

Control of the Helical Chirality in Octahedral Complexes by a Chiral Macrobicyclic Cavity Possessing Six Convergent Hydroxyl Groups

Paul Baret, Virginie Beaujolais, Didier Gaude, Christian Coulombeau and Jean-Louis Pierre*

Abstract: The (*aR,aR,aR*) and (*aS,aS,aS*) enantiomers of a chiral macrobicyclic ligand with a bicapped tris(binaphthol) structure were synthesized. Complexation of gallium(III), chromium(III) and iron(III) centres in the chiral cavities of these two ligands yielded exclusively one octahedral configuration in each case: the (*aR,aR,aR*) enantiomer gave a Λ complex and the (*aS,aS,aS*) enantiomer a Δ complex. These assignments were established by CD spectroscopy for chromium and iron centres and by molecular modelling.

Keywords

chirality • coordination modes • macrocyclic ligands • octahedral complexes • supramolecular chemistry

Introduction

The design of host molecules capable of strong and stereoselective complexation of metal ions is an important area of molecular recognition. Octahedral complexation of transition metal ions with three bidentate ligands usually leads to racemic mixtures of Λ and Δ isomers. The importance of the absolute configuration of the octahedral metal centre has been demonstrated through the recognition of iron(III)–siderophore complexes by membrane receptor proteins.^[1–6]

Chiral siderophore analogues have been shown to undergo stereoselective formation of Δ or Λ coordination isomers upon complexation of metal ions such as iron(III), gallium(III), chromium(III) or cobalt(III).^[7–14] The source of the stereoselective chelation has been ascribed to nonbonded, weakly polar interactions between substituents of the chiral moieties peripheral to the metal centre. In all of these examples, the ligand chirality arises from amino acid derived subunits. The direct control of the Δ or Λ coordination by means of intrinsically chiral bidentate moieties with axial

chirality has been reported for tris(binaphtholate) complexes of tungsten(VI).^[15]

The pioneering work of Vögtle^[16–18] and Raymond^[19–24] on bicapped tris(catecholate) iron(III) complexes inspired us to synthesize the iron(III) complex of a macrobicyclic ligand containing three conformationally racemizable 2,2'-dihydroxybiphenyl subunits.^[25] We describe herein the synthesis and complexation properties of a new chiral macrobicyclic ligand, the bicapped tris(binaphtholate) **LH₆** (Figure 1). Since chiral and

