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Synthesis, characterization, and fluorescence behavior of four novel macrocyclic emissive ligands containing a flexible 8-hydroxyquinoline unit

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ABSTRACT

Four emissive macrocyclic ligands mono-substituted with an 8-hydroxyquinoline pendant arm are presented. The new compounds have been used for metal-ion detection, which results from the competition between PET (photo-induced electron transfer) and PPT (photo-induced proton transfer) mechanisms. Solid metal complexes with divalent Cu(II), Zn(II), and Cd(II), and trivalent metal ions Al(III) and Cr(III) have been also synthesized and characterized. The compounds have been isolated as mononuclear or dinuclear (Cu(II)) complexes, confirming the stoichiometry observed in solution.

1. Introduction

The development of compounds that selectively respond to specific metal ions and thus can be used as ion sensors is an area of growing interest.[1] Emphasis has been placed on the development of compounds that can detect the presence of specific metal ions through guest-modulated effects, e.g., changes in redox potentials,[2] UV–vis absorption spectra,[3] or fluorescence spectra[1] as a result of the interaction between the sensor and the target ion. Particular attention has been paid to fluorescence chemosensors, since fluorescence modulation allows the detection of the target ions at very low concentrations;[1b] moreover, fluorescent sensors offer several distinct advantages such as selectivity, time response, and spatial resolution.

8-Hydroxyquinoline (8-HQ) and derived compounds are known to be the best chelating agents after EDTA and its derivatives, due to their guest-modulated chromogenic and fluorescent behavior. Accordingly, they have been used in chromatography,[4] for the detection of metal ions,[5] in the preparation of organic light emitting diode devices,[6] in electrochemiluminiscence,[7] etc. 8-HQ forms stable five-membered chelate rings with metal centers, and very stable complexes of the type $M(HQ)^+$, $M(HQ)_2$ or $M(HQ)_3$ with divalent transition and post-transition metal ions.[8] Macrocycles containing quinoline side arms have been employed as analytical reagents in absorption spectrometry, fluorometry, solvent extraction, and chromatography.[9] The potential use of some of these compounds as pesticides has also been explored.[10]

A number of azacrown ethers containing 8-hydroxyquinoline (**I**,[11] **II**,[5c] **III**[12]), 5-chloro-8-hydroxyquinoline (**IV**[5c]), and 8-hydroxy-5-*N*,*N*-dimethylaminosulfonylquinoline (**V**[12]) have been reported (see Scheme 1). Prodi[5a] and co-workers reported systems **VI.a** and **VI.b** for the recognition of Mg(II) and Hg(II), respectively. In these complexes, the pK_a values for the hydroxyl groups of the 8-HQ moieties were low enough to become fluorescent in slightly acidic solutions.[5c,10,13] Addition of Mg(II) to **VI.a** or Hg(II) to **VI.b** in neutral MeOH–H_2O (1:1) solutions results in the strong enhancement of the luminescence bands at 520 nm and 476 nm, respectively. All these ligands have been designed to detect transition and post-transition

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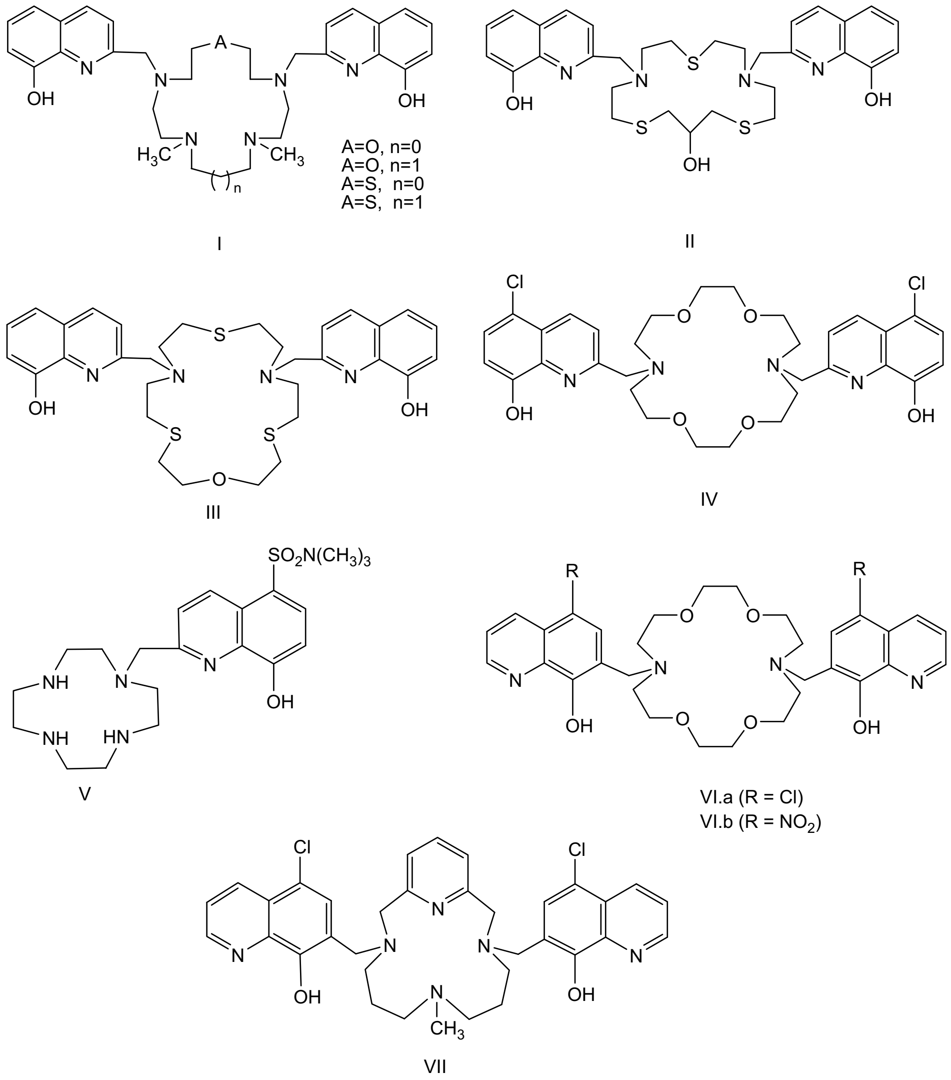


Scheme 1. Macrocyclic ligands with quinoline pendant arms reported for Pb^{2+}(**I**, **II**, **III**, **VII**), Co^{2+}(**I**), Ni^{2+}(**I**), Cu^{2+}(**I**, **II**), Zn^{2+}(**I**, **II**, **III**, **V**, **VII**), Cd^{2+}(**I**, **II**, **III**, **VII**), Hg^{2+}(**VI**), K^{+}(**IV.b**), Mg^{2+}(**VI.a**), and Ba^{2+}(**IV**).

