DALTON
FULL PAPER

Synthesis and kinetic behaviour of lanthanide(III) complexes with the mixed pendant-arm macrocyclic ligand 1,7-bis(carboxymethyl)-4,10-bis(1-methylimidazol-2-ylmethyl)-1,4,7,10-tetraazacyclododecane †

Fabrizio Mani, Roberto Morassi, Piero Stoppioni and Alberto Vacca

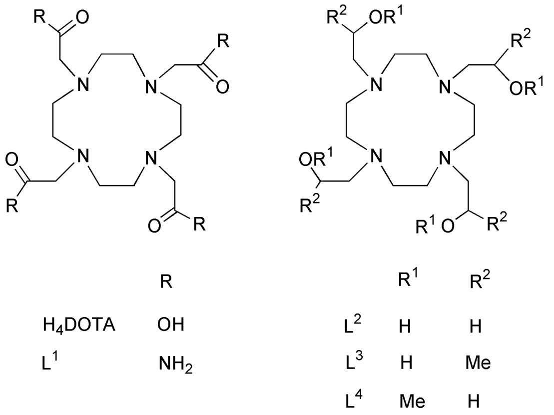
Dipartimento di Chimica, Università di Firenze, via Maragliano 77, 50144 Firenze, Italy.
E-mail: stopmora@chim1.unifi.it

Received 27th February 2001, Accepted 22nd May 2001
First published as an Advance Article on the web 3rd July 2001

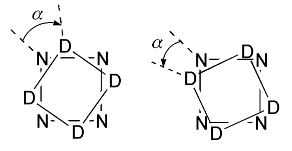
The La^{III}, Eu^{III} and Lu^{III} complexes with the potentially octadentate new ligand 1,7-bis(carboxymethyl)-4,10-bis(1-methylimidazol-2-ylmethyl)-1,4,7,10-tetraazacyclododecane (H_2L) which bears two pairs of different dangling groups in *trans* positions on the cyclen skeleton, have been synthesized. The low-temperature limiting NMR spectra (^1H and ^{13}C) of the compounds support the presence in solution of one species with an approximately prismatic geometry for the lanthanum derivative and of two isomers with nearly square-prismatic and -antiprismatic geometries for the europium and the lutetium complexes. Both the dangling groups and the ethylenic moieties of the ligand are rigid in all the species at low temperature. The rigidity is lost at higher temperatures yielding a dynamic behaviour which proceeds through both ring inversion and rearrangement of the pendant arms. The kinetic parameters for the ring inversion of the lanthanum derivative have been obtained from the temperature-dependent ^{13}C NMR spectra in D_2O: $k(298\ K) = 107\ s^{-1}$; $\Delta H^{\ddagger} = 61.4\ kJ\ mol^{-1}$; $\Delta S^{\ddagger} = -0.4\ J\ K^{-1}\ mol^{-1}$.

Introduction

In recent years considerable attention has been addressed to metal complexes of 1,4,7,10-tetraazacyclododecane (cyclen) bearing pendant arms.[1] Depending on the number of substituent groups on the macrocycle framework, as well as on the requirements of the metal ions employed, the substituted cyclen ligands easily adapt to coordination numbers of six or eight and to geometries broadly referable to the octahedral[2–4] or square-antiprismatic type.[5] For these reasons such molecules appear to be suitable to coordinate both transition and rare-earth metal ions. The complexes with these ligands exhibit notable thermodynamic and kinetic stability and, in connection with this feature, they have important applications in biology and in medicine, including: (i) the design of luminescent chelates for immunoassays,[6] (ii) the use of Gd-containing contrast agents in diagnostic medicine[7] and (iii) the labelling and specific cleavage of DNA and RNA.[8] The octadentate ligands efficiently encapsulate the lanthanide ions leaving the possibility for one further interaction either with a solvent molecule,[9] an essential feature for contrast agents,[10] or with RNA oligomers to be hydrolyzed.[8] Representative examples of such ligands include (Scheme 1) 1,4,7,10-tetraazacyclododecanetetraacetic acid (H_4DOTA), providing anionic donors on the dangling groups, and molecules bearing four neutral donors on the arms of the tetraazacyclododecane.[11] The solid state X-ray characterization of Ln^{III} complexes revealed that the eight coordination sites, four nitrogen atoms of the macrocycle and four donors from the dangling groups, are arranged in two parallel squares, tilted by an angle α (Scheme 2). According to the value of α, the coordination polyhedron can range from a regular antiprism ($\alpha = 45°$) to a prism ($\alpha = 0°$). Neither limiting case has been observed so far in the crystal structures of the complexes and most of the known geometries cluster around two values: $\alpha = 40°$ and 15°. The LnDOTA complexes (Ln = Eu,[12] Gd,[13] Lu[14]) belong to the former group; the LaDOTA,[15] LaDOTAM [DOTAM = 1,4,7,10-tetrakis(2-carboxyethyl)-1,4,7,10-tetraazacyclododecane],[16] EuTHP [THP = 1,4,7,10-tetrakis(2-hydroxypropyl)-1,4,7,10-tetraazacyclododecane],[17] $YDOTPBz_4$ [$DOTPBz_4$ = 1,4,7,10-tetrakis(methylenebenzylphosphinic acid)-1,4,7,10-tetraazacyclododecane][18] can be assigned to the latter.