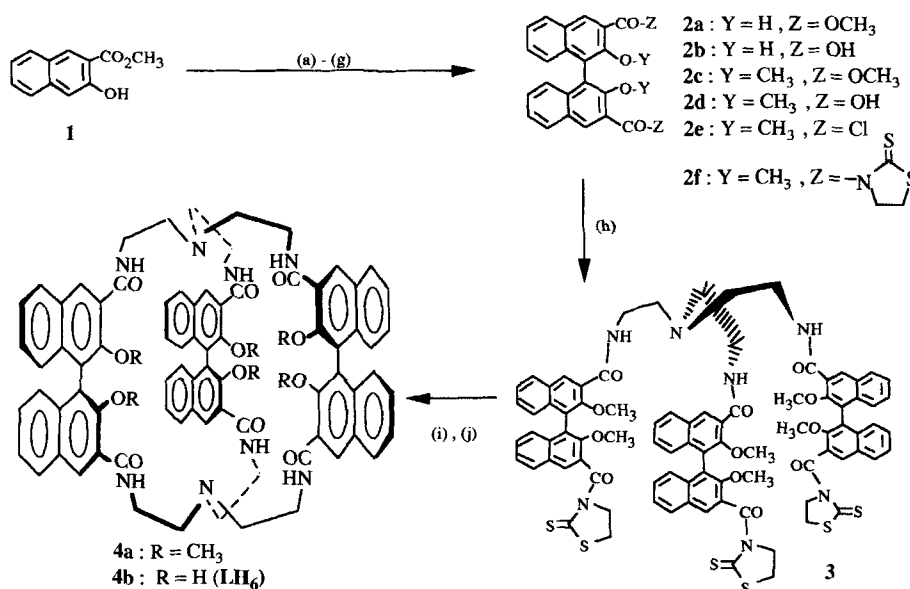


Figure 1. Synthetic pathway to **LH₆**: a) CuCl_2 , PhCH_2NH_2 , methanol (**2a**, 63% yield) [26]. b) NaOH , ethanol; acidic treatment (**2b**, 99% yield). c) Resolution of racemic **2b** [27]. d) $(\text{CH}_3\text{O})_2\text{SO}_2$, K_2CO_3 , acetone (**2c**, 90% yield). e) NaOH , methanol, acidic treatment (**2d**, 97% yield). f) SOCl_2 (**2e**, 99% yield, used without further purification). g) NaH , 2-mercaptobenzothiazole, THF (**2f**, 99% yield). h) TREN (0.3 equiv), CH_2Cl_2 ; chromatography (silica gel) (**3**, 46% yield). i) TREN (1 equiv), CHCl_3 , high-dilution technique (**4a**, 38% yield). j) BBr_3 , CH_2Cl_2 (**4b**, **LH₆**, 93% yield).

[*] Prof. Dr. J.-L. Pierre, Prof. Dr. P. Baret, Dr. V. Beaujolais, Prof. Dr. C. Coulombeau, Dr. D. Gaude
LEDSS, UMR CNRS 5616,
Université J. Fourier
BP 53, F-38041 Grenoble Cedex 9 (France)
Fax : Int. code + (4)7651-4836
e-mail: jean-louis.pierre@ujf-grenoble.fr

optically stable binaphthol subunits were used, both the (*aR,aR,aR*) and the (*aS,aS,aS*) ligands could be obtained in enantiomerically pure form.

Results and Discussion

Syntheses of Ligand LH_6 (Figure 1): Oxidative coupling of **1** afforded the racemic mixture **2b**,^[126] which was resolved into (*aR*)-**2b** and (*aS*)-**2b** according to Cram.^[127] The optically pure precursors **2c** and **2d** were obtained and identified according to published procedures.^[128–30] The methyl-protected enantiomerically pure (*aR,aR,aR*) and (*aS,aS,aS*) bicapped ligands **4a** were obtained from the corresponding tripods **3** by using high-dilution techniques based on Raymond's methodology employing 2-mercaptothiazolide derivatives.^[123] Removal of the methyl groups with BBr_3 gave the two enantiomers of LH_6 .

Metal complexes: The following metal complexes of LH_6 were formed.

Gallium(III): Diamagnetic gallium(III) has been used extensively as a substitute for iron(III) in NMR studies.^[12, 13, 31, 32] Both ions have the same charge and similar ionic radii in six-coordinate complexes. Since neither high-spin d^5 iron(III) nor d^{10} gallium(III) have any crystal field stabilization, they are similar in their ligand exchange rates. The gallium complexes were prepared from (*aR,aR,aR*)- and (*aS,aS,aS*)- LH_6 through an exchange procedure involving gallium acetylacetonate. The complexes formed exhibited identical NMR spectra. The enantiomeric relationship between these two complexes was revealed by the polarimetric measurements (complex from the (*aR,aR,aR*) ligand: $[\alpha]_{589}^{21} = +213$, $[\alpha]_{578}^{21} = +222$; complex from the (*aS,aS,aS*) ligand: $[\alpha]_{589}^{21} = -211$, $[\alpha]_{578}^{21} = -221$). NMR analysis showed a single set of signals with a pattern similar to that observed for the tris(methyl-protected) free ligand. This establishes the isomeric purity of the complexes. On the basis of the NMR data, the structure of the $[\text{LGa}]^{3-}$ complex anion in solution was assigned D_3 symmetry. Partial crystallization experiments were used to confirm that only one isomer had been formed for each ligand: no changes were observed in the NMR spectra of samples from the liquid phase and from the solid phase. Surprisingly, the gallium complexes $\text{K}_3[\text{LGa}]$ obtained from (*aR,aR,aR*)- and (*aS,aS,aS*)- LH_6 were found to be less stable than the corresponding iron(III) complexes (see below); they decomposed within a few days in solution, but were more stable in the solid state. Nevertheless, before decomposition, no isomerization was observed (no change in the NMR spectrum): the constrained bicapped structure does not allow inversion of the octahedral centre, contrary to simple trisbidentate complexes.^[132] It should be emphasized that octahedral inversion would lead to diastereoisomeric material, since the ligand LH_6 cannot racemize under the experimental conditions. $\text{Ga}(\text{acac})_3$ was added progressively to LH_6 (in D_2O , NaOD), and the complexation was monitored by ^1H NMR spectroscopy. The 1:1 stoichiometry for the complex was thus confirmed. The absence of exchange at ambient temperature between free and complexed ligand indicates that the complex is not labile before decomposition: kinetic lability, resulting from the absence of ligand field

stabilization, would favour the release of the metal and the exchange between free and complexed ions. Exchange has been observed for the simple tris(bidentate) complexes.^[121]