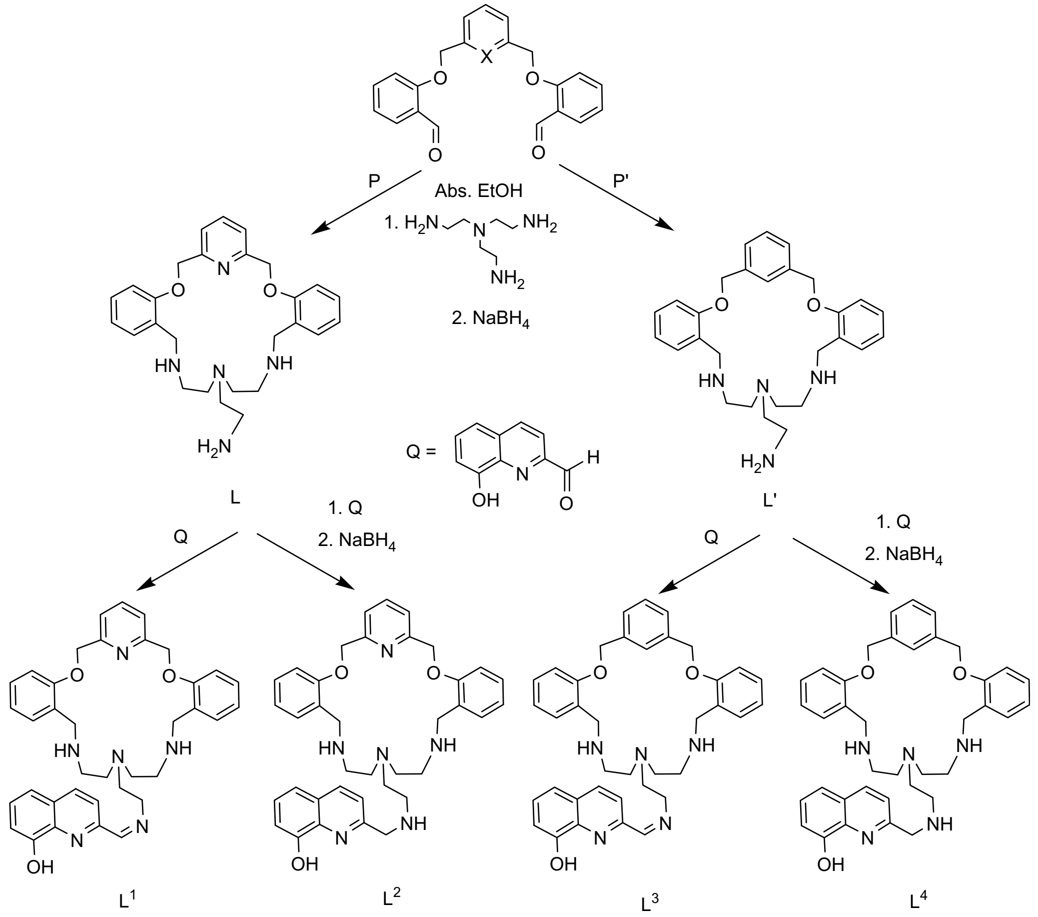
metal ions through guest associated modulation of the absorption and fluorescence spectra of the ligands.[14] Less attention has been paid to macrocycles containing a pyridine head. Delgado and co-workers have published a small tetraaza donor macrocyclic system (**VII**) substituted with two 5-chloro-8-hydroxyquinoline units; its interaction with Cu(II), Zn(II), Cd(II), and Pb(II) were studied, but no fluorescence data were reported.[15]

The biological and biomedical significance of Cu(II), Zn(II), Cd(II), Al(III) or Cr(III) makes the detection of these metal ions crucial.[16] The design and synthesis of fluorescence chemosensors for Cu(II) have become a very active research area, due to the adverse effects of this metal ion when present in large concentration.[17–19] Elements from group 12 (Zn(II), Cd(II), and Hg(II)) are also attracting considerable attention, due to the biological importance of Zn(II) and the toxicological effects of Cd(II) and Hg(II).[20] Zn(II) acts as a catalytic or co-catalytic factor in the active sites of more than 300 enzymes and, due to their chemical similarities, Zn(II) can be easily substituted by Cd(II). Their d^{10} electron configurations make Zn(II), Cd(II), and Hg(II) spectroscopically silent; thus, research is now focused on the design of fluorescence chemosensors capable of determining their concentration in solution, especially in living cells.[21]

Al(III) is widely used in water treatment, as food additive and in medicine; Cr(III) is used in harden and stainless steel, in alloys to prevent corrosion, and as inorganic catalyst. Many analytical (sample destructive) methods are used for the analysis of both metal ions; however, fewer examples of the use of fluorescence chemosensors (a non-destructive technique) have been reported. Most of the research has focused on chemosensors for aluminum,[22] but less attention has been paid to the detection of chromium.[23]

As an extension of our work on the synthesis of macrocyclic receptors possessing pyridine units[24] for metal-ion chelation, herein we report the synthesis and characterization of four new emissive macrocycles, L^1–L^4 (see Scheme 2). The starting material for L^1 and L^2 was the N$_5$O$_2$-donor ligand L, containing a free amine pendant arm.[25] The precursor to L^3 and L^4 (L′) was obtained via Schiff-base condensation of 2,2-(1,3-phenylenebis(methyleneoxy))dibenzaldehyde, and tris(2-aminoethyl)amine (tren-amine), followed by an in situ reductive demetalation reaction with NaBH$_4$. Condensation of an 8-hydroxyquinoline unit with the free amine pendant arm yielded the macrocycles L^1–L^4. The new ligands have been fully characterized by the usual techniques.

The protonation behavior and sensing capability toward divalent Cu(II), Zn(II), and Cd(II), and trivalent Al(III) and Cr(III) metal ions have been studied by UV–vis and fluorescent emission spectroscopy, and by MALDI-TOF-MS spectrometry. In order to compare with the results obtained in solution, some solid metal complexes with the same metal ions were synthesized and characterized; these results are also discussed.



Scheme 2. Schematic synthetic route for ligands L^1–L^4 in absolute ethanol.

2. Results and discussion

2.1. Synthesis and characterization of the free ligands L^1–L^4 and metal complexes

2.1.1. *Schiff-base macrocycles L^1 and L^3*

We have previously reported the synthesis of the macrocycle L[25] obtained by a template cyclocondensation of tren-amine with 2,6-bis(2-formylphenoxymethyl)pyridine (P).[26] Macrocyclic ligand L′ was synthesized by the same template method, via cyclocondensation of tren-amine with 2,2-(1,3-phenylenebis(methyleneoxy))dibenzaldehyde (P′) in the presence of $Ba(ClO_4)_2\cdot 2H_2O$, followed by an in situ demetalation reaction with $NaBH_4$.

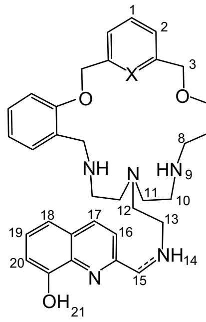
Subsequent condensation of L and L′ with 8-hydroxyquinoline-2-carbaldehyde using a one-step procedure, yielded L^1 and L^3; both ligands were isolated as air-stable orange solids, ca. 73.3% and 62.3% yield, respectively. The infrared spectra (KBr discs) show bands at 1642 (L^1) and 1641 (L^3) cm^{-1}, corresponding to the imine bond, and no peaks attributable to unreacted amine or carbonyl groups were present. The absorption bands corresponding to the ν(C=C) and ν(C=N) vibrations of the pyridine groups appear in the expected positions, 1597, 1453 cm^{-1}, and 1600, 1453 cm^{-1}, respectively. The MALDI-TOF-MS spectrum of L^1 shows a parent peak at *m*/*z* 617, corresponding to the protonated form of the ligand $[L^1H]^+$. For L^3, the base peak in the FAB mass spectrum and in the MALDI-TOF-MS was at *m*/*z* 616, attributable to the protonated form $[L^3H]^+$. Elemental analysis data confirm that both Schiff-base ligands have been isolated. L^1 and L^3 were studied by ^1H NMR in $CDCl_3$; the spectra confirm the integrity of the ligands in solution (Table 1). Both ^1H NMR spectra show a peak at ca. 8.2 ppm, corresponding to the imine protons, and no signals corresponding to the primary amine or aldehyde protons are present.

2.1.2. *Synthesis and characterization of the amine macrocycles L^2 and L^4*

Following a one-step procedure involving the reduction of L^1 and L^3 with $NaBH_4$, macrocyclic ligands L^2 and L^4 were isolated as air-stable yellow solids, ca. 45.3 and 59.4% yield, respectively. The absence of a band at ca. 1640 cm^{-1} in the infrared spectra (KBr disc) confirms the reduction of the imine group. The absorption bands

Table 1
^1H NMR shifts (ppm) for L^1, L^2, L^3, and L^4 in CD_3Cl solutions (see Scheme 3 for labeling)

	L^1	L^2	L^3	L^4
$H_{1,2}$; H_{4-7}; H_{16-20}	7.9–6.7 (m), 16H	7.8–6.8 (m), 16H	8.1–6.7 (m), 17H	8.0–6.5 (m), 17H
H_3	4.9 (s), 4H	5.3 (s), 4H	5.1 (s), 4H	5.0 (s), 4H
H_8	3.7 (m), 4H	3.7–3.6 (m), 4H	3.8 (s), 4H	3.7 (s), 4H
$H_{10,13}$	3.4 (m), 6H	3.6–3.5 (m), 6H	2.9–2.1 (m), 6H	2.6–2.1 (m), 6H
$H_{11,12}$	2.5 (m), 6H	2.8–2.3 (m), 6H	2.9–2.1 (m), 6H	2.6–2.1 (m), 6H
H_{15}	8.2 (s), 1H	4.0 (s), 2H	8.4 (s), 1H	3.4 (s), 2H
H_{21}	5.6 (s), 1H	5.9 (s), 1H	4.5 (s), 1H	4.0 (s), 1H



Scheme 3. Ligands L^1–L^4 with numbered atoms.

corresponding to ν(C=C) and ν(C=N) vibrations of the pyridine groups appear at 1597, 1451 cm^{-1}, and 1600, 1453 cm^{-1}, respectively.