Scheme 1



Scheme 2

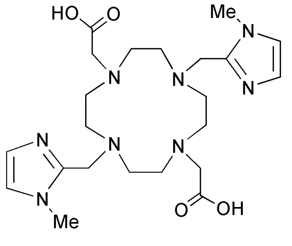
The lanthanides are tightly bound to the eight donors also in solution, where intermolecular and intramolecular processes occur.[14,16] Only one isomer is observed at low temperature with the ligands L^1–L^4 (Scheme 1).[19] The DOTA complexes, on the other hand, give rise to an equilibrium between two diastereoisomers.[20,21] Although some mixed ligands bearing three identical groups and one different have been described and their coordination properties toward lanthanide ions have

---

† Electronic supplementary information (ESI) available: $^{13}C\{^1H\}$ spectrum of the $[LaL]^+$ cation at 278 K in D_2O, $^{13}C\{^1H\}$ spectrum of the $[LuL]^+$ cation at 272 K in D_2O and Eyring plot for the ring inversion of the $[LaL]^+$ cation in D_2O. See http://www.rsc.org/suppdata/dt/b1/b101874o/

been investigated,[22] up to now the occurrence of dynamic processes for such complexes has not been described.

In this paper we report the synthesis of three lanthanide complexes with the new ligand 1,7-bis(carboxymethyl)-4,10-bis(1-methylimidazol-2-ylmethyl)-1,4,7,10-tetraazacyclododecane (H_2L), providing two neutral and two anionic donors on the different pairs of dangling groups which are in *trans* positions on the cyclen skeleton. The behaviour in solution of the complexes has been investigated by means of variable-temperature ^1H and ^{13}C NMR measurements.



H_2L

Experimental

Commercial solvents were dried from appropriate drying agents just before use according to standard procedures. NMR spectra were obtained with a Varian Gemini g300bb spectrometer, equipped with a variable-temperature unit, operating at 300 MHz (^1H) and 75.46 MHz (^{13}C). Positive chemical shifts are to high frequency relative to Me_4Si; CD_3CN was used as an internal reference; the spectra of the lutetium trifluoromethanesulfonate complex were referenced to the anion multiplet. The variable-temperature accessories were checked against methanol and ethylene glycol. The $^{13}C\{^1H\}$ NMR spectra of the $[LaL]^+$ cation in the range δ 58–46 were analyzed with the program CAHOS;[23] this can perform a line-shape fitting by simultaneous refinement of several spectral parameters. Mass spectra were obtained with an API 365 PESCIEX spectrometer equipped with an ESI source. Elemental analyses were performed by the Microanalytical Laboratory of the Department of Chemistry of the University of Florence. The hydrobromide $H_2L\cdot5HBr\cdot EtOH$ was prepared according to the published procedure.[4] Hydrated (nitrates) and anhydrous (trifluoromethanesulfonates) lanthanide (La^{III}, Eu^{III}, Lu^{III}) salts (Aldrich) were used as received.

Syntheses

1,7-Bis(carboxymethyl)-4,10-bis(1-methylimidazol-2-ylmethyl)-1,4,7,10-tetraazacyclododecane, H_2L. The pentahydrobromide $H_2L\cdot5HBr\cdot EtOH$ (1.5 g, 1.6 mmol) was dissolved in the minimum amount of water and the resulting solution was then loaded on a DOWEX 50W-X4 cation-exchange resin in the H^+ form[24] and eluted with water followed by 0.5 M NH_3 and then by 1 M NH_3. The ligand was isolated by removing the solvent under reduced pressure from the neutral and the basic solutions. The highly hygroscopic compound may be recrystallized from absolute ethanol and dry toluene. The ligand (300 mg; yield 36%) crystallizes with two molecules of water, $H_2L\cdot2H_2O$. Found: C, 51.7; H, 7.9; N, 21.5. Calc. for $C_{22}H_{40}N_8O_6$: C, 51.6; H, 7.9; N, 21.9%. EI mass spectrum *m*/*z*, relative intensity (assignment, mass): 477.4, 60% (H_2L + H, 477.6). $^{13}C\{^1H\}$ NMR (D_2O, 298 K, $C_M = 2.3 \times 10^{-2}$, pD = 6.5): δ 168.7 (CO_2H), 144.1 (C2 imidazole), 123.1, 122.9 (C4, C5 imidazole), 56.3 (CH_2CO_2H), 51.0, 48.2 (CH_2 macrocycle), 46.9 (CH_2 imidazole) and 33.5 (CH_3 imidazole).