Chromium(III): Chromic ions induce kinetic inertness leading to stable optical isomers, and the d–d transition of the d^3 complexes is allowed. Diastereoisomeric chiral chromic complexes and, in some cases, the resolution of optical isomers have been described by Raymond et al.^[110, 33–37] The absolute configurations have been assigned in some examples. X-ray data have been reported for $\text{K}_3[\text{Cr}(\text{Cat})_3] \cdot 1.5\text{H}_2\text{O}$.^[38]

Stable chromic complexes $\text{K}_3[\text{LCr}]$ were prepared from (*aR,aR,aR*)- and (*aS,aS,aS*)- LH_6 through an exchange procedure involving chromic acetylacetonate. The complexes were crystallized, but the crystalline material was unfortunately not suitable for X-ray structure determination. Titration of the ligands with the chromic salt, monitored by UV/Vis spectroscopy, established a 1:1 stoichiometry of ion and ligand in the complex. FAB^+ mass spectra in an NBA matrix confirmed the purity of the complexes. From each enantiomer of LH_6 , only one isomer of the complex was formed. This was demonstrated by partial crystallization experiments; the CD spectra were unmodified for the liquid phase and for the solid phase.

Iron(III): The ferric complexes $\text{K}_3[\text{LFe}]$ were similarly prepared from each enantiomer of LH_6 through an exchange procedure involving ferric acetylacetonate.^[125] Titration of the ligands with the ferric salt, monitored by UV/Vis spectroscopy, established a 1:1 stoichiometry of ion and ligand in the complex. The FAB^- mass spectra corroborated the 1:1 stoichiometry. The crystalline material was not well-suited for X-ray structure determination. Partial crystallization experiments showed that only one isomer was formed (CD spectra unmodified for the liquid phase and for the solid phase).

Stereochemistry: It has been established that tripodate ligands force complexes to form in a *fac* arrangement.^[121] This is all the more true for LH_6 , which can be regarded as a tripodate ligand with its three "feet" connected by a second TREN (tris-(2-aminoethyl)amine) moiety. Only a *cis (fac)* arrangement of each set of three hydroxyl groups is possible (Figure 4), and the Δ and Λ isomers are therefore the only two that need be considered for a given ligand. Thus, the diastereoisomers Δ -(*aR,aR,aR*)- or Λ -(*aR,aR,aR*)- $[\text{LM}]^{3-}$ can be formed from (*aR,aR,aR*)- LH_6 , and Δ -(*aS,aS,aS*) or Λ -(*aS,aS,aS*) diastereoisomers from (*aS,aS,aS*)- LH_6 . Only one isomer has been detected in both cases, and the complexes obtained from the (*aR,aR,aR*) and (*aS,aS,aS*) enantiomers of LH_6 are also enantiomers. It appears that the chirality of the ligand leads to the formation of only one of the two possible diastereomeric metal complexes; in other words, the configuration (Δ or Λ) of the created chiral octahedral centre is entirely controlled by the chirality of the ligand.

The chirality of the metal centre was investigated by circular dichroism (CD) for the chromium and ferric complexes (see below).

Chromium complex: The electronic spectra in methanol (the same spectrum is obtained for the two enantiomers) are similar

to those of other Cr^{III} complexes with oxygen donor ligands. The main bands are at 558 nm ($\epsilon = 78.4 \text{ M}^{-1} \text{ cm}^{-1}$), 375 nm ($\epsilon = 9.26 \times 10^3 \text{ M}^{-1} \text{ cm}^{-1}$) and 236 nm ($\epsilon = 1.97 \times 10^5 \text{ M}^{-1} \text{ cm}^{-1}$) (Figure 2). The wavelength and the intensity of the well-resolved band at 558 nm are characteristic for the spin-allowed ${}^4A_{2g} \rightarrow {}^4T_{2g}$ d–d transition. The highest-energy ${}^4A_{2g} \rightarrow {}^4T_{1g}$ d–d transition is masked by the transitions of the ligand. The CD spectrum (visible region) of the complex from the (*aS,aS,aS*) ligand is shown in Figure 2 (the CD spectrum of

