (\text{number of counts})^2$, and for [Cd((S)-thphpc12)](ClO₄)₂ counting statistics alone were used. Neutral atom scattering factors with anomalous dispersion corrections were used. Hydrogen atoms of the hydroxyl oxygen atoms of [Cd((S)-thphpc12)(p-toluenesulfonate)]ClO₄ were located from a difference map and their positional and isotropic displacement parameters refined. Those of the *p*-toluenesulfonate methyl group were also located from a difference map, but their coordinates were not refined. All other hydrogen atoms were placed at calculated positions and, although their coordinates and isotropic displacement parameters were not refined, the coordinates were readjusted several times during the refinements. A Flack parameter²⁰ was refined for [Cd((S)-thphpc12)(p-toluenesulfonate)]ClO₄ (-0.01(2)), but a similar procedure for [Cd((S)-thphpc12)](ClO₄)₂ did not refine satisfactorily and instead the structure was refined using the entire Friedel independent data set. The synthetic scheme precluded the presence of a center of symmetry in both space groups and this was confirmed by intensity statistics, the structure solution, and the program BUNYIP.²¹ In [Cd((S)-thphpc12)](ClO₄)₂ the peak of 1.94 \AA^{-3} in the difference map is near Cd1.

Results and Discussion

Synthesis and Structure of (S)-thphpc12. The ligand (S)-thphpc12, which occurs as a viscous, pale-yellow oil, was

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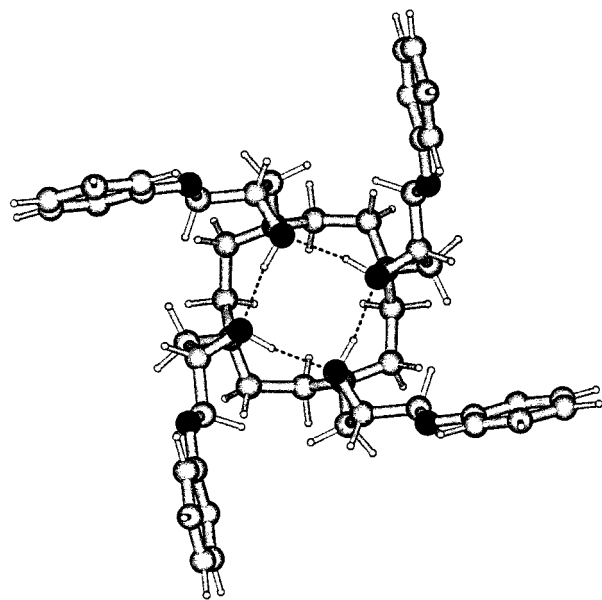
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Table 1. Crystal Data and Refinement Summary for [Cd((S)-thphpc12)](ClO₄)₂ and [Cd((S)-thphpc12)(*p*-toluenesulfonate)]ClO₄

empirical formula	[Cd(C ₄₄ H ₆₀ N ₄ O ₈)]-(ClO ₄) ₂	[Cd(C ₄₄ H ₆₀ N ₄ O ₈)-(C ₇ H ₇ O ₃ S)](ClO ₄)
<i>M</i>	1076.26	1155.85
cryst syst	triclinic	triclinic
space group	<i>P</i> 1	<i>P</i> 1
<i>a</i> /Å	9.8736(2)	10.640(1)
<i>b</i> /Å	10.8633(3)	11.907(1)
<i>c</i> /Å	23.4208(6)	12.174(1)
α /deg	77.326(1)	111.96(1)
β /deg	80.511(1)	91.77(1)
γ /deg	73.931(1)	113.94(1)
<i>U</i> /Å ³	2340.6(1)	1276.5(3)
λ /Å	0.71073	0.71073
<i>Z</i>	2	1
cryst color and shape	colorless plate	pale pink prism
cryst size/mm	0.80 × 0.64 × 0.04	0.46 × 0.32 × 0.30
diffractometer type	siemens SMART diffractometer	CAD-4/PC diffractometer
<i>D</i> _c /g cm ⁻³	1.527	1.504
<i>F</i> (000)	1124	602
<i>T</i> /K	142(2)	150(2)
<i>T</i> _{min} , <i>T</i> _{max}	0.31, 0.97	0.781, 0.887
μ /mm ⁻¹	0.66	0.59
θ _{max} /deg	30.5	27.5
<i>h</i> , <i>k</i> , <i>l</i> ranges	-14 → 5, -14 → 15, -32 → 30	-13 → 13, -15 → 3, -15 → 15
<i>R</i> _{int}	0.06	0.02
no. of reflns measd	15 383	14 769
no. of unique reflns	12 859	5848
no. used in refinement (<i>F</i> ² > 0)	11 938	5844
no. of params refined	1208	672
<i>R</i> (<i>F</i>) ^a	0.054	0.029
w <i>R</i> (<i>F</i> ²)	0.143	0.038
goodness of fit	1.26	1.69
final shift/error (max, av)	0.0009, 0.00007	0.004, 0.0002
min, max $\Delta\rho$ /e Å ⁻³	-2.13, 1.94	-0.42, 0.76