$Na[LnL](CF_3SO_3)_2\cdot3H_2O$ (Ln = La, Eu, Lu). Neat ligand $H_2L\cdot2H_2O$ (0.2 mmol) was added to a solution of $Ln(CF_3SO_3)_3$ (Ln = La, Eu, Lu) (0.2 mmol) in dry MeCN (15 cm^3) and the resulting suspension was warmed (*ca.* 70 °C) for 12 h. After cooling, solid Na_2CO_3 was added and the suspension stirred for 1 h; the solid was eliminated by filtration on a sintered glass. The solution was concentrated to a volume of 5 cm^3 and dry toluene (10 cm^3) added. The resulting solution was kept overnight at 4 °C and the deposited solid was collected; yield 60%. $Na[LaL](CF_3SO_3)_2\cdot3H_2O$ found: C, 29.3; H, 4.0; N, 11.1. Calc. for $C_{24}H_{40}F_6LaN_8NaO_{13}S_2$: C, 29.2; H, 4.1; N, 11.3%. $Na[EuL](CF_3SO_3)_2\cdot3H_2O$; found: C, 28.5; H, 4.3; N, 10.9. Calc. for $C_{24}H_{40}EuF_6N_8NaO_{13}S_2$: C, 28.8; H, 4.0; N, 11.2%. $Na[LuL](CF_3SO_3)_2\cdot3H_2O$; found: C, 27.9; H, 4.2; N, 10.4. Calc. for $C_{24}H_{40}F_6LuN_8NaO_{13}S_2$: C, 28.1; H, 3.9; N, 10.9%.

$Na[LnL](NO_3)_2\cdot3H_2O$ (Ln = La, Eu, Lu). The complexes were obtained through the same procedure used for the trifluoromethanesulfonates by adding the ligand to the lanthanide nitrate dissolved in water (10 cm^3). The pH of the resulting solution was then adjusted to 7.5 by adding Na_2CO_3 dissolved in water. The solid was obtained after addition of *n*-butanol; yield 65%. $Na[LaL](NO_3)_2\cdot3H_2O$; found: C, 32.1; H, 5.2; N, 16.8. Calc. for $C_{22}H_{40}LaN_{10}NaO_{13}$: C, 32.4; H, 5.2; N, 17.2%. $Na[EuL](NO_3)_2\cdot3H_2O$; found: C, 31.6; H, 5.2; N, 16.4. Calc. for $C_{22}H_{40}EuN_{10}NaO_{13}$: C, 31.9; H, 4.7; N, 16.9%. $Na[LuL](NO_3)_2\cdot3H_2O$; found: C, 30.7; H, 5.0; N, 16.0. Calc. for $C_{22}H_{40}LuN_{10}NaO_{13}$: C, 31.1; H, 4.7; N, 16.5%. The ^1H and ^{13}C NMR spectra of the complex cations are not affected by the counter ion in the investigated temperature range. Accordingly, for brevity, only the NMR data of the trifluoromethanesulfonates are reported. The $^{13}C\{^1H\}$ spectra of the compounds exhibit at 298 K a quartet (δ 120.4; J = 316.6 Hz) due to the anion.

$Na[LaL](CF_3SO_3)_2\cdot3H_2O$: NMR ($D_2O$, 278 K, $C_M = 5.1 \times 10^{-2}$, pD = 7.4, J/Hz). $^{13}C\{^1H\}$: δ 180.1 (CO_2^-), 147.5 (C2 imidazole), 126.3, 123.4 (C4, C5 imidazole), 60.7 ($CH_2CO_2^-$), 54.5, 53.8, 51.2, 49.2 (CH_2 macrocycle), 51.8 (CH_2 imidazole) and 33.5 (CH_3 imidazole). ^1H: δ 6.81 (2H, d, J = 1.2, H imidazole), 6.66 (2H, d, J = 1.2, H imidazole), 4.06 (2H, d, J = 16.6, CH_2 acetate), 3.55 (2H, d, J = 16.7, CH_2 acetate), 3.38 (10H, m, CH_3 imidazole, CH_2 macrocycle), 3.26 (2H, d, J = 17.1, CH_2 imidazole), 2.94 (2H, t, J = 12.3, CH_2 macrocycle), 2.80 (2H, t, J = 12.7, CH_2 macrocycle), 2.72 (2H, d, J = 17.1, CH_2 imidazole), 2.33 (6H, m, CH_2 macrocycle) and 2.09 (2H, d, J = 11.9, CH_2 macrocycle).