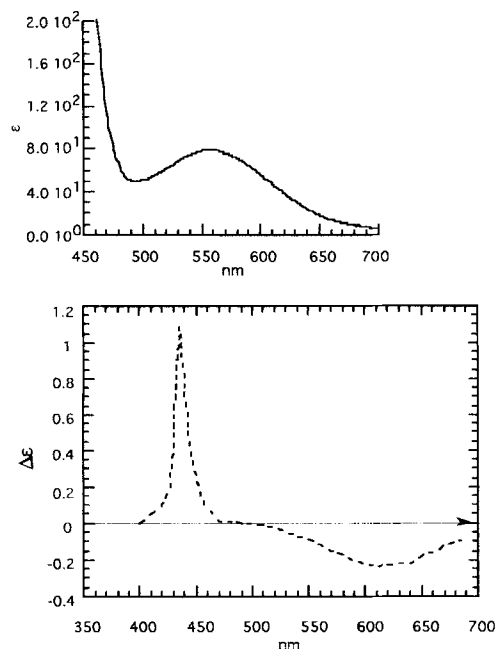


Figure 2. UV/Vis (top) and CD (bottom) spectra in methanol of the chromium(III) complex from the (*aS,aS,aS*) enantiomer of LH_6 .

the complex from the (*aR,aR,aR*) ligand is the mirror image of the CD spectrum in Figure 2). The CD bands in the visible region are at 610 nm ($\Delta\epsilon = -0.31 \text{ M}^{-1} \text{ cm}^{-1}$) and 430 nm ($\Delta\epsilon = +1.1 \text{ M}^{-1} \text{ cm}^{-1}$).

Assuming D_3 coordination point symmetry, the ${}^4A_{2g} \rightarrow {}^4T_{2g}$ octahedral transition factors into ${}^4A_2 \rightarrow {}^4A_1 + {}^4E$, which gives transitions of A_2 and E symmetry. The A_2 and low-energy E (designated E_a) transitions should be opposite in sign. A widely used empirical rule for d^3 complexes^[39] predicts a Δ absolute configuration when the low-energy transition with E symmetry is negative. The negative low-energy band at 650 nm allows us to assign the Δ configuration to the complex from the (*aS,aS,aS*) ligand. In the same way, the Λ configuration can be assigned to the complex from the (*aR,aR,aR*) ligand.

Ferric complex: The assignment of the absolute configuration of the metal centre is more challenging because it is not possible to use the forbidden d–d transition for circular dichroism studies. We therefore used the LMCT transition, which is sensitive to chirality. Since there are no spin-allowed d–d transitions for ferric high-spin d^5 systems, the absorption maximum in the UV/Vis spectrum observed at 483 nm ($\epsilon = 8660$) was assigned (D_3 symmetry) to the $e_{\pi 1} \rightarrow e^a$ LMCT transition (the lower ener-

gy $a_2 \rightarrow e^a$ LMCT transition was not observed). The CD spectrum of the ferric complex from the (*aS,aS,aS*) ligand exhibits a positive Cotton effect for the LMCT band at 420 nm ($\Delta\epsilon = 8.3 \text{ M}^{-1} \text{ cm}^{-1}$) (Figure 3). An opposite effect (and equal

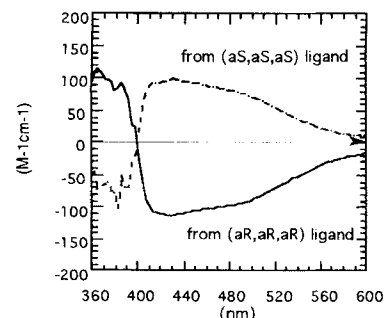


Figure 3. CD spectra of the enantiomeric iron(III) complexes in methanol.

in intensity) is observed for the ferric complex from the (*aR,aR,aR*) ligand; this confirms the enantiomeric relationship of the two complexes. The chiral tris(catecholate) ferric complexes of D_3 symmetry exhibit a positive effect for the $e_{\pi 1} \rightarrow e^a$ LMCT transition (from +1.5 to $3.8 \text{ M}^{-1} \text{ cm}^{-1}$) for the Δ isomers^[7, 11, 12, 40] (the Cotton effect is of reverse sign for the $a_2 \rightarrow e^a$ LMCT transition). These results are consistent with the assignments of Δ -(*aS,aS,aS*) and Λ -(*aR,aR,aR*) to the absolute configurations of our complexes; nevertheless, the correlation with the CD spectra of catecholates should be treated with caution.