$$^a R(F) = \frac{\sum(|F_o| - |F_c|)}{\sum|F_o|}. \quad wR(F^2) = \frac{\sum w(|F_o^2| - |F_c^2|)}{\sum w|F_o^2|}.$$

prepared in quantitative yield through the reaction of the optically pure epoxide (2*S*)-(+)-3-phenoxy-1,2-epoxypropane with cyclen. (2*S*)-(+)-3-Phenoxy-1,2-epoxypropane was obtained through the known reaction of sodium phenoxide with commercially available (2*S*)-glycidyl tosylate.¹³ Molecular orbital calculations performed using Gaussian 94⁴ indicate that the global energy minimized structure of (S)-thphpc12 in the gas phase, shown in Figure 1, is one in which it has C₄ symmetry with the four nitrogen atoms and the four oxygen atoms defining opposite faces of an approximate cube. The O₄ plane is twisted by 3° in a clockwise direction with respect to the N₄ plane giving the molecule a Δ helicity. This configuration accommodates the formation of four hydrogen bonds (H···O = 1.80 Å, O—H···O angle = 170.59°) between the hydrogen atom of each hydroxyl group and the oxygen atom of a neighboring group. Although the C₂ axes of the aromatic rings and the C₄ axis of the molecule do not align parallel to one another, the axes connecting carbon atoms 2 and 5 on each aromatic ring and the C₄ axis do achieve this arrangement, thereby creating a cavity within the molecule. This cavity, however, is broader than the one shown in Scheme 1 where the C₂ axes are so aligned. The spacial extent of the four aromatic rings gives the cavity significant openings between its four defining walls and although there are apparent face to edge alignments between neighboring aromatic rings (inter-ring angle = 88.58°) the rings are too distant from one another for them to experience significant attractive forces. Face to edge attractions between

**Figure 1.** Global energy-minimized structure of (S)-thphpc12 determined through Gaussian 94 using the LanL2DZ basis set. Hydrogen bonds are shown as broken lines. Oxygen, nitrogen, and carbon atoms are strongly, moderately, and lightly shaded, respectively.**Table 2.** Bond Lengths (Å) and Angles (deg) Derived from Molecular Orbital Calculations on (S)-thphpc12 and [Cd((S)-thphpc12)]²⁺ Using the Gaussian 94 LanL2DZ Basis Set

	(S)-thphpc12	[Cd((S)-thphpc12)] ²⁺
O—O distance	2.76	2.91
N—N distance	3.20	3.05
O plane—N plane distance	2.89	2.56
Cd—O distance	—	2.38
Cd—N distance	—	2.55
Cd—O plane distance	—	1.20
Cd—N plane distance	—	1.36
adjacent phenyl centroid—centroid distance	8.93	9.37
adjacent inter-phenyl plane angle	88.58	82.56
H···O distance	1.80	2.85
O—H···O angle	170.59	—
twist angle ϕ^b	+3	-22