$Na[EuL](CF_3SO_3)_2\cdot3H_2O$: $^{13}C\{^1H\}$ NMR (D_2O, 275 K, $C_M = 7.8 \times 10^{-2}$, pD = 7.4, J/Hz); isomer in higher amount: δ 190.4 (CO_2^-), 176.3 (C2 imidazole), 114.6, 111.6 (C4, C5 imidazole), 96.2, 91.9, 88.3, 87.2, 86.0, 82.5 (CH_2 macrocycle, acetate and imidazole) and 34.2 (CH_3 imidazole). Isomer in lower concentration: δ 189.4 (CO_2^-), 178.8 (C2 imidazole), 114.4, 112.7 (C4, C5 imidazole), 97.2, 93.5, 83.4, 76.8, 75.5, 60.6 (CH_2 macrocycle, acetate and imidazole) and 30.1 (CH_3 imidazole).

$Na[LuL](CF_3SO_3)_2\cdot3H_2O$: NMR ($D_2O$, 272 K, $C_M = 8.1 \times 10^{-2}$, pD = 7.8, J/Hz). $^{13}C\{^1H\}$: isomer in higher amount: δ 180.5 (CO_2^-), 148.3 (C2 imidazole), 125.2, 124.5 (C5, C4 imidazole), 61.4 ($CH_2CO_2^-$), 55.3, 54.5, 50.9, 49.2 (CH_2 macrocycle), 51.7 (CH_2 imidazole) and 33.8 (CH_3 imidazole). Isomer in lower concentration: δ 182.2 (CO_2^-), 148.9 (C2 imidazole), 126.1, 124.2 (C5, C4 imidazole), 66.7 ($CH_2CO_2^-$), 58.5, 57.6, 56.7, 56.5 (CH_2 macrocycle), 57.1 (CH_2 imidazole) and 33.6 (CH_3 imidazole). ^1H: δ 6.84 (2H, s, H imidazole), 6.57 (0.7H, s, H imidazole, minor isomer), 6.50 (1.3H, s, H imidazole, major isomer), 4.1 (1.3H, d, J = 16.2, CH_2 acetate, major isomer), 3.86 (2H, m), 3.72 (1.3H, d, J = 16.3, CH_2 acetate, major isomer), 3.38 (6H, CH_3 imidazole), 3.20 (5H, m), 2.89 (6H, m), 2.55 (4H, m), 2.34 (4H, m), 1.85 (0.7, m).

Results and discussion

Synthesis of the ligand and of the metal complexes

The ligand 1,7-bis(carboxymethyl)-4,10-bis(1-methylimidazol-

2-ylmethyl)-1,4,7,10-tetraazacyclododecane, H_2L, has been obtained through elution of the pentahydrobromide, $H_2L\cdot5HBr\cdot EtOH$, with NH_3 solutions on a cation exchange resin in the H^+ form. The ligand crystallizes with two molecules of water. Its $^{13}C\{^1H\}$ NMR spectrum in D_2O exhibits one signal for each group of equivalent carbon atoms.

The reaction of hydrated nitrates and anhydrous trifluoromethanesulfonates of lanthanides (La, Eu and Lu) with the ligand yields solid compounds which invariantly contain the species [LnL]Y (Ln = La^{III}, Eu^{III}, Lu^{III}. Y = CF_3SO_3, NO_3), NaY and H_2O in a 1 : 1 : 3 ratio. The solids are very soluble in polar solvents (water, methanol and ethanol). The complex cations are stable in solution for weeks in the range pH 5–10, as expected for such ligands.[25] The $^{13}C\{^1H\}$ and ^1H NMR spectra of nitrate and triflate complexes in D_2O exhibit at the same temperature, in the range of investigated temperatures, resonances which have the same shape and shift. Such behaviour rules out the penetration of the poorly coordinating anions in the inner coordination sphere of the metal.