The ESI mass spectrum of L^2 shows a peak at 619 amu attributable to $[L^2H]^+$. For L^4, the highest peak in the FAB mass spectrum is at 618 amu, attributable to $[L^4H]^+$. Both peaks were observed also in the MALDI-TOF-MS spectra. Ligands L^2 and L^4 were studied by ^1H NMR in $CDCl_3$; the NMR spectra confirm the integrity of the ligands in solution. The absence of a peak at ca. 8.2 ppm in the ^1H NMR spectra confirms the reduction of the imine protons (see Table 1).

2.1.3. *Synthesis and characterization of the metal complexes*

The coordination ability of ligands L^1 to L^4 toward hydrated transition and post-transition metal salts was studied in solution and in solid state. Reaction of L^1 and L^3 with Al(III) chloride in a 1:1 metal–ligand ratio in ethanol led to two compounds of formula $[AlL^1](Cl)_3{\cdot}5H_2O$ and $[AlL^3](Cl)_3{\cdot}6H_2O$ in good yields, 55.3 and 59.2%, respectively. The complexes were characterized by elemental analysis, IR, and ESI MS or FABMS spectra. The reaction was attempted also with the Zn(II) and Cr(III) salts, but only the aluminum products gave satisfactory microanalytical results. The ESI mass spectrum of $[AlL^1](Cl)_3{\cdot}5H_2O$ displays peaks corresponding to the $[M_2L^1]^+$, $[M_2L^1X_z]^+$ (z=3 and 5) fragments, and the FAB mass spectrum of $[AlL^3](Cl)_3{\cdot}6H_2O$ displays a peak corresponding to the fragment $[M_3L^3X_2]^+$, confirming the formation of both complexes; the higher nuclearity suggests some complex formation in the gas phase. The IR spectra of the complexes were recorded as KBr discs. In both cases, the band due to the imine bond is shifted to lower wave numbers when compared to its position in the spectrum of the free ligand, and the ν(C=C) and ν(C=N) stretching modes of the pyridine rings appear at higher wave numbers than those on the spectrum of the free ligand. Both effects suggest that the N_{py} atom of the quinoline pendant group could be involved in the coordination to the metal ion.[27] The broad absorption band in the region 3450–3380 cm^{-1} present is probably due to the existence of lattice and/or coordinated water in the molecule, and make it difficult to see the bands due to the ν(O–H) and ν(N–H) stretching vibrations, which would appear in this region.

Ligands L^2 and L^4 reacted easily with transition and post-transition ions producing air-stable solid complexes, which were characterized by elemental analysis, IR, ESI MS (L^2 complexes), and FABMS (L^4 complexes). The elemental analysis data indicate the formation of mononuclear complexes with empirical formulas $CdL^2(ClO_4)_2{\cdot}xC_2H_6O$, $ZnL^2(NO_3)_2{\cdot}xH_2O$, $CrL^2(NO_3)_3{\cdot}xH_2O$, $ML^4(NO_3)_2{\cdot}xH_2O$ (M=Zn, Cd), $CrL^4(NO_3)_3{\cdot}xH_2O$, $AlL^2(Cl)_3{\cdot}xH_2O$, $AlL^4(Cl)_3{\cdot}xH_2O$ and the dinuclear complexes $Cu_2L^2(NO_3)_4{\cdot}xC_2H_6O$ and $Cu_2L^4(NO_3)_4{\cdot}xH_2O$. The ESI mass spectra for L^2 complexes display peaks corresponding to the $[ML^2]^+$, $[ML^2X]^+$, $[ML^2X_2]^+$, $[M_2L^2X]^+$, $[M_2L^2X_2]^+$ fragments, and the FAB mass spectra for L^4 complexes display a peak attributable to the $[ML^4]^+$ fragment, confirming the formation of the complexes in both cases. The IR spectra of all the complexes were recorded as KBr discs and all show similar features. As in the free ligands there are split bands associated with ν(C=C) and ν(C=N) vibrations of the pyridine rings, which have undergone a shift toward higher wave numbers on complexation.[27] As in the complexes with L^1 and L^3, the presence of an intense broad band at ca. 3400 cm^{-1} makes it difficult to see the bands corresponding to the ν(O–H) and ν(N–H), which would appear in this region. The spectra of the nitrate complexes show a band at 1384 cm^{-1} associated with the presence of ionic nitrate. For $CdL^2(ClO_4)_2{\cdot}2C_2H_6O$, bands attributable to the asymmetric Cl–O stretching mode at ca. 1088 cm^{-1} (ν_3) and the asymmetric Cl–O bending mode (ν_4) at ca. 627 cm^{-1} can be observed. The highest energy band shows considerable splitting, with three maxima at ca. 1050, 1088, and 1121 cm^{-1}, suggesting some interaction of at least one of the ClO_4^- anions with the metal.[28]

2.2. Spectrophotometric and spectrometric studies

2.2.1. *Spectrophotometric studies: UV–vis and Fluorescence emission spectroscopy*

Ligands L1–L4 have a low solubility in water. In addition in water–absolute ethanol solutions (50:50, v/v) those ligands precipitated. For the aforementioned reasons all the spectroscopic studies have been done in absolute ethanol.

The absorption spectra of ligands L^1, L^2, L^3 and L^4 in absolute ethanol solution show one band centered at 248–250 nm, attributable to the π–π* transitions in the ligand. The band presents a long tail, up to 400 nm. The spectrum is independent of the acidic conditions, and addition of up to 5 equiv of HBF_4 does not affect the absorption band; this result is in agreement with other polyamine macrocyclic ligands containing aromatic units. The spectra for L^1 and L^2 show an emission band centered at 524 nm. The intensity of this band increases with the addition of protons, achieving a plateau when 4 equiv of HBF_4 is added. The spectra for L^3 and L^4 (without the pyridine head) show the emission band centered at 514 nm; addition of acid results in an increase of this band, also achieving a plateau with the addition of 4 equiv. These results suggest that the pyridine ring present in the macrocyclic skeleton of L^1 and L^2 may not be protonated on these conditions. Addition of a tetrabutylammonium hydroxide solution to an ethanolic solution of ligands L^1 and L^3 reduced the intensity of the emission in ca. 50%; 2 equiv of base is enough to achieve a plateau. A generic spectrophotometric characterization is shown in Figure 1.

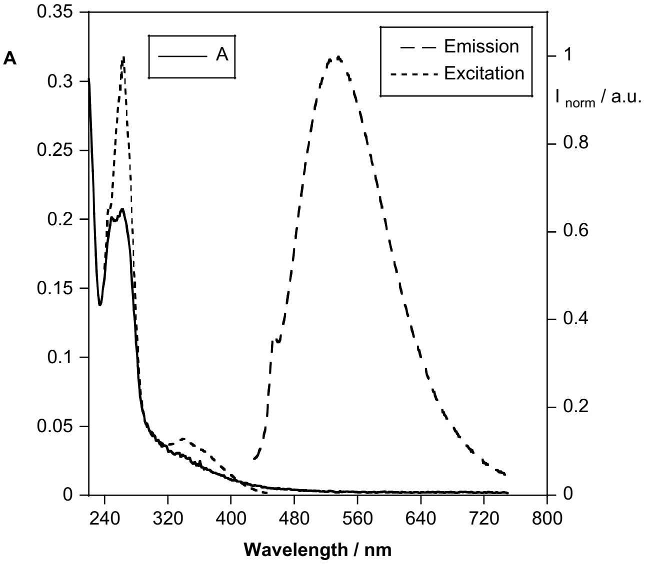


Figure 1. Absorption, emission, and excitation spectra of ligand L^2 in absolute ethanol solution ($[L^2]=1.0\times10^{-5}$ M, λ_{exc}=400 nm, λ_{em}=530 nm).