^a The globalized minimum energies for Δ (S)-thphpc12 and Λ [Cd((S)-thphpc12)]²⁺ are -2516.973 908 2 and -2563.296 895 7 H, respectively where 1 H = 2622.99 kJ mol⁻¹. ^b The twist angle, ϕ , is the clockwise (+) or anticlockwise (-) angle of rotation of the O₄ plane with respect to the N₄ plane determined by viewing the molecule from the O₄ plane in the direction of the N₄ plane and noting the direction and angle of displacement of an oxygen atom with respect to the nitrogen atom to which it is connected.

benzene rings have been calculated to maximize at a centroid to centroid separation in the range 4.99–5.19 Å,²³ whereas the separation calculated in this work for (S)-thphpc12 is 8.93 Å. Full details of calculated bond lengths and angles are given in Table 2.

The ¹³C NMR spectrum of (S)-thphpc12 in CDCl₃ shows coalescence of the two resonances arising from the inequivalent carbon atoms of each ethano link of the cyclen macrocycle, predicted by the modeling, as the sample is heated above 223 K. None of the other seven resonances undergo coalescence. This phenomenon has been noted previously with related

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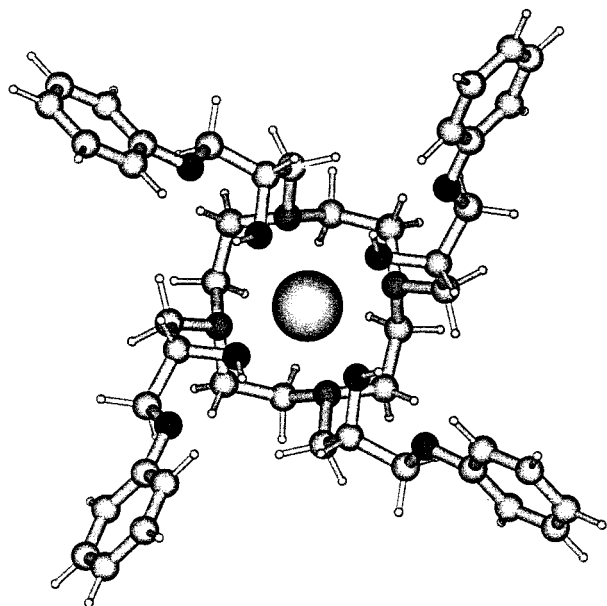


Figure 2. Global energy-minimized structure of $[\text{Cd}((S)\text{-thphpc12})]^{2+}$ determined through Gaussian 94 using the LanL2DZ basis set. Oxygen, nitrogen, and carbon atoms are strongly, moderately, and lightly shaded, respectively.

ligands,^{2,3,8,9} and besides indicating that the ligand exists in solution as a single diastereomer, of C_4 symmetry, as predicted for the gas phase, shows that there is continual site exchange between the two carbon atoms of the cyclen macrocycle which can be accounted for by repeated double inversions at each nitrogen center.

Synthesis and Structure of $[\text{Cd}((S)\text{-thphpc12})]^{2+}$. The Cd(II) complex of (*S*)-thphpc12 was formed as the diperchlorate salt by the addition of cadmium perchlorate hexahydrate to an ethanolic solution of the ligand. In DMF solution the complex behaves as a 1:2 electrolyte indicating little or no association between the perchlorate anions and the complex cation in this solvent. Gaussian 94 calculations predict a structure for the cation in the gas phase which is broadly similar to that of the free ligand, but with an eight-coordinate Cd(II) ion positioned centrally between the N_4 and O_4 planes, as shown in Figure 2. Predicted bond lengths and angles are given in Table 2. The introduction of the Cd(II) ion results in the loss of all hydrogen bonding interactions between the hydroxyl groups as well as the potential for face to edge interactions, since the aromatic rings are no longer favorably aligned. The predicted helicity of the complex; an anticlockwise twist angle of 22° , is more marked in the complex than in the free ligand.