NMR spectra of the diamagnetic $[LnL]^+$ cations (Ln = La, Lu)

The $^{13}C\{^1H\}$ spectrum of the $[LaL]^+$ cation at 278 K exhibits eleven peaks which have been assigned, taking into account also their changes with the temperature, as follows: δ 180.1 to the carboxylate functionalities, δ 147.5, 126.3 and 123.4 to the carbon atoms of the imidazole ring, δ 60.7 and 51.8 to the methylenic carbon atoms of the acetate and of the imidazole arms, respectively, δ 54.5, 53.8, 51.2 and 49.2 to the ethylenic carbons of the tetraazamacrocycle, and δ 33.5 to the carbon of the methyl group of imidazole. On increasing the temperature the four signals due to the macrocycle broaden (Fig. 1), collapse and then merge to afford at 375 K two resonances at δ 53.2 and 52.5; the signals due to the other carbon atoms remain narrow undergoing a small drift. The proton NMR spectrum of the lanthanum derivative shows eleven resonances at 278 K (see Experimental section) which have been assigned with the aid of the data of a 2D COSY experiment. The imidazole protons appear as a pair of doublets at low field and those of the methyl group yield a singlet at δ 3.38. The protons of the CH_2 moieties bridging the macrocycle and the pendant donor groups yield two pairs of doublets having similar coupling constants (*ca.* 17 Hz): those due to the $CH_2CO_2^-$ occur at δ 4.06 and 3.55, those of the CH_2-imidazole at δ 3.76 and 2.72. Such resonances are typical for two non-equivalent AB systems.[20,24] The ethylenic moieties of the macrocycle present two signals partially buried in the methyl resonance of imidazole, two triplets at δ 2.94 and 2.80 (coupling constant *ca.* 12.5 Hz), overlapping doublets centered at δ 2.33 and a doublet at δ 2.09 ($J = 11.9$ Hz). The chemical shifts of the resonances, occurring in two regions, δ *ca.* 3.0 and 2.33, the multiplicity and the coupling constants which are observed for not overlapping signals are typical for two non-equivalent ABCD systems exhibiting large geminal and axial couplings with the equatorial ones being small. Such data parallel those observed for the DOTA ethylenic groups in the diamagnetic complexes at low temperature.[20,24] By increasing the temperature the three resonances due to the protons of methylimidazole remain narrow, undergoing a low field shift; all the other resonances broaden, collapse, and then merge to afford a spectrum which exhibts at 371 K narrow signals at δ 4.85 and 3.99 for the CH_2 of the dangling groups and two unresolved resonances centered at δ 3.83 and 3.57 due to the ethylenic moieties of the macrocycle.

The ^{13}C NMR spectrum of $[LuL]^+$ cation at 272 K exhibits two distinct sets of resonances (see Experimental section) which clearly show the presence of two isomers in 1 : 2 ratio, as determined from the intensity of the signals due to carbon atoms of the same group. On increasing the temperature all the signals collapse and then merge to afford at 371 K one narrow resonance for each group of chemically equivalent carbon atoms [δ 179.6 (CO_2^-), 148.2, 125.3 124.1 (imidazole carbons), 62.8 and 53.3 (CH_2 acetate and CH_2 imidazole, respectively), 53.6 and 53.4 (CH_2 ethylenic) and 33.4 (CH_3 imidazole)]. The resonances due to the minor isomer broaden quicker as the temperature is increased; at 293 K they have collapsed while the resonances due to the major isomer have undergone only a small broadening. The proton spectrum at 275 K is rather complicated owing to the presence of the two isomers and a complete assignment of the resonances has not been possible; however, some useful points may be outlined. The resonances due to the two hydrogens of the imidazole ring occur at low field: the protons bound to the imidazole C5 which points outside the ligand shell, yield one signal (δ 6.84) having intensity typical for two atoms; the two C4–H which point inside the ligand environment, exhibit two resonances (δ 6.57 and 6.50) and the sum of their intensities corresponds to two protons. Such results point out that the C4–H are in two different magnetic environments which should originate from a different layout of the dangling goups. Several overlapping resonances occur in the range δ 4.16–2.20 and among them a narrow singlet (δ 3.38) is safely assigned to the methyl hydrogens of the imidazole. A COSY experiment has revealed groups of cross-peaks as those observed for the signals of ethylenic moieties of the lanthanum derivative; such data are consistent with two inequivalent ABCD systems. Weaker resonances due to the minor isomer are observed at δ 3.87, 2.23 and 1.75. By increasing the temperature the signals due to the C5–H and CH_3 remain narrow, undergoing a low field shift; all the other resonances broaden, collapse, and then merge to afford a spectrum which exhibits at 371 K narrow signals at δ 4.91 and 3.99 for the CH_2 of the dangling groups and two unresolved resonances centered at δ 3.90 and 3.65 due to the ethylenic moieties of the macrocycle.