Table 2
Optical data for the metal complexes of L^1, L^2, L^3 and L^4 in absolute ethanol solutions (λ_{exc}=400 nm; 25 °C)

Metal complex	λ_{max} (nm); log ε	λ_{em} (nm)
$AlL^1(Cl)_3 \cdot 5H_2O$	269; 4.46	546
$AlL^2(Cl)_3 \cdot 2H_2O$	261; 4.20	543
$AlL^3(Cl)_3 \cdot 6H_2O$	260; 4.19	545
$AlL^4(Cl)_3 \cdot 5H_2O$	262; 4.77	545
$CrL^2(NO_3)_3 \cdot 6H_2O$	255; 4.61	535
$CrL^4(NO_3)_3 \cdot 2H_2O$	251; 4.61	536
$Cu_2L^2(NO_3)_4 \cdot 3C_2H_6O$	266; 4.80	—
$Cu_2L^4(NO_3)_4 \cdot 3H_2O$	275; 4.35	—
$ZnL^2(NO_3)_2 \cdot 6H_2O$	265; 4.41	573
$ZnL^4(NO_3)_2 \cdot 3H_2O$	273; 4.21	565
$CdL^2(ClO_4)_2 \cdot 2C_2H_6O$	260; 4.56	508
$CdL^4(NO_3)_2 \cdot 3H_2O$	248; 4.17 269; 4.18 300; 3.76	505

The photophysical properties of compounds including 8-HQ as chromophore have been studied in detail.[29] In their fluorescence spectra, a non-structured band centered between 360 and 460 nm, strongly dependent on the solvent, was observed.[29] In our case, the emission band is red-shifted in at least 60 nm, which could facilitate their potential applications in biological systems. The emissive compounds could be irradiated in the presence of bio-molecules without any damage to the chromophores present in aminoacids, peptides, proteins, DNA, etc.

The relative fluorescence quantum yields of ligands L^1 to L^4 were determined using a 0.1 M solution of quinine sulfate in 0.5 M H_2SO_4 as standard (ϕ=0.546); the values obtained were always below 1×10^{-3}.[30,29c] The fluorescence of chemosensors with 8-HQ units is weak due to the competition between the intermolecular photo-induced proton transfer (PPT) from the hydroxyl group of the molecule, and the photo-induced electron transfer (PET) from the amines.[5a] Moreover, in proton–donor solvents, a PPT process involving solvent molecules opens another way to further deactivate fluorescence. Consequently, both PPT and PET processes can quench the fluorescence emission in substituted quinolines. The quenching effect observed after the addition of tetrabutylammonium hydroxide is consistent with this explanation; in this case, the PET mechanism is stronger than the PPT.

The sensing behavior of the compound toward Zn(II), Cd(II), Cu(II), Al(III), and Cr(III) has been studied in solution, using absolute ethanol as the solvent. For comparison purposes, all the synthesized metal complexes have been also optically characterized and the data are given in Table 2.

Addition of increasing amounts of anhydrous zinc and cadmium triflates to an ethanolic solution of L^2 or L^4 ($1.00E^{-5}$ M), at 298 K, led to a decrease in the absorption band centered at 249 nm, and the appearance of a new band centered at ca. 270 nm. This spectrum has a long tail up to 400 nm. In this region, the absorption increases with the addition of metal ions, suggesting the involvement of the quinoline ring in the metal complexation. An isosbestic point at 260 nm was observed for all the metal titrations, confirming the presence of two species in solution, the free ligand, and the metal

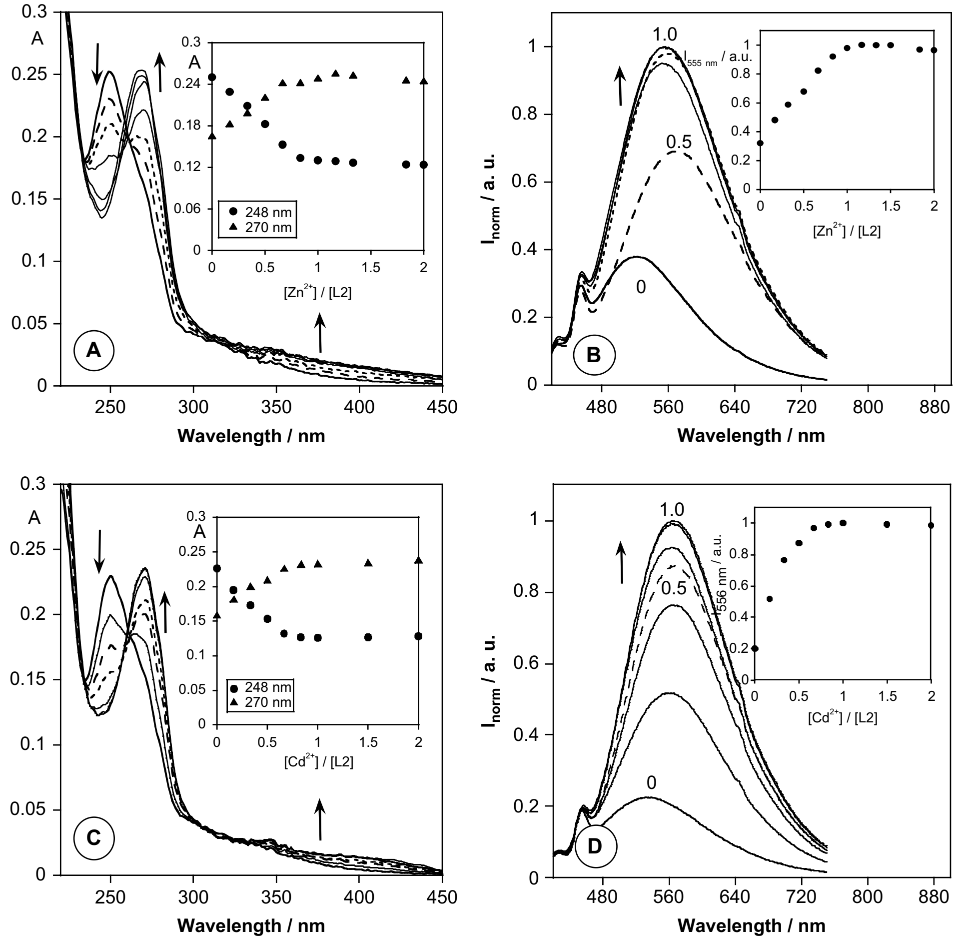


Figure 2. Absorption (A and C) and fluorescence emission (B and D) titration of absolute ethanol solutions of L^2 as a function of increasing amounts of Zn^{2+} (A and B) or Cd^{2+} (C and D) ions. The inset shows the absorption at 248 and 270 nm, and the normalized fluorescence intensity at 555 nm ($[L^2]=1.00\times E^{-5}$ M, λ_{exc}=400 nm).

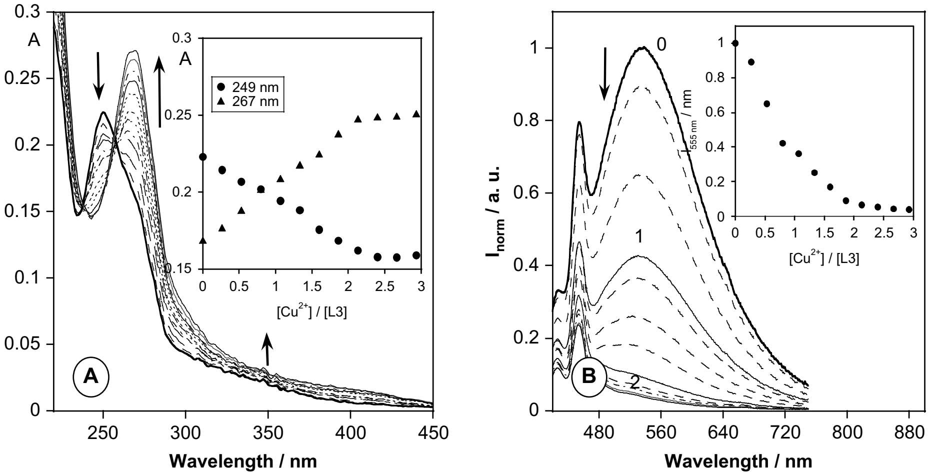


Figure 3. Absorption (A) and fluorescence emission (B) titrations of absolute ethanol solution of L^2 as a function of increasing amounts of Cu^{2+} ions. The inset shows the absorption at 249 and 257 nm, and the normalized fluorescence intensity at 555 nm ([L^2]=1.00×E^{-5} M, λ_{exc}=400 nm).

complex. As an example, Figure 2 depicts the absorption and emission metal titration of L^2 with Zn(II) and Cd(II).

Excitation at 400 nm (quinoline tail) gave emission spectra centered at 555 nm. The band is red-shifted upon complexation, as it can be seen in Figure 2B and D for Zn(II) and Cd(II), respectively. The same behavior was observed when the metal ion used was Al(III). A *Chelation Enhanced Fluorescence (CHEF)* effect was observed in all cases. This well known phenomenon is consistent with the involvement of the amines and the quinoline ring in complexation. The lone pairs of the nitrogen atom are bound to the metal ion preventing the PET processes, while the 8-HQ is coordinated to the metal preventing the PPT process; thus, complexation results in an enhancement of the fluorescence signal.