The helicity predicted in the gas phase for $[\text{Cd}((S)\text{-thphpc12})]^{2+}$ is evident in DMSO- d_6 solution from the ^{13}C NMR spectrum of $[\text{Cd}((S)\text{-thphpc12})](\text{ClO}_4)_2$ in which the carbon atoms of each five-membered chelate ring formed by the macrocycle resonate at well-separated frequencies at 295 K. Increasing the sample temperature to 373 K caused no coalescence of these resonances indicating that the complex is of substantially greater rigidity than (*S*)-thphpc12. The total number of resonances in the spectrum corresponds to the number expected of a single diastereomer having C_4 symmetry, showing that the molecule has a definite structural preference for one helicity over the other.

Crystals of $[\text{Cd}((S)\text{-thphpc12})](\text{ClO}_4)_2$ suitable for X-ray diffraction data collection were grown by vapor diffusion of diethyl ether into a solution of the compound in acetone. Solution of the crystal structure indicated that the two crystal-

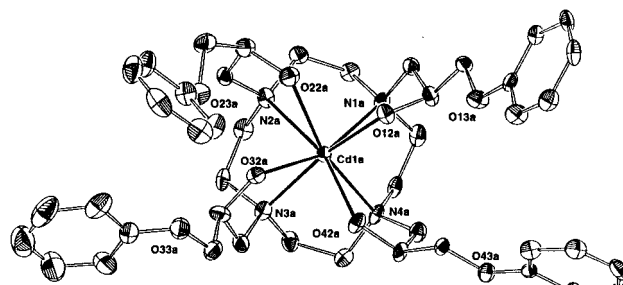


Figure 3. ORTEP²² view of one of the $[\text{Cd}((S)\text{-thphpc12})]^{2+}$ cations in crystalline $[\text{Cd}((S)\text{-thphpc12})](\text{ClO}_4)_2$ with displacement ellipsoids shown at the 50% probability level. Hydrogen atoms are omitted.

Table 3. Important Bond Lengths (Å) in the Crystal Structures of $[\text{Cd}((S)\text{-thphpc12})](\text{ClO}_4)_2$ and $[\text{Cd}((S)\text{-thphpc12})(p\text{-toluenesulfonate})]\text{ClO}_4$

bond	complex		
	$[\text{Cd}((S)\text{-thphpc12})](\text{ClO}_4)_2$ molecule a	$[\text{Cd}((S)\text{-thphpc12})](\text{ClO}_4)_2$ molecule b	$[\text{Cd}((S)\text{-thphpc12})(p\text{-toluenesulfonate})]\text{ClO}_4$
Cd–N12	2.454(17)	2.451(16)	2.520(4)
Cd–N22	2.410(18)	2.463(16)	2.472(4)
Cd–N32	2.467(17)	2.430(18)	2.498(4)
Cd–N42	2.456(16)	2.451(19)	2.439(3)
Cd–O12	2.437(17)	2.444(18)	2.546(4)
Cd–O22	2.578(16)	2.385(18)	2.376(2)
Cd–O32	2.376(17)	2.544(15)	2.581(4)
Cd–O42	2.431(18)	2.497(16)	2.518(4)

lographically unique molecules in this structure are very similar in appearance when superimposed. The four pendant arms have similar dispositions except for minor differences in the tilt of the phenyl groups. The stereochemistry of the cation (shown in Figure 3) is similar to that predicted for the gas phase by Gaussian 94, although the precise C_4 symmetry is lacking and the plane of the four oxygen atoms is rotated by approximately $+18^\circ$ with respect to the plane of the four nitrogen atoms. The Cd(II) ion-to-donor atom bond lengths are given in Table 3. A significant difference, however, relates to the disposition of the aromatic rings. These, as it has been noted in the discussion of the modeling, have insignificant attractions between them and, presumably, are highly susceptible to the vagaries of crystal packing forces when condensing into the solid state. The perchlorate ions are located in the crystal structure in positions which are remote from the molecular cavity, but which permit, in each case, the formation of hydrogen bonds between two of the perchlorate oxygen atoms and hydrogen atoms from adjacent pairs of hydroxyl groups.