Molecular modelling studies show that the Δ -(*aS,aS,aS*) complex has a lower energy than the Λ -(*aS,aS,aS*) complex. The former complex retains its original configuration during the minimization process, leading to a total energy of $8.9 \text{ kcal mol}^{-1}$; it adopts a structure that is substantially flattened along the C_3 principal axis (Figure 4). With the Λ -(*aS,aS,aS*) complex, the minimization process without constraints leads to configurational inversion of the metal centre and formation of the same conformer as for the Δ -(*aS,aS,aS*) complex. Minimized with constraints on the iron and oxygen atoms, the Λ -(*aS,aS,aS*) complex adopts a structure which, after elimination of constraints, retains its configuration upon minimization with an energy of $116.6 \text{ kcal mol}^{-1}$ (Figure 4).

In a further step, the iron atom was removed from the final structures obtained above to give the two conformers of the ligand preorganized for Δ and Λ complexation. The lower-energy conformer ($\Delta E = 107.7 \text{ kcal mol}^{-1}$) corresponds to the Δ -(*aS,aS,aS*) configuration. The noticeable energy difference between the two conformers arises from van der Waals terms and from the stacking of the aromatic rings, which is only possible for the flattened Δ -(*aS,aS,aS*) isomer; the electrostatic interactions are not stabilizing. It should be emphasized that it is the trend in the energy values and not their absolute magnitude that is of importance. A similar preference for the Δ -(*aS,aS,aS*) isomer has been calculated by a similar method for the tungsten(VI) complex of binaphtholate.^[15] The calculations strongly support the assignment of the Δ -(*aS,aS,aS*) configuration to the unique isomer obtained with the (*aS,aS,aS*) isomer of LH_6 .

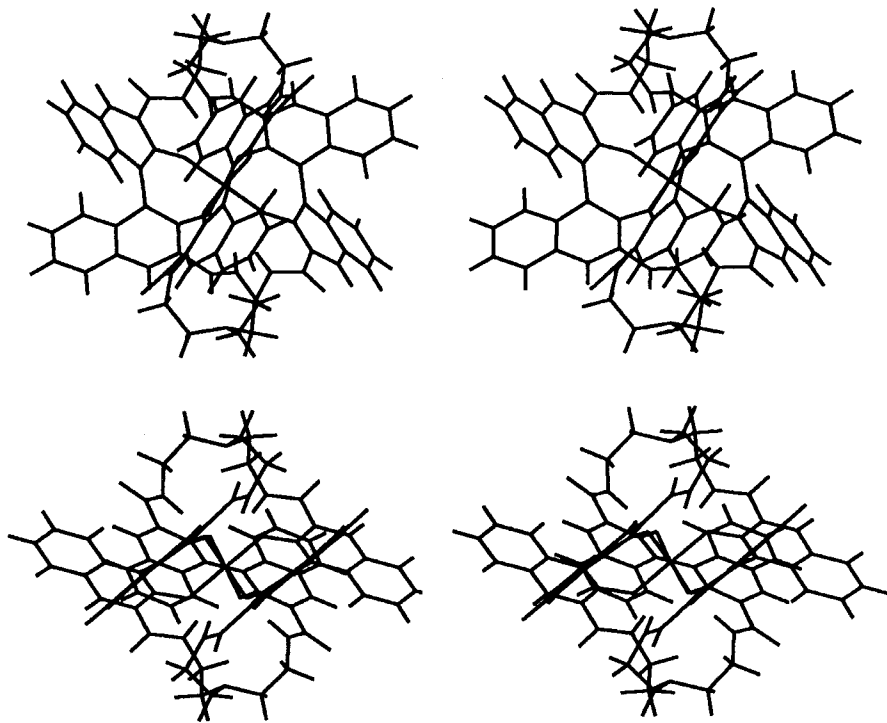


Figure 4. Stereoviews of *A*-(*a,S,a,S,a,S*) (top) and *A*-(*a,S,a,S,a,S*) (bottom) $[LFe]^{3-}$ complexes (generated by molecular modelling).

Conclusion

We have presented the first example of an optically active macrobicyclic ligand bearing six convergent hydroxyl groups and examined its ability to stereospecifically control the chirality in octahedral complexation. The putative absolute configurations assigned to the iron(III) complexes of **LH₆** are in agreement with the assignments established for the chromic complexes. The two metals have the same charge and similar ionic radii in six coordinate complexes, and the chiral control upon complexation by **LH₆** is undoubtedly the same. The configuration assignments have also been corroborated by molecular modelling studies.