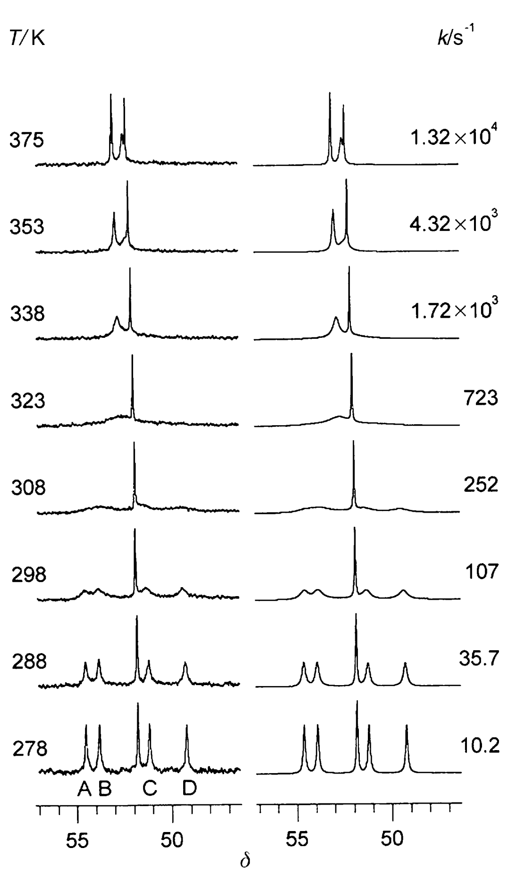


Fig. 1 $^{13}C\{^1H\}$ spectra of the macrocyclic carbons of the $[LaL]^+$ cation at different temperatures (left) compared with spectra calculated by line-shape analysis (right). The simulation has been performed by assuming an ABCD $\rightleftharpoons$ DCBA exchange mechanism.

NMR spectra of the paramagnetic $[EuL]^+$ complex

The low-temperature (275 K) ^{13}C NMR spectrum exhibits twenty-two narrow signals clustering in four regions (δ *ca.* 190–176, 115–112, 97–60 and 34–30; see Experimental section), which have different intensity; they may be clearly grouped, according to their intensity, in two sets, each containing eleven signals, one for two equivalent carbon atoms of the ligand. These data point to the presence in solution of two isomers in a 1 : 1.7 ratio.

The proton spectrum exhibits at 275 K resonances in the range δ+30 to −22; they appear too broad to allow the detection of any coupling pattern. Upon raising the temperature both the ^1H and ^{13}C signals broaden and collapse. The proton spectrum at 371 K, the highest reached temperature, presents a broad signal for each of the chemically equivalent protons of the dangling groups and of the ethylenic moieties. The ^{13}C spectrum at the same temperature exhibits narrow resonances at δ 191.0, 177.4. 120.4, 97.0, 83.2 and 73.8 due to the carbon atoms of the dangling groups and a broad resonance at δ 83.7 due to the ethylenic moieties of the macrocycle that has not reached, as suggested also by the ^1H spectrum, the upper limit form.

The DOTA lanthanide complexes present in solution two isomers having nearly square-antiprismatic and -prismatic geometry, respectively, and their relative amounts change markedly from the lighter to the heavier metal ion. It has been established for the LuDOTA complex[20,24] that the isomer in higher concentration has a geometry approaching the square antiprism, corresponding quite closely to the solid-state structure determined for Eu–,[12] Gd–[13] and Lu–DOTA.[14] On the other hand, the major isomer of the LaDOTA complex has been assigned a square-prismatic structure containing an inverted layout of the acetate arms, as found in the solid-state structure of the LaDOTAM[16] and of $Na[La(HDOTA)La(DOTA)]\cdot 10H_2O$.[15] ^1H and ^{13}C NMR data of the major isomer of the diamagnetic lanthanum and lutetium DOTA complexes have quite similar patterns and differ for a low field shift of the ^{13}C signals on going from the prismatic to the antiprismatic structure.[20]