Synthesis and Structure of Inclusion Compounds Derived from $[\text{Cd}((S)\text{-thphpc12})]^{2+}$ and $[\text{Pb}((S)\text{-thphpc12})]^{2+}$. To test the ability of the cavity in (*S*)-thphpc12 to retain aromatic guest molecules $[\text{Cd}((S)\text{-thphpc12})](\text{ClO}_4)_2$ and $[\text{Pb}((S)\text{-thphpc12})](\text{ClO}_4)_2$ (prepared in the same way as the Cd(II) complex) were exposed, in separate experiments, to sodium *p*-toluenesulfonate and sodium *p*-nitrophenolate in either acetonitrile or methanol solution. In all four cases sodium perchlorate was eliminated from the mixture and it was possible to isolate and recrystallize the resulting complex as the mono-inclusion anion mono-perchlorate salt. With the exception of $[\text{Pb}((S)\text{-thphpc12})(p\text{-toluenesulfonate})]\text{ClO}_4$ these complexes all have conductivities in DMF indicating that they are 1:1 electrolytes, in contrast to both host complex diperchlorate salts which are 1:2 electrolytes under the same conditions, implying that the aromatic anion, except in the case of $[\text{Pb}((S)\text{-thphpc12})(p\text{-toluenesulfonate})]\text{ClO}_4$, is immobilized within the cavity. These indications of

Table 4. $^{13}\text{C}\{^1\text{H}\}$ NMR Chemical Shifts for Free and Included Sodium *p*-Toluenesulfonate and Sodium *p*-Nitrophenolate

compound	chemical shifts (ppm) of the guest molecule resonances ^{a,b}		
	C ₁ ,C ₄	C _{2/6} ,C _{3/5}	C ₇
sodium <i>p</i> -toluenesulfonate (<i>p</i> -Ts)	145.91, 138.00	128.36, 125.79	20.86
[Cd((<i>S</i>)-thphpc12)(<i>p</i> -Ts)]ClO ₄	145.58, 138.16	128.39, 125.77	20.84
[Pb((<i>S</i>)-thphpc12)(<i>p</i> -Ts)]ClO ₄	145.79, 138.05	128.37, 125.77	20.83
sodium <i>p</i> -nitrophenolate (<i>p</i> -NO ₂)	180.82, 127.99	127.75, 119.59	—
[Cd((<i>S</i>)-thphpc12)(<i>p</i> -NO ₂)]ClO ₄	173.95, 133.97	126.84, 118.21	—
[Pb((<i>S</i>)-thphpc12)(<i>p</i> -NO ₂)]ClO ₄	177.50, 131.58	127.12, 118.99	—

^a 0.05 M in DMSO-*d*₆ at 295 K. ^b Carbon atoms are numbered such that C₁ and C₄ are the *ipso*-carbon atoms and C₇ is the *p*-toluenesulfonate methyl group.