Experimental Section

Materials and Equipment: Solvents were purified by standard techniques. The amine TREN was distilled from sodium. All other compounds were of reagent grade and were not further purified. Spectra were collected on custom-built 200 MHz or 250 MHz FT Brucker (¹H and ¹³C NMR), Nicolet Impact 400 (FT-IR), Kontron Uvikon 930 (UV/Vis) and Nermag R1010C (mass spectra) spectrometers. The multiplicity in ¹³C NMR was determined by DEPT techniques. CD spectra were recorded on a Jobin Yvon CD6 dichrograph. Rotation angles were obtained with a Perkin-Elmer 341 polarimeter. Molecular modelling calculations were performed using Insight/Discover package of Biosym on an IBM RS 6000 42-T station; a force-field ESFF was used. For ligand syntheses, see Figure 1.

2c: ¹H NMR (250 MHz, CDCl₃): δ = 3.46 (s, 6H, OCH₃); 7.12 (d, 2H, *J* = 8.7 Hz, ArH); 7.40–7.55 (m, 4H, ArH); 8.07 (d, 2H, *J* = 8.7 Hz, ArH); 8.87 (s, 2H, H₄); ¹³C NMR (75 MHz, CDCl₃): δ = 62.3 (OCH₃); 125.4 (CH); 126.2 (C_{quat}); 126.4 (CH); 127.3 (C_{quat}); 129.2 (C_{quat}); 130.0 (CH); 130.3 (CH); 136.5 (C_{quat}); 137.5 (CH); 153.7 (C=O); 164.6 (C=O); IR (NaCl, cm⁻¹): ν̃ = 1779 (C=O).

2f: The bis(2-mercaptothiazolide) was prepared in quantitative yield on a 11 mmol scale by adaptation of the published procedure^[23] and used without

further purification. Yellow solid, m.p. 153–155 °C. ¹H NMR (200 MHz, CDCl₃): δ = 3.21–3.43 (m, 10H, CH₂, OCH₃); 4.49–4.73 (m, 4H, CH₂); 7.13 (d, 2H, *J* = 7.8 Hz, ArH); 7.25 (t, 2H, ArH); 7.34 (t, 2H, ArH); 7.80 (d, 2H, *J* = 7.8 Hz, ArH); 7.94 (s, 2H, H₄); ¹³C NMR (50 MHz, CDCl₃): δ = 29.1 and 55.7 (CH₂); 61.7 (OCH₃); 123.3 (C_{quat}); 125.4 (CH); 125.8 (CH); 128.1 (C_{quat}); 128.2 (CH); 128.7 (CH); 129.3 (C_{quat}); 129.7 (C_{quat}); 130.5 (CH); 135.5 (C_{quat}); 152.5 (C=O); 168.3 (C=O); IR (NaCl, cm⁻¹): ν̃ = 1676 (C=O); MS (FAB⁺, NBA matrix): *m/z* = 605 [*M* + H⁺], 573, 486.

3: Under high-dilution conditions, TREN (305 μL, 2.0 mmol in 120 mL CH₂Cl₂) was slowly added (3 d), under nitrogen, to a solution of **2f** (5.8 g; 11 mmol in 1 L CH₂Cl₂). The yellow solid obtained by evaporation of the solvent was purified by column chromatography (SiO₂; 0 to 5% gradient of methanol in CH₂Cl₂); TLC, *R_f* = 0.7, CH₂Cl₂/CH₃OH : 9/1. Yellow solid, 1.5 g; 0.93 mmol; m.p. 215–220 °C. (*aR,aR,aR*)-**3**: [*α*]_D²⁵ = +11 (*c* = 0.38, CH₂Cl₂). (*aS,aS,aS*)-**3**: [*α*]_D²⁵ = -12 (*c* = 0.37, CH₂Cl₂). ¹H NMR (200 MHz, CDCl₃): δ = 2.83–2.90 (6H, m, CH₂); 3.27 (9H, s, OCH₃); 3.29–3.38 (15H, m, CH₂, OCH₃); 3.57–3.60 (6H, m, CH₂); 4.55–4.69 (6H, m, CH₂); 7.01 (3H, d, *J* = 8.3 Hz, ArH); 7.11–7.39 (15H, m, ArH); 7.85 (6H, d, *J* = 8.3 Hz, ArH); 7.97 (3H, s, ArH); 8.12–8.15 (3H, m, NH); 8.65 (3H, s, ArH). ¹³C NMR (50 MHz, CDCl₃): δ = 29.0 (CH₂); 38.0 (CH₂); 53.4 (CH₂); 55.6 (CH₂); 61.6 (OCH₃); 61.9 (OCH₃); 123.5 (C_{quat}); 125.1 (C_{quat}); 125.4 (CH); 125.6 (2 CH); 126.0 (C_{quat}); 128.1 (CH); 128.3 (CH); 128.8 (CH); 129.3 (CH); 129.4, (C_{quat}) 129.8 (C_{quat}); 130.0 (CH); 130.2 (CH); 133.5 (CH); 135.1 (C_{quat}); 135.2 (C_{quat}); 152.5 (C=O); 153.4 (C=O); 165.5 (C=O); 166.1 (C=O). IR (NaCl, cm⁻¹): ν̃ = 3398 (NH), 1650 (C=O). MS (FAB⁺, NBA matrix): *m/z* = 1604 [*M* + H⁺], 1393, 1252, 1088, 1033, 999, 529. Anal. calcd (found) for C₈₇H₇₅O₁₃N₇S₆·1.5 CH₂Cl₂: C 61.48 (61.54); H 4.55 (4.87); N 5.67 (6.05); S 11.11 (11.69).