The ^{13}C NMR spectrum of the present lanthanum derivative at the low-exchange limit exhibits resonances for the acetate and the ethylenic moieties which compare to those of the LaDOTA square-prismatic main isomer. Consequently, an analogous structure may be assigned to the $[LaL]^+$ cation. According to results previously reported,[19,20] the absence of changes in the magnetic environments of the pendant arm carbon atoms in the investigated range of temperatures suggests that an intramolecular exchange between two enantiomers occurs on increasing the temperature. The enantiomerization should proceed through simultaneous intramolecular exchanges: (a) ring inversion and (b) rotation around the NCH_2 pendant arms. The exchange between the two magnetic environments of the NCH_2 ring carbon atoms may be characterized by a four-site line-shape analysis.[23] Typical experimental and calculated ^{13}C NMR spectra for the cation are displayed in Fig. 1. The dependence of the rate constants on the temperature was fitted by the Eyring equation, yielding the parameters $k(298\ \mathrm{K}) = 107\ \mathrm{s}^{-1}$, $\Delta H^\ddagger = 61.4 \pm 1.9\ \mathrm{kJ\ mol}^{-1}$, $\Delta S^\ddagger = -0.4 \pm 5.8\ \mathrm{J\ K}^{-1}\ \mathrm{mol}^{-1}$. These kinetic parameters for the ring inversion compare with those reported by Desreaux for LaDOTA[24] and are significantly higher than those found for lanthanide complexes having four neutral donors on the arms.[19] The high barrier to the ring inversion in the present $[LaL]^+$ cation implies that the ligand cage, once formed, is very tight and shows little flexibility.

The line-shape analysis of the ^{13}C NMR peaks due to the macrocyclic carbon atoms provides kinetic information on the ring inversion only, whatever the rate of rotation of the arms. However, the ^1H NMR spectra show that both ring inversion and arm rotation do occur simultaneously in the temperature range studied, as indicated by the loss of rigidity of the NCH_2CH_2N, $NCH_2CO_2^-$ and $NCH_2C_3N_2H_2Me$ moieties upon increasing the temperature. The measurement of the rate constants for processes (a) and (b) from the ^1H NMR data has not been attempted owing to the complexity of the exchanging system. However, the occurrence of both processes in the temperature range studied indicates that the order of magnitude of their rate constants should not be very different and is further evidence for the interconversion between the two enantiomers as described for complexes with DOTA and L^1.

Among the two isomers of the $[LuL]^+$ complex in solution, that in higher amount has ^{13}C resonances whose shifts parallel those found for the lanthanum derivative and, accordingly, the same nearly prismatic geometry may be assigned; the minor isomer exhibits resonances downfield shifted and these data point to a nearly antiprismatic geometry. According to the results obtained for the lanthanum and the lutetium derivatives, it appears reasonable to assume that the major and the minor isomers of the $[EuL]^+$ cation at low temperature have a prismatic and an antiprismatic geometry, respectively. These results point out that the prismatic geometry is the most stable for the three $[LnL]^+$ cations (Ln = La, Eu, Lu). In this regard the present compounds differ from those with DOTA. The stabilization of the nearly prismatic structure in the $[LnL]^+$ complexes is likely to be related to the two heterocyclic imidazole rings. In fact an analogous prismatic structure made up of eight nitrogens has been found in the sodium[26] and manganese[27] complexes with a pyrazole functionalized tetraazamacrocycle.

Acknowledgements

We acknowledge financial support by the Italian Ministero dell'Università e della Ricerca Scientifica e Tecnologica.

References

1 L. F. Lindoy, in *The Chemistry of Macrocyclic Ligand Complexes*, Cambridge University Press, Cambridge, 1989; R. D. Hancock and A. E. Martell, *Chem. Rev.*, 1989, **89**, 1875; P. V. Bernhardt and G. A. Lawrence, *Coord. Chem. Rev.*, 1990, **104**, 297; D. Parker, K. Pulukkody, T. J. Norman, A. Harrison, L. Royle and C. Walker, *J. Chem. Soc., Chem. Commun.*, 1992, 1441; R. Dhillon, A. K. W. Stephens, S. L. Whitbread, S. F. Lincoln and K. P. Wainwright, *J. Chem. Soc., Chem. Commun.*, 1995, 97; D. Parker and J. A. Williams, *J. Chem. Soc., Dalton Trans.*, 1996, 3613.

2 H. Maumela, R. D. Hancock, L. Carlton, J. H. Reibenspies and K. P. Wainwright, *J. Am. Chem. Soc.*, 1995, **117**, 6698.

3 M. Di Vaira, F. Mani, N. Nardi, P. Stoppioni and A. Vacca, *J. Chem. Soc., Dalton Trans.*, 1996, 2679.

4 M. Di Vaira, F. Mani and P. Stoppioni, *J. Chem. Soc., Dalton Trans.*, 1998, 1879.

5 G. B. Drew, *Coord. Chem. Rev.*, 1977, **24**, 179; I. Murase, I. Ueda, N. Marubayashi, S. Kida, N. Matsumoto, M. Kudo, M. Toyohara, K. Hiate and M. Mikuriya, *J. Chem. Soc., Dalton Trans.*, 1990, 2763; L. H. Tan, M. R. Taylor, K. P. Wainwright and P. A. Duckworth, *J. Chem. Soc., Dalton Trans.*, 1993, 2921.