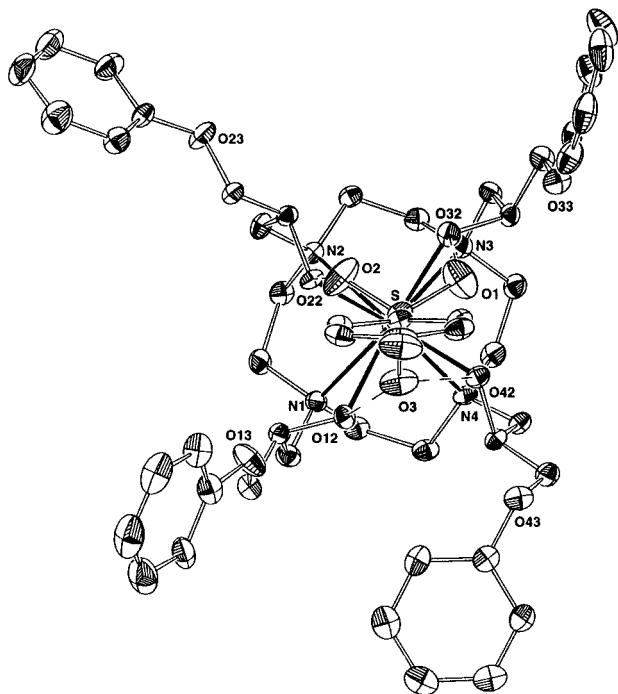


Figure 4. [Cd((*S*)-thphpc12)(*p*-toluenesulfonate)]⁺ inclusion cation viewed perpendicular to the plane of the hydroxyl oxygen atoms (O12, O22, O32, O42). Displacement ellipsoids are at the 50% probability level. Hydrogen bonds between sulfonate oxygen atoms and hydroxyl oxygen atoms are shown as broken lines. Hydrogen atoms are omitted.

relative stability are supported by the magnitude of changes in the chemical shift of resonances attributable to the guest molecule when seen in the ^{13}C NMR spectrum of the host-guest complex and compared to the free guest. These spectra were all recorded in DMSO-*d*₆ at identical concentration and temperature and are tabulated in Table 4. From it it may be seen that the carbon atoms of the guest molecule that are most affected are the *ipso*-carbon atoms (C₁ and C₄), and these more so in the case of the Cd(II) complexes than the Pb(II) complexes and more in the case of the *p*-nitrophenolate complexes than the *p*-toluenesulfonate complexes; all of which correlates with [Pb((*S*)-thphpc12)(*p*-Ts)]ClO₄ being the least stable complex as shown by its relatively high conductivity. The spectra are in all cases consistent with the [M((*S*)-thphpc12)]²⁺ moiety retaining its 4-fold symmetry and being present as a single diastereomer. The introduction of these guest molecules does not significantly alter the chemical shift value of the resonances arising from the [M((*S*)-thphpc12)]²⁺ moiety.

Crystals of [Cd((*S*)-thphpc12)(*p*-toluenesulfonate)]ClO₄ suitable for a crystal structure determination by X-ray diffraction were grown by recrystallizing the inclusion compound from methanol. Solution of the crystal structure verified that the *p*-toluenesulfonate moiety is located within the molecular cavity

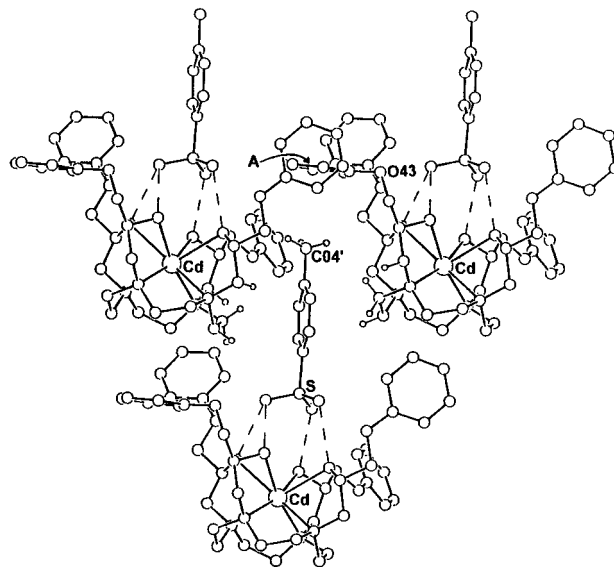


Figure 5. View of the crystal structure of [Cd((*S*)-thphpc12)(*p*-toluenesulfonate)]ClO₄ showing the environment of one (central) guest anion. Hydrogen bonds are shown as broken lines. Hydrogen atoms (smallest circles) on the methyl carbon atom C04' are shown as those with close contacts to the phenyl ring from neighboring molecules.