As it can be seen in Figure 2A and B, a plateau is reached after addition of one metal equivalent, suggesting that the macrocyclic unit is coordinated to one metal ion. This result confirms the stoichiometry observed for the solid metal complexes synthesized. Copper(II) ions are well know to quench excited states.[31] Addition of increasing amounts of all d^n metals studied leads to the formation of non-emissive complexes. These results are in agreement with the fluorescence behavior observed for the analytically pure complexes isolated (see Experimental section).

Figure 3 shows the absorption and emission spectra of L^2 in the presence of increasing amounts of Cu(II); the inset shows the normalized fluorescence intensity at 555 nm. Upon addition of 2 equiv of metal ion, the emission disappears, achieving a plateau;

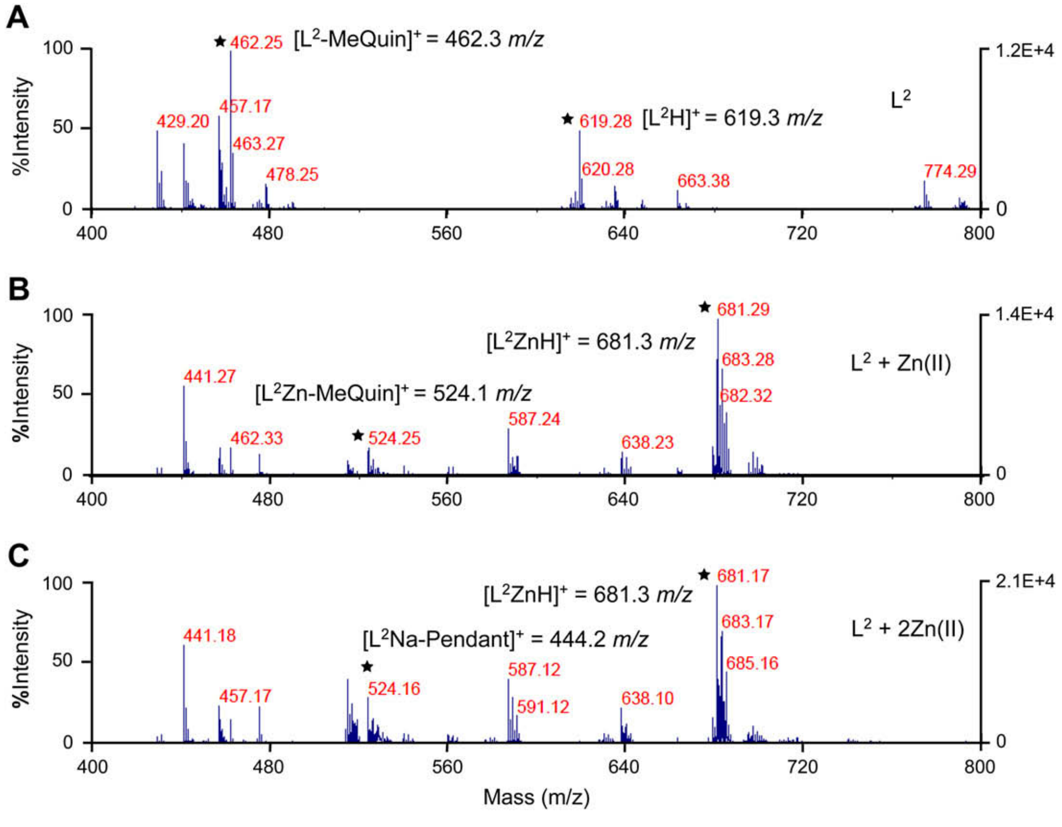


Figure 4. (A) MALDI-TOF-MS spectra of L^2 using dithranol as MALDI matrix, (B) in the presence of 1 equiv of Zn(II), and (C) in the presence of 2 equiv of Zn(II).

this suggests the formation of a dinuclear complex. A similar CHEQ effect was observed in the presence of Cr(III), but the plateau was achieved for one metal ion, suggesting the formation of a mononuclear complex. Both results agree with the stoichiometry found in the solid metal complexes synthesized.

Protonation and/or complexation of a pyridine ring lead to a quenching effect for molecules that incorporate both a pyridine and an emissive chromophore unit in their structure.[32] The presence of the pyridine head in L^1 and L^2 creates another inverse PET mechanism for quenching the emission. The analogous ligands L^3 and L^4, without the pyridine unit, were synthesized for comparative purposes. Unfortunately, the results observed with L^3 and L^4 are similar to those ligands L^1 and L^2, due to the strong PPT and PET processes mentioned previously.

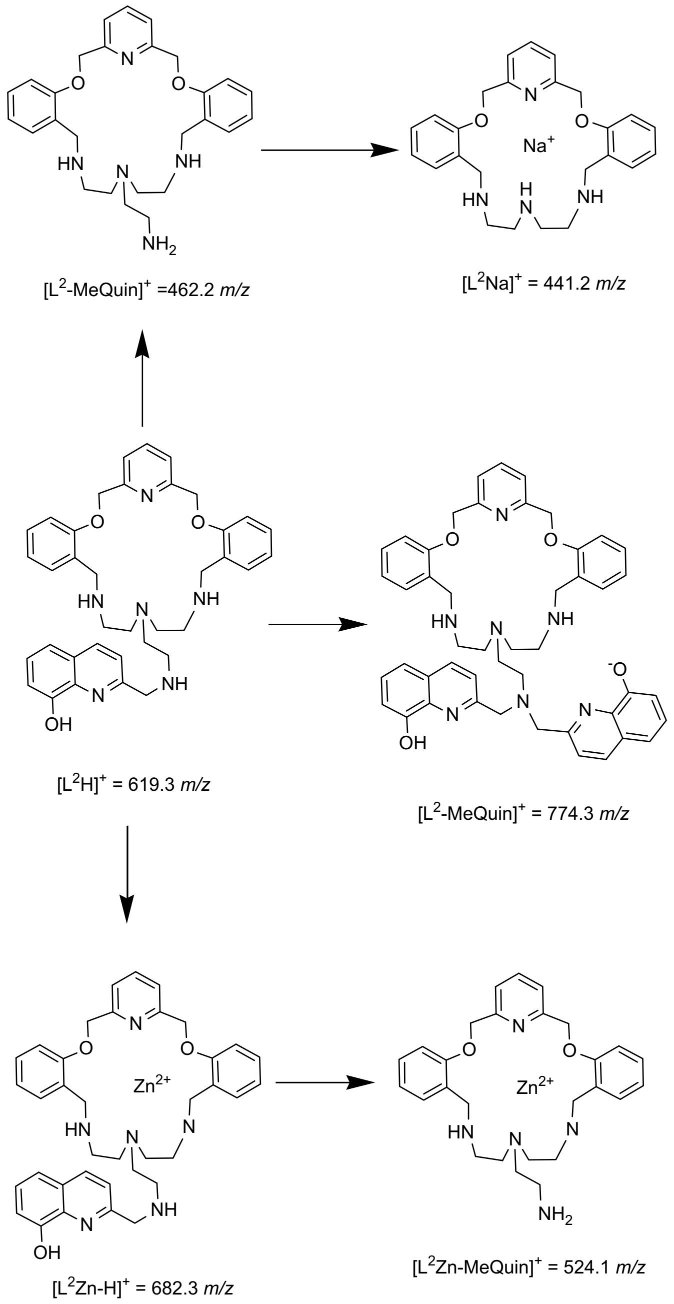
The fluorescence quantum yields for all the complexes have been calculated using a solution of quinine sulfate as pattern. In all cases, and in accordance with the results obtained for the free ligands, the values are very small, always below 10^{-3}. This quenching can be attributed to the high number of donor atoms present in the ligands; some of them may not be coordinated to the metal centers, specially the nitrogens that activate the quenching through the PET phenomena. As it can be observed in Table 2, the maximum of the emission for each metal complex is slightly different, opening up the possibility of using these ligands to recognize these metals in solution.

2.2.2. Spectrometric studies by MALDI-TOF-MS spectrometry

Taking into account the biological importance of Zn(II) ions, and the environmental problems by Al(III) excess, these two metal ions were selected for the gas phase studies by MALDI-TOF-MS using ligands L^2 and L^4 as molecular probes. To perform the metal titrations, both ligands were dissolved in chloroform and the metal salts in absolute ethanol. Two different strategies were explored. First, three solutions containing the ligand (1 μL), the MALDI matrix (dithranol), and the metal salt (1 μL) were mixed and then applied in the MALDI-TOF sample holder. The second method consisted of a layer by layer addition: a solution of L^2 or L^4 mixed with the matrix (dithranol) was spotted in the MALDI-TOF plate and then dried; subsequently, 1 μL of the solution containing the metal salt was placed on the sample holder, which was then inserted in the ion source. For the second case, the chemical reaction between the ligand and the metal salts occurred in the holder, and the complex species were produced in gas phase.