6 V. Balzani, J.-M. Lehn, J. van de Loosdrecht, A. Mecati, N. Sabbatini and R. Ziessel, *Angew. Chem., Int. Ed. Engl.*, 1991, **30**, 190; D. Parker and J. A. G. Williams, *Chem. Commun.*, 1996, 3613; D. Parker and J. A. G. Williams, *Chem. Commun.*, 1998, 245.

7 D. Parker, *Chem. Br.*, 1994, 833; *Comprehensive Supramolecular Chemistry*, eds. J.-M. Lehn, D. D. Macnicol, J. L. Atwood, J. E. Davies, D. N. Rienhoudt and F. Vogtle, Pergamon, Oxford, 1996, vol. 10, ch. 17.

8 B. Barbier and A. Brack, *J. Am. Chem. Soc.*, 1998, **110**, 6880; Y. Matsumoto and M. Komiyama, *J. Chem. Soc., Chem. Commun.*, 1990, 1050; K. O. Aileen and J. R. Morrow, *Inorg. Chem.*, 1994, **33**, 5036.

9 S. H. Koenig and R. D. Brown, *III Prog. Nucl. Magn. Reson. Spectrosc.*, 1991, **22**, 487.

10 K. Kumar and M. F. Tweedle, *Pure Appl. Chem.*, 1993, **65**, 515.

11 J. R. Morrow and K. O. A. Chin, *Inorg. Chem.*, 1993, **32**, 3357; J. R. Morrow, K. Aures and D. Epstein, *J. Chem. Soc., Chem. Commun.*, 1995, 2431.

12 M. R. Spirlet, J. Rebizant, J. F. Desreux and M. F. Loncin, *Inorg. Chem.*, 1984, **23**, 359.
13 J.-P. Dubost, M. Legar, D. Meyer and M. Schaefer, *C. R. Acad. Sci. Paris, Ser. II*, 1991, **312**, 349.
14 S. Aime, A. Barge, M. Botta, M. Fasano, J. D. Ayala and G. Bombieri, *Inorg. Chim. Acta*, 1996, **246**, 423.
15 S. Aime, A. Barge, F. Benetollo, G. Bombieri, M. Botta and F. Uggeri, *Inorg. Chem.*, 1997, **36**, 4287.
16 J. R. Morrow, S. Amin, C. H. Lake and M. R. Churchill, *Inorg. Chem.*, 1993, **32**, 4566.
17 K. O. A. Chin, J. R. Morrow, C. H. Lake and M. R. Churchill, *Inorg. Chem.*, 1994, **33**, 656.
18 S. Aime, A. S. Batsanov, M. Botta, J. A. K. Howard, D. Parker, K. Senanayake and G. Williams, *Inorg. Chem.*, 1994, **33**, 4696.
19 P. A. Pittet, D. Früh, V. Tissières and J. C. Bünzli, *J. Chem. Soc., Dalton Trans.*, 1997, 895.
20 S. Aime, M. Botta and G. Ermondi, *Inorg. Chem.*, 1992, **31**, 4291.
21 S. Aime, M. Botta, M. Fasano, M. P. M. Marques, C. F. G. C. Geraldes, D. Pubanz and A. E. Merbach, *Inorg. Chem.*, 1997, **36**, 2059.
22 S. I. Kang, R. S. Ranganathan, J. E. Emswiler, K. Kumar, J. Z. Gougoutas, M. F. Malley and M. F. Tweedle, *Inorg. Chem.*, 1993, **32**, 2912.
23 F. Cecconi, C. A. Ghilardi, P. Innocenti, S. Midollini, A. Orlandini, A. Ienco and A. Vacca, *J. Chem. Soc., Dalton Trans.*, 1996, 2821.
24 J. F. Desreux, *Inorg. Chem.*, 1980, **19**, 1319.
25 E. Tóth, E. Brucher, I. Lázár and J. Tóth, *Inorg. Chem.*, 1994, **33**, 4070.
26 B. Cosimelli, M. Di Vaira, F. Mani and P. Stoppioni, *J. Chem. Soc., Dalton Trans.*, 1991, 331.
27 M. Di Vaira, F. Mani and P. Stoppioni, *J. Chem. Soc., Dalton Trans.*, 1992, 1127.