Table 5. Hydrogen-Bonding Geometry (Å and deg) in the Crystal Structure of [Cd((*S*)-thphpc12)(*p*-toluenesulfonate)]ClO₄

hydrogen bond	O—H	H···O	O···O	O—H···O
O32—H321···O1	0.86(7)	1.94(7)	2.791(5)	170(5)
O22—H221···O2	0.98(6)	1.70(6)	2.656(5)	164(8)
O12—H121···O3	0.75(5)	2.14(5)	2.792(5)	146(4)
O42—H421···O3	0.82(5)	2.10(5)	2.902(4)	168(7)

(shown in Figures 4 and 5) and shows that the principal retaining forces arise by way of hydrogen bonds between the hydroxyl groups of the ligand and the three oxygen atoms of the sulfonate moiety. Thus, each of the sulfonate oxygen atoms positions itself so that it is within 2.14(5) Å of one of the pendant hydroxyl hydrogen atoms. Full details are given in Table 5. The plane of the phenyl ring lies across the S—O3 bond direction and O3 is the acceptor for two hydrogen bonds, one each from O12 and O42. O1 and O2 of the sulfonate moiety are the acceptors in two single hydrogen bonds from O32 and O22, respectively. The distance of the Cd(II) ion from the plane of the three sulfonate oxygen atoms is 5.17(2) Å which is too large for a significant ionic interaction. No particular alignment, between any of the aromatic rings that would suggest the presence of significant interactions between them, is evident. However, there is an attractive C—H/ π interaction between the tosylate methyl group and the pendant phenyl ring attached to O43 of the molecule at 1 + *x*, 1 + *y*, *z* (labeled A in Figure 5) with distances between the three hydrogen atoms and the ring in the range 3.04(1) to 3.09(1). The C—H/ π contacts observed here are much

shorter than the sum of the van der Waals radii for a methyl group and an sp^2 carbon atom which amounts to 3.7 Å.²⁴ The remainder of the complex is superficially similar to the host molecule as shown by the bond lengths detailed in Table 3.

Since the crystal structure of $[Cd((S)\text{-thphpc12})(p\text{-Ts})]ClO_4$ indicated that the aromatic rings of the host molecule are not involved, at least in the solid state, in stabilizing the guest molecule within the cavity, it became of interest to ascertain the importance of these aromatic moieties to the inclusion process by repeating the inclusion-complex forming reactions using analogous host molecules that are devoid of aromatic entities. To do this we investigated the reaction of $[Cd(\text{thec12})](ClO_4)_2$ and $[Cd(S\text{-thpc12})](ClO_4)_2$ with sodium *p*-toluenesulfonate under identical conditions to those described above (thec12 and *S*-thpc12 are analogous to (*S*)-thphpc12 except that they have H or Me, respectively, in place of the phenoxyethyl substituent). The importance of the aromatic moieties was immediately obvious when it was found that sodium *p*-toluenesulfonate, which by itself is insoluble in acetonitrile, was not taken into solution by the nonaromatic hosts even after several hours in refluxing acetonitrile. Thus it appears that the aromatic moieties play a crucial role in generating a hydrophobic

cavity into which the *p*-toluenesulfonate ion is first induced, and then locked, by way of the hydrogen bonding seen in the crystal structure. In a similar way it was of interest to know how essential the metal ion is to the inclusion process, especially as the gas phase modeling predicts a similar geometrical arrangement of the ligand with or without Cd(II) present. We tested this by forming the di-*p*-toluenesulfonate salt of (*S*)-thphpc12 and measuring its conductivity in DMF. The result of this was a conductivity value of $95 \Omega^{-1} \text{ cm}^2 \text{ mol}^{-1}$ slightly above that expected for a 1:1 electrolyte and greater than the $84 \Omega^{-1} \text{ cm}^2 \text{ mol}^{-1}$ shown by the Cd(II) inclusion complex. This suggests weaker retention of *p*-toluenesulfonate within the structure of the diprotonated macrocycle than within the Cd(II) complex.

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Supporting Information Available: Listings of atomic positional parameters, atomic anisotropic displacement parameters and fully labeled structural diagrams. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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