The results were the same in both cases. Addition of one metal equivalent led to the formation of the mononuclear complex. Addition of increasing amounts of metal ion did not produce any peaks attributable to the formation of dinuclear complexes. The results with Al(III) and Zn(II) confirm both the stoichiometry observed in the synthesized solid metal complexes, and the data obtained in solution by absorption and fluorescence emission spectroscopy.

Figure 4 summarizes the MALDI-TOF-MS spectra for ligand L^2. In the presence of 1 and 2 equiv of Zn(II), peaks at *m*/*z* 619.3, attributable to the protonated ligand $[L^2H]^+$, and *m*/*z* 462.2, attributed to the loss of the methyl-8-HQ group, were observed. Small peaks at higher mass values, attributable to species with two, three and four pendant arms, can be observed; these are indicative of the interaction of the quinoline group with the ligand in the gas phase (see Scheme 4). After addition of the metal salt, the peak corresponding to the protonated ligand disappears, and new peaks at *m*/*z* 682.3, 524.2, and 441.2, attributable to the $[L^2Zn–H]^+$, $[L^2Zn–MeQuinoline]^+$, and $[L^2Na\text{-pendant}]^+$ species, respectively, were observed.



Scheme 4. MALDI-TOF-MS fragmentation peak observed for L^2 and $L^2Zn(II)$ complex.

3. Conclusions

Four macrocyclic ligands containing an 8-HQ pendant arm have been synthesized and fully characterized. The protonation behavior and sensing capability of these ligands toward divalent, Cu(II), Zn(II), Cd(II), and trivalent, Al(III) and Cr(III) metal ions have been studied by UV–vis and fluorescent emission spectroscopy. Several metal complexes have also been synthesized and characterized, confirming the stoichiometry and all the data obtained in solution.

The photophysical characterization of the ligands shows two quenching mechanisms active, PPT and PET. Coordination with Zn(II), Cd(II), and Al(III) partially prevents this quenching trough a CHEF effect. Cu(II) and Cr(III) gave non-emissive complexes due to the quenching, via a CHEQ effect, of the low emission observed for the free macrocycles. Both phenomena could be used for sensing purposes, opening up the possibility of using these ligands in solution for metal-ion recognition.

Titrations of L^2 and L^4 with Zn(II) and Al(III) solutions were followed by MALDI-TOF-MS spectrometry. In all cases, the formation of the complex peak was observed. These results confirm the formation of the metal complexes also in the gas phase.

4. Experimental

4.1. General

The chemical analysis of the dialdehyde precursor, 2,2-(1,3-phenylenebis(methyleneoxy))dibenzaldehyde, was carried out on a Carlo Erba 1106 CHN analyser. Elemental analyses of the ligands were performed on a Fisons Instruments EA1108 micro analyser by the Universidade de Santiago de Compostela. The IR spectra of the precursors were recorded on a Pye Umicam SP3-100 infrared spectrometer. Infrared spectra of free ligands were recorded as KBr discs on a BIO-RAD FTS 175-C spectrometer. FAB mass spectra were recorded using a KRATOS MS50TC spectrometer with 3-nitrobenzyl alcohol as the matrix. The ^{1}H NMR spectrum of the dialdehyde precursor was recorded on a JEOL GSX 270 FT NMR spectrometer. The ^{1}H, ^{13}C NMR, COSY, DEPT, and HMQC spectra were recorded on a Bruker 500 MHz spectrometer, using CD_3Cl as the solvent.

MALDI-TOF-MS spectra have been performed in a MALDI-TOF-MS model Voyager DE-PRO Biospectrometry Workstation equipped with a nitrogen laser radiating at 337 nm from Applied Biosystems (Foster City, United States) from the MALDI-TOF-MS Service of the REQUIMTE, Chemistry Department, Universidade Nova de Lisboa. The acceleration voltage was 2.0×10^4 kV with a delayed extraction (DE) time of 200 ns. The spectra represent accumulations of 5×100 laser shots. The reflection mode was used. The ion source and flight tube pressures were less than 1.80×10^{-7} and 5.60×10^{-8} Torr, respectively. The MALDI mass spectra of the soluble samples (1 or 2 µg/µL) such as the ligand and metal complexes were recorded using the conventional sample preparation method for MALDI-MS. In the metal titrations by MALDI 1 µL of the metal sample was put on the sample holder on which the chelating ligand had been previously spotted with the matrix (dithranol). The sample holder was inserted in the ion source. Chemical reaction between the ligand and metal salts occurred in the holder and complex species were produced.

Absorption spectra were recorded on a Shimadzu UV-2501PC or in a Perkin Elmer lambda 35 spectrophotometer. Fluorescence emission spectra were recorded on a Horiba–Jobin–Yvon SPEX Fluorolog 3.22 or a Perkin Elmer LS45 espectrofluorimeters. The linearity of the fluorescence emission versus concentration was checked in the concentration range used (10^{-4} to 10^{-6} M). A correction for the absorbed light was performed when necessary. All spectrofluorimetric titrations were performed as follows: the stock solutions of the ligand (ca. 1×10^{-3} M) were prepared by dissolving an appropriate amount of the ligand in a 50 mL volumetric flask and diluting to the mark with absolute ethanol UVA-sol. All measurements were performed at 298 K. The titration solutions (ca. $[L]=1.0\times10^{-5}$ M) were prepared by appropriate dilution of the stock solutions. Titrations of the ligand were carried out by addition of microliter amounts of standard solutions of the ions in absolute ethanol. HBF_4 and tetrabutylammonium hydroxide were used to change the acidic conditions of the ethanolic solutions. Luminescence quantum yields were measured using a solution of quinine sulfate in H_2SO_4 (0.1 M) as a standard $[\Phi_F]=0.546$].[30]

4.2. Chemicals and starting material

Salicylaldehyde, 1,3-bis(bromomethyl)benzene, tris(2-aminoethyl)amine, 8-hydroxyquinoline-2-carbaldehyde, and hydrated chloride, nitrate, and perchlorate salts were commercial products from Alfa and Aldrich. Solvents used were of reagent grade and purified by the usual methods. CD_3Cl (99.8%) was obtained from Aldrich. All triflate metallic salts were purchased from Strem, chemicals for research. The starting materials, 2,6-bis(2-formylphenoxymethyl)pyridine[26] and the macrocyclic ligand L[25] were synthesized as previously published.

4.3. Synthesis

4.3.1. Synthesis of 2,2-(1,3-phenylenebis(methyleneoxy))-dibenzaldehyde

A solution of NaOH (1.512 g, 37.8 mmol) in 50 mL of distilled water was added dropwise to a solution of salicylaldehyde (4.710 g, 37.8 mmol) in 10 mL in absolute ethanol. After heating gently for approximately 10 min, 1,3-bis(bromomethyl)benzene (4.741 g, 18.9 mmol) was added dropwise. Absolute ethanol (80 mL) was slowly added, and the resulting solution refluxed gently for 4 h while maintaining magnetic stirring. The solution was then allowed to cool and a white solid appeared. The solid was filtered off and dried. The compound is air stable, soluble in chloroform and dichloromethane, moderately soluble in hexane, absolute ethanol, diethyl ether, and methanol and insoluble in distilled water.

$C_{22}H_{18}O_4\cdot 0.5H_2O$. Mp (°C): 80–85 °C. Anal. Calcd for $C_{22}H_{19}O_{4.5}$: C, 74.36; H, 5.07. Found: C, 74.30; H, 5.04%. Yield: 78%. IR (NaCl windows, cm^{-1}): 1690 [ν(C=O)], 1600 [ν(C=C)]. MS (FAB$^+$, m/z): 347 [L′H]$^+$.

^{1}H NMR ($CDCl_3$), δ (ppm): 10.5 (s), 2H (CO*H*); 7.9–7.0 (m), 12H (aromatics); 5.2 (s), 4H (aromatic-C*H*$_2$–O).