4a: Under high-dilution conditions, TREN (85 μL, 0.57 mmol in 130 mL CHCl₃) and **3** (900 mg., 0.56 mmol in 150 mL CHCl₃) were simultaneously and slowly (4 d) added, under nitrogen, to CHCl₃ (600 mL) at reflux. After concentration of the solution to a volume of 300 mL, the mixture was washed with brine and then dried on Na₂SO₄. The product was purified by chromatography (SiO₂; 0 to 5% gradient of methanol in CH₂Cl₂). Whitish solid (300 mg., 0.22 mmol); m.p. > 250 °C. (*aR,aR,aR*)-**4a**: [*α*]_D²⁵ = +60° (*c* = 0.32 in CH₂Cl₂). *R_f* (SiO₂) = 0.5, CH₂Cl₂/CH₃OH = 9/1. ¹H NMR (200 MHz, CDCl₃): δ = 2.95 (s, 30H, NCH₂, OCH₃); 3.49–3.59 (m, 6H, NHCH₂); 3.74–3.86 (m, 6H, NHCH₂); 6.88 (d, 6H, *J* = 8.4 Hz, H₅); 7.21 (t, 6H, *J* = 8.4 Hz, H₆); 7.37 (t, 6H, *J* = 8.2 Hz, H₇); 7.91 (d, 6H, *J* = 8.2 Hz, H₈); 8.09–8.14 (m, 6H, NH); 8.72 (s, 6H, H₄); ¹³C NMR (50 MHz, CDCl₃): δ = 38.1 (NHCH₂); 53.1 (NCH₂); 61.5 (OCH₃); 124.8 (C_{quat}); 125.0 (C₅) 125.3 (C_{quat}); 125.8 (C₇); 128.1 (C₆); 129.3 (C₈); 130.0 (C_{quat}); 133.6 (C₄); 134.8 (C_{quat}); 153.2 (C=O); 164.8 (C=O); IR (NaCl, cm⁻¹): ν̃ = 3386 (NH), 1654 (C=O); MS (FAB⁺, NBA matrix): *m/z* = 1392 [*M* + H⁺], 978. Anal. calcd (found) for C₈₄H₇₈N₈O₁₂·1 CH₂Cl₂·1 CH₃OH: C 68.50 (68.29); H 5.62 (5.59); N 7.49 (7.82).

4b: Macrobicycle **4a** (570 mg, 0.41 mmol), in 30 mL of CH₂Cl₂ at 0 °C, was treated under nitrogen with a solution of BBr₃ in CH₂Cl₂ (1 M, 4.1 mL). The mixture was stirred at 25 °C for 15 h and then treated with 10 mL of water and stirred for 1 h. The product was precipitated by adding 100 mL of water and 200 mL of chloroform (pH of the aqueous phase 1.5). The solid was filtered. The product was purified by dissolution in 4 M NaOH, washing with CH₂Cl₂ and precipitation by addition of 4 N HBr. The yellowish solid was dried under vacuum (497 mg, 0.38 mmol). (*aR,aR,aR*)-**4b**: [*α*]_D²⁵ = 228 (*c* = 0.11 in methanol); (*aS,aS,aS*)-**4b**: [*α*]_D²⁵ = -231 (*c* = 0.13 in methanol). ¹H NMR (200 MHz, NaOD–D₂O): δ = 2.84–3.08 (m, 12H, CH₂); 3.22–3.30 (m, 6H, CH₂); 3.93–4.00 (m, 6H, CH₂); 6.68–6.73 (m, 6H, ArH); 6.98–7.02 (m,