4.3.2. Template synthesis of the macrocyclic ligand L′

A solution of tris(2-aminoethyl)amine (0.512 g, 1 mmol) in methanol (25 mL) was added dropwise to a refluxing solution of 2,2-(1,3-phenylenebis(methyleneoxy))dibenzaldehyde (0.346 g, 1 mmol) and barium perchlorate (0.336 g, 1 mmol) in methanol (75 mL). The resulting solution was gently refluxed with magnetic stirring for ca. 4 h. The solution was allowed to cool and $NaBH_4$ (0.378 g, 10 mmol) was added; magnetic stirring was maintained for a further 2 h period. The mixture was filtered off and evaporated to dryness. The residue was then extracted with water–chloroform. The organic layer was dried over anhydrous Na_2SO_4 and evaporated to yield a yellow oil that was dried under vacuum.

$C_{28}N_4O_2H_{36}\cdot 4H_2O$ *(L′)*. Anal. Calcd for $C_{28}N_4O_6H_{44}$: C, 63.15; H, 8.30; N, 10.53. Found: C, 62.90; H, 8.63; N, 10.85%. Yield: 70.3%. IR (KBr, cm^{-1}): 1601 [ν(C=C)]. MS (FAB, m/z): 461 [L′H]$^+$.

^{1}H NMR of L′ ($CDCl_3$), δ (ppm): 7.7–6.7 (m), 12H (Ph); 5.0 (s), 4H (Ph–C*H*$_2$–O); 3.6 (s), 4H (Ph–C*H*$_2$–NH); 2.6–2.0 (m), 12H (–C*H*$_2$C*H*$_2$); 1.7 (s) (–N*H*).

^{13}C NMR ($CDCl_3$), δ (ppm): 156.9–111.9, 18C (aromatics); 70.2, 2C (aromatic-CH$_2$-O); 49.1, 2C (aromatic-*C*H$_2$–NH); 57.5–53.8, 6C (–*C*H$_2$*C*H$_2$).

4.3.3. Synthesis of the imine macrocyclic ligands L^1 and L^3: general method

A solution of 8-hydroxyquinoline-2-carbaldehyde (0.069 g, 0.4 mmol) for L^1 (0.034 g, 0.2 mmol) and for L^3 in absolute ethanol (10 mL) was added dropwise to a refluxing solution of L (0.184 g, 0.4 mmol) and L′ (0.092 g, 0.2 mmol) in the same solvent (70 mL for L^1 and 35 mL for L^3). The resulting solution was gently refluxed with magnetic stirring for ca. 4 h. The color changed from yellow to orange in both cases. The solution was allowed to cool, filtered off to eliminate the solid precipitate, and then concentrated in the rotary evaporator. The resulting orange oil was stirred with acetonitrile (to eliminate possible excess of L or L′) and then with cold diethyl ether. The orange powder precipitates, later characterized as L^1 or L^3, were separated by centrifugation and dried under vacuum.

$C_{37}N_6O_3H_{40}\cdot 2H_2O$ *(L^1)*. Mp (°C): 170–175. Anal. Calcd for $C_{37}N_6O_5H_{44}$: C, 68.10; H, 6.74; N, 12.88. Found: C, 68.59; H, 6.10; N, 12.98%. Yield: 73.3%. IR (KBr, cm^{-1}): 1642 [ν(C=N)$_{\text{imine}}$]; 1597, 1453 [ν(C=C) and ν(C=N)$_{\text{py}}$]. MS (ESI, m/z): 617 [L^{1}H]$^+$; MS (MALDI-TOF-MS, m/z): 616 [L^{1}H]$^+$.

^{1}H NMR of L^1 ($CDCl_3$), δ (ppm): 8.2 (s), 1H,(*H*C=N)$_{\text{imine}}$; 7.9–6.7 (m), 16H (aromatics); 5.6 (s), 1H (O*H*); 4.9(s), 4H (Py–C*H*$_2$–O); 3.7 (m), 4H (Ph–C*H*$_2$–NH); 2.0 (s) (–N*H*); 3.4–2.5 (m), 12H (–C*H*$_2$C*H*$_2$).

$C_{38}N_5O_3H_{41}\cdot 3H_2O$ (L^3). Mp (°C): 165–170; Anal. Calcd for $C_{38}N_5O_6H_{47}$: C, 68.15; H, 7.02; N, 10.45. Found: C, 68.20; H, 7.53; N, 10.08%. Yield: 62.3%. IR (KBr, cm^{-1}): 1641 [$\nu(C{=}N)_{imine}$]; 1600, 1453 [$\nu(C{=}C)$ and $\nu(C{=}N)_{py}$]. MS (FAB^+, m/z): 616 $[L^3H]^+$. MS (MALDI-TOF-MS, m/z): 616 $[L^3H]^+$.

^1H NMR of L^3 ($CDCl_3$), δ (ppm): 8.4 (s), 1H $(C{=}N)_{imine}$; 8.1–6.7 (m), 17H (aromatics); 4.5 (s), 1H (OH); 5.1 (s) 4H (Py–CH_2–O); 3.8 (s), 4H (Ph–CH_2–NH); 2.9–2.1 (m), 12H (–CH_2CH_2).

4.3.4. Synthesis of the amine macrocyclic ligands L^2 and L^4: general method

$NaBH_4$ was added in excess (20%) to a solution of L^1 (0.123 g, 0.2 mmol) and L^3 (0.062 g, 0.1 mmol) in methanol at room temperature. The resulting solutions were gently refluxed with magnetic stirring for 4 h; within that time, the color changed slowly from orange to pale yellow. The mixtures were filtered off and evaporated to dryness. The residues were then extracted with water–chloroform. The organic layer was dried over anhydrous Na_2SO_4 and evaporated to yield a yellow oil that was stirred with diethyl ether. The yellow powder formed was separated by centrifugation and dried under vacuum. These compounds were characterized as L^2 and L^4.

$C_{37}N_6O_3H_{42}\cdot 2H_2O$ (L^2). Mp (°C): 175–180; Anal. Calcd for $C_{37}N_6O_5H_{46}$: C, 66.07; H, 7.14; N, 12.50. Found: C, 66.70; H, 6.90; N, 12.20%. Yield: 45.3%. IR (KBr, cm^{-1}): 1597, 1451 [$\nu(C{=}C)$ and $\nu(C{=}N)_{py}$]. MS (ESI, m/z): 619 $[L^2H]^+$. MS (MALDI-TOF-MS, m/z): 619 $[L^2H]^+$.

^1H NMR of L^2($CDCl_3$), δ (ppm): 7.8–6.8 (m), 16H (aromatics); 5.9 (s), 1H (O*H*); 5.3 (s) 4H (Py–CH_2–O); 3.7–3.6 (m), 4H (Ph–CH_2–NH); 3.6–2.3 (m), 12H (–CH_2CH_2); 4.0 (s), 2H (8-HQ-CH_2NH).

$C_{38}N_5O_3H_{43}\cdot 8H_2O$ (L^4). Anal. Calcd for $C_{38}N_5O_{11}H_{59}$: C, 59.90; H. 7.75; N, 9.20. Found: C, 60.57; H, 7.45; N, 8.85%. Yield: 59.4%. IR (KBr, cm^{-1}): 1600, 1453 [$\nu(C{=}C)$ and $\nu(C{=}N)_{py}$]. MS (FAB^+, m/z): 618 $[L^4{+}H]^+$. MS (MALDI-TOF-MS, m/z): 618 $[L^4H]^+$.

^1H NMR of L^4($CDCl_3$), δ (ppm): 8.0–6.5 (m), 17H (Ph); 4.0 (s) 1H,(OH); 5.0 (s) 4H (Py–CH_2–O); 3.7 (s), 4H (Ph–CH_2–NH); 2.6–2.1 (m), 12H (–CH_2CH_2); 3.4 (s), 2H (8-HQ-CH_2NH).

4.3.5. General procedure for metal complexes with ligands L^1 and L^3

Hydrate aluminum chloride (0.02 mmol) in ethanol (5 mL) was added dropwise to a stirred solution of L^1 or L^3 (0.02 mmol) in the same solvent (15 mL). The resulting mixture was gently heated and magnetically stirred for 4 h. The solution was then concentrated in a rotary evaporator to ca. 5 mL. A small volume of diethyl ether (ca. 3 mL) was slowly infused into the solution producing powdery precipitates. The products were separated by centrifugation and dried under vacuum. The compounds are air stable, soluble in absolute ethanol, methanol, and dimethyl sulfoxide and insoluble in acetonitrile, ether, and water. Attempts to grow single crystals of the complexes were unsuccessful. This reaction was attempted also with the Zn(II) and Cr(III) nitrates, but in both cases the microanalytical results were unsatisfactory.