12H, *ArH*); 7.74–7.79 (m, 6H, *ArH*); 8.44 (s, 6H, H_2); ^{13}C NMR (50 MHz, $\text{NaOD}-\text{D}_2\text{O}$): δ = 36.7 (NHCH_2); 54.6 (NCH_2); 120.4 (CH); 122.2 (C_{quat}); 123.6 (CH); 124.1 (C_{quat}); 127.1 (CH); 129.3 (CH); 129.4 (CH); 137.1 (C_{quat}); 163.5 (C=O); 170.8 (C=O); IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3382, 3259, 3035, 1649; MS (FAB $^+$, NBA matrix): m/z = 1307 [$\text{LH}_6 + \text{H}^+$], 880. Anal. calcd (found) for $\text{C}_{78}\text{H}_{66}\text{N}_8\text{O}_{12} \cdot 2\text{HBr} \cdot 8\text{H}_2\text{O}$: C 58.07 (57.91); H 5.25 (5.16); N 6.95 (6.77).

Gallium complexes: Alcoholic KOH (0.5 M, 390 μL) and $\text{Ga}(\text{acac})_3$ (14.6 mg, 0.039 mmol) were added to of (*aR,aR,aR*)- LH_6 (51 mg, 0.039 mmol) in methanol (15 mL) under argon. The yellow solution was stirred for 24 h and the solvent then removed. The complex was purified on a Sephadex G25 column with methanol elution. MS (FAB $^+$, NBA matrix): m/z = 1487 [LHK_3Ga], 1449 [$\text{LH}_2\text{K}_2\text{Ga}$], 1411 [LH_3KGa]. [α] $_{589}^{21}$ = +213; [α] $_{578}^{21}$ = +222 (c = 0.34 in methanol) [(*aS,aS,aS*) enantiomer: [α] $_{589}^{21}$ = -211; [α] $_{578}^{21}$ = -221]. ^1H NMR (300 MHz, CD_3OD): δ = 2.05 (m, 12H, CH_2); 2.43 (m, 12H, CH_2); 6.42 (d, 6H, J = 8.3 Hz, *ArH*); 6.75 (m, 6H, *ArH*); 6.90 (m, 6H, *ArH*); 7.60 (d, 6H, J = 8.3 Hz, *ArH*); 7.77 (s, 6H, H_4).

Chromium complexes: LCrK_3 complexes were obtained by a similar procedure using $\text{Cr}(\text{acac})_3$. After purification on a Sephadex G25 column (methanol) the complexes were crystallized by slow diffusion of diethyl ether. Yield: 94%. UV/Vis (CH_3OH , nm, $\text{m}^{-1}\text{cm}^{-1}$): 558 (ϵ = 78.4), 375 (ϵ = 9.26 $\times 10^3$), 236 (ϵ = 1.97×10^5). MS (FAB $^-$, NBA matrix): m/z = 1392 [LHKCr], 1354 [LH_2Cr], 1381 [LH_3K_2], 1343 [LH_4K], 1305 [LH_5]. Anal. calcd (found) for $\text{C}_{78}\text{H}_{60}\text{O}_{12}\text{N}_8\text{CrK}_3 \cdot 5\text{H}_2\text{O}$: C 60.03 (59.84); H 4.52 (4.99); N 7.18 (7.22); Cr 3.33 (3.56).

Iron complexes: LFeK_3 and LFeNa_3 complexes were similarly obtained, using $\text{Fe}(\text{acac})_3$; Yield: 85–95%. UV/Vis (CH_3OH , nm, $\text{m}^{-1}\text{cm}^{-1}$): 483 (ϵ = 8.66×10^3), 377 (ϵ = 8.86×10^3), 236 (ϵ = 1.64×10^5). MS (FAB $^-$, NBA matrix): m/z = 1396 [LHKFe], 1358 [LH_2Fe]. (FAB $^+$, Thioglycerol matrix): m/z = 1383 [LH_3NaFe], 1360 [LH_4Fe], 1307 [LH_5]. HRMS (FAB $^+$, Thioglycerol matrix): calcd for $\text{C}_{78}\text{H}_{64}\text{O}_{12}\text{N}_8\text{Fe}$: 1360.3993; found 1360.3899. Anal. calcd (found) for $\text{C}_{78}\text{H}_{60}\text{O}_{12}\text{N}_8\text{FeNa}_3 \cdot 6\text{H}_2\text{O}$: C 61.04 (59.94); H 4.43 (4.74); N 7.31 (7.11); Fe 3.65 (3.65).

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