*$AlL^1Cl_3\cdot 5H_2O$ (**1**).* Color: yellow; Anal. Calcd for $C_{37}N_6O_3H_{40}Cl_3Al\cdot 5H_2O$: C, 52.88; H, 5.95; N, 10.00. Found: C, 52.33; H, 6.31; N, 9.45%. Yield: 55.3%. IR (KBr, cm^{-1}): 1599, 1456 [$\nu(C{=}C)$ and $\nu(C{=}N)_{py}$]. MS (ESI, m/z): 619 $[L^1]^+$, 670 $[Al_2L^1]^+$, 775 $[Al_2L^1Cl_3]^+$, 847 $[Al_2L^1Cl_5]^+$.

*$AlL^3Cl_3\cdot 6H_2O$ (**2**).* Color: yellow. Anal. Calcd for $C_{38}N_5O_9H_{53}Cl_3Al$: C, 53.24; H, 6.18; N, 8.17. Found: C, 53.51; H, 5.90; N, 8.24%. Yield: 59.2%. IR (KBr, cm^{-1}): 1629 [$\nu(C{=}N)_{imin}$]; 1602, 1457 [$\nu(C{=}C)$ and $\nu(C{=}N)_{py}$]. MS (FAB, m/z): 765 $[Al_3L^3Cl_2]^+$.

4.3.6. General procedure for complexes with the amine macrocycles L^2 and L^4

The appropriate metal salt (0.02 mmol) in absolute ethanol (5 mL) was added dropwise to a stirred solution of the ligand L^2 or L^4 (0.02 mmol) in the same solvent (15 mL). The resulting mixture was gently heated and magnetically stirred for 4 h. The solution was then concentrated in a rotary evaporator to ca. 5 mL. A small volume of diethyl ether (ca. 3 mL) was slowly infused into the solution producing powdery precipitates. The products were separated by centrifugation and dried under vacuum. The compounds were air stable, soluble in ethanol, methanol, and dimethyl sulfoxide and insoluble in acetonitrile, ether, and water. Attempts to grow single crystals of the complexes were unsuccessful.

*$AlL^2(Cl)_3\cdot 2H_2O$ (**3**).* Color: yellow. Anal. Calcd for $C_{37}N_6O_5H_{46}Cl_3Al$: C, 56.25; H, 5.84; N, 10.66. Found: C, 56.83; H, 4.96; N, 11.32%. Yield: 62.3%. IR (KBr, cm^{-1}): 1604, 1457 [$\nu(C{=}C)$ and $\nu(C{=}N)_{py}$]. MS (ESI, m/z): 713 $[AlL^2Cl_2]^+$.

*$AlL^4(Cl)_3\cdot 5H_2O$ (**4**).* Color: yellow. Anal. Calcd for $C_{38}N_5O_8H_{53}AlCl_3$: C, 54.26; H, 6.30; N, 8.33. Found: C, 54.35; H, 5.74; N, 8.15%. Yield: 52.8%. IR (KBr, cm^{-1}): 1603, 1456 [$\nu(C{=}C)$ and $\nu(C{=}N)_{py}$]. MS (FAB, m/z): 618 $[L^4]^+$, 683 $[AlL^4Cl]^+$.

*$CrL^2(NO_3)_3\cdot 6H_2O$ (**5**).* Color: yellow. Anal. Calcd for $C_{37}N_9O_{18}H_{54}Cr$: C, 46.05; H, 5.60; N, 13.07. Found: C, 46.28; H, 5.79; N, 13.45%. Yield: 54.4%. IR (KBr, cm^{-1}): 1601, 1457 [$\nu(C{=}N)_{py}$ and $\nu(C{=}C)$]; 839, 1384 [$\nu(NO_3^-)$]. MS (ESI, m/z): 619 $[L^2]^+$, 696 $[CrL^2Na]^+$, 754 $[CrL^2Na(NO_3)]^+$, 790 $[CrL^2\,(NO_3)_2]^+$.

*$CrL^4(NO_3)_3\cdot 2H_2O$ (**6**).* Color: yellow. Anal. Calcd for $C_{38}N_8O_{14}H_{47}Cr$: C, 51.17; H, 5.27; N, 12.57. Found: C, 51.23; H, 5.12; N, 12.87%. Yield: 49.8%. IR (KBr, cm^{-1}): 1601, 1459 [$\nu(C{=}C)$ and $\nu(C{=}N)_{py}$]; 840, 1383 [$\nu(NO_3^-)$].

*$Cu_2L^2(NO_3)_4\cdot 3C_2H_6O$ (**7**).* Color: green. Anal. Calcd for $C_{43}N_{10}O_{18}H_{60}Cu_2$: C, 45.62; H, 5.30; N, 12.37. Found: C, 45.56; H, 5.28; N, 11.90%. Yield: 63.8%. IR (KBr, cm^{-1}): 1599, 1454 [$\nu(C{=}C)$ and $\nu(C{=}N)_{py}$]; 839, 1384 [$\nu(NO_3^-)$]. MS (ESI, m/z): 619 $[L^2]^+$, 680 $[CuL^2]^+$, 766 $[Cu_2L^2(H_2O)]^+$, 806 $[Cu\;L^2(NO_3)_2]^+$, 822 $[CuL^2(NO_3)_2(H_2O)]^+$, 867 $[Cu_2L^2(NO_3)_2]^+$.

*$Cu_2L^4(NO_3)_4\cdot 3H_2O$ (**8**).* Color: green. Anal. Calcd for $C_{38}N_9O_{18}H_{49}Cu_2$: C, 43.60; H, 4.68; N, 12.04. Found: C, 43.25; H, 4.20; N, 12.04%. Yield: 41.5%. IR (KBr, cm^{-1}): 1602, 1458 [$\nu(C{=}C)$ and $\nu(C{=}N)_{py}$]; 840, 1383 [$\nu(NO_3^-)$]. MS (FAB, m/z): 679 $[CuL^4]^+$.

*$ZnL^2(NO_3)_2\cdot 6H_2O$ (**9**).* Color: yellow. Anal. Calcd for $C_{37}N_8O_{15}H_{54}Zn$: C, 48.50; H, 5.89; N, 12.23. Found: C, 48.50; H, 4.86; N, 12.44%. Yield: 59.0%. IR (KBr, cm^{-1}): 1600, 1454 [$\nu(C{=}C)$ and $\nu(C{=}N)_{py}$]; 839, 1384 [$\nu(NO_3^-)$]. (ESI,m/z): 619 $[L^2]^+$, 681 $[ZnL^2]^+$.

*$ZnL^4(NO_3)_2\cdot 3H_2O$ (**10**).* Color: yellow. Anal. Calcd for $C_{38}N_7O_{12}H_{49}Zn$: C, 53.00; H, 5.69; N, 11.39. Found: C, 53.51; H, 5.32; N, 11.15%. Yield: 68.3%. IR (KBr, cm^{-1}): 1606, 1458 [$\nu(C{=}C)$ and $\nu(C{=}N)_{py}$]; 838, 1383 [$\text{v}(NO_3^-)$]. MS (FAB, m/z): 639 $[L^4Na]^+$, 680 $[ZnL^4]^+$, 701 $[ZnL^4H_2O]^+$.

*$CdL^2(ClO_4)_2\cdot 2C_2H_6O$ (**11**).* Color: brown. Anal. Calcd for $C_{41}N_6O_{13}H_{54}Cl_2Cd$: C, 48.16; H, 5.28; N, 8.22. Found: C, 48.11; H, 5.34; N, 8.51%. Yield: 71.4%. IR (KBr, cm^{-1}): 1599, 1454 [$\nu(C{=}C)$ and $\nu(C{=}N)_{py}$]; 624, 636, 1087, 1109, 1121 [$\nu(ClO_4^-)$]. MS (ESI, m/z): 619 $[L^2]^+$, 731 $[Cd\;L^2]^+$, 929 $[CdL^2\,(ClO_4)]^+$, 942 $[Cd_2L^2(ClO_4)]^+$.

*$CdL^4(NO_3)_2\cdot 3H_2O$ (**12**).* Color: brown. Anal. Calcd for $C_{38}N_7O_{12}H_{49}Cd$: C, 50.25; H, 5.40; N, 10.80. Found: C, 50.70; H, 5.87; N, 10.07%. Yield: 58.3%. IR (KBr, cm^{-1}): 1600, 1454 [$\nu(C{=}C)$ and $\nu(C{=}N)_{py}$]; 838, 1384 [$\nu(NO_3^-)$]. MS (FAB, m/z): 728 $[CdL^4]^+$, 790 $[CdL^4(NO_3^-)]^+$.

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