

A Fluxional Lanthanum(III) Polypyridyl Complex. A Nuclear Magnetic Resonance Investigation

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The lanthanum(III) complex of the potentially octadentate polypyridyl ligand 6,6'-bis[bis(2-pyridylmethyl)aminomethyl]-2,2'-bipyridine (**L**) has been prepared. The dynamics of [La(**L**)]Cl₃·4H₂O (**1**) in acetonitrile and methanol solution has been studied by NMR spectroscopy. The spectra were assigned by means of one-dimensional ¹H NMR and two-dimensional COSY spectroscopy. The assignment showed the presence of two pairwise equivalent pyridine rings and a two-fold symmetry in the cation in **1**. The two-dimensional EXSY spectrum revealed a slow interconversion of the two pairs [*k*_{obs} = 0.43(2) s⁻¹ in acetonitrile at 285 K]. The first-order rate constant for the interconversion was determined in the temperature range 270–315 K. This gave the thermodynamic activation parameters $\Delta H^\ddagger = 69(1)$ kJ mol⁻¹ and $\Delta S^\ddagger = -9(2)$ J mol⁻¹ K⁻¹ in acetonitrile and $\Delta H^\ddagger = 71(2)$ kJ mol⁻¹ and $\Delta S^\ddagger = 4(6)$ J mol⁻¹ K⁻¹ in methanol solution.

The search for europium(III)-based luminescent tags is currently an attractive research field, especially in relation to the design of time-resolved fluoroimmunoassays.^{1–6} For this type of application, an europium(III) complex must be strongly emissive in aqueous solution and four requirements must be fulfilled: (a) the ligand must include highly absorbing chromophores close to the first coordination sphere of the metal centre, (b) the energy transfer from the ligand-centred excited state(s) to the metal centre must be fast and efficient, (c) the complex must be stable in aqueous solution and (d) the ligand must exclude water ligands from the first coordination sphere of the metal centre. Recently² we prepared the europium(III) and gadolinium(III) complexes of the potentially octadentate polypyridyl ligand 6,6'-bis[bis(2-pyridylmethyl)aminomethyl]-2,2'-bipyridine (**L**) (Fig. 1). The crystal structure of the gadolinium(III) complex revealed the presence of one uncoordinated, dangling, pyridine group and two chloride ions coordinated to the metal centre.² In aqueous and methanol solution, however, luminescence studies of the europium(III) complex indicate that all the pyridine groups are coordinated to the metal ion.² In order to gain more insight into the solution structure and dynamics of these complexes we have prepared the diamagnetic lanthanum(III) com-

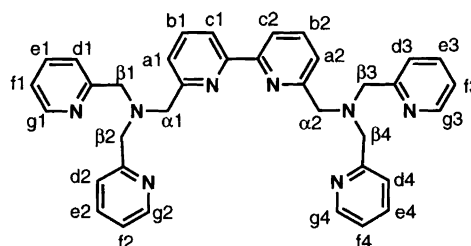


Fig. 1. Structure of the polypyridine ligand, **L**, illustrating the labeling of the protons. The coordinated lanthanum(III) ion is for clarity not shown.

plex of **L**, and here we report a detailed NMR study of this complex in acetonitrile-*d*₃ and methanol-*d*₄ solutions.

Experimental

Materials. The compound **L** was synthesized according to methods described earlier.⁷

Preparation of [La(L**)]Cl₃·4H₂O (**1**).** A mixture of LaCl₃·7H₂O (386 mg, 1.04 mmol), **L** (600 mg, 1.04 mmol), trimethyl orthoformate (8 ml, 74 mmol) and acetonitrile (40 ml) was refluxed for 2 h. The solvent was evaporated off and the yellow–white residue was redissolved in ethanol (20 ml). The solution was filtered and the complex was reprecipitated by addition of diethyl ether (200 ml). The product was washed with diethyl

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ether and air-dried, giving 650 mg (70%) of a white product. Calc. For $C_{36}H_{42}N_8LaCl_3O_4$: C, 48.25; H, 4.72; N, 12.50; Cl, 11.87. Found: C, 48.08; H, 4.65; N, 12.37; Cl, 11.41. UV (CH_3CN , λ_{max}/nm , $\epsilon_{max}/M^{-1}cm^{-1}$): (316, 10.0×10^3), (262, 17.1×10^3).

Physical methods

NMR spectroscopy. One-dimensional 1H spectra and a two-dimensional COSY spectrum were recorded on a Varian Unity 400 MHz spectrometer. One-dimensional 1H spectra were recorded at 253, 273, 298 and 323 K on a solution of complex **1** in acetonitrile. Each spectrum was recorded with a spectral width of 6 kHz, an acquisition time of 3.744 s and a total recording time of 2 min. A one-dimensional spectrum was recorded at 298 K on a solution of complex **1** in methanol with the same parameters. A COSY experiment⁸ was recorded at 298 K on the solution of complex **1** in acetonitrile. The spectra were referenced to the residual 1H signal of the solvent methyl group at 1.95 and 3.35 ppm for acetonitrile- d_3 and methanol- d_4 , respectively.

Two-dimensional EXSY-spectra⁹ were recorded on a Varian Unity-Inova 500 MHz spectrometer. The spectra were recorded with two transients for each complex data point in the t_1 dimension according to the States-TPPI phase-cycling scheme.¹⁰ Each EXSY spectrum was recorded with 320 complex points in the t_1 dimension and 320 complex points in the t_2 dimension and with a spectral width of 6 kHz in both dimensions. The pre-scan delay was 6.0 s. A series of 8 EXSY spectra with varying exchange delays were recorded for each of the four temperatures 270, 285, 300 and 315 K for each solution condition. The exchange delays for the series recorded at 270 K were 0.16, 0.4, 0.7, 1.0, 2.0, 3.0, 5.0 and 8.0 s. For the series recorded at 285 and 300 K exchange delays were 0.12, 0.16, 0.2, 0.4, 0.7, 1.0, 2.0 and 5.0 s. Finally, for the series recorded at 315 K, the exchange delays were 0.04, 0.08, 0.16, 0.4, 0.7, 1.0, 2.0 and 5.0 s. The total recording time of all 64 EXSY spectra were approximately 4.5 days.

In the NMR experiments the concentration of complex **1** was in the range 0.002–0.015 M.

Least-squares fitting. Estimation of exchange rates: The signal heights of the two diagonal signals and the two exchange cross peaks corresponding to the two exchanging forms of H^g on the pyridine rings were measured in each series of EXSY spectra. The corresponding 32 signal heights for each series of EXSY spectra of the complex in acetonitrile solution were fitted to the analytical expression for the general two-site exchange model¹¹ by means of a non-linear least-squares minimization procedure.¹² In each calculation, five parameters were estimated including the exchange rate constant, k_{BA} , between the two sites A and B, the longitudinal relaxation rates for each site, $R_1(A)$ and $R_1(B)$, and the equilibrium magnetization on each site, $M_0(A)$ and $M_0(B)$. The exchange rates at 315 K for the methylene protons were estimated

in the same fashion. In order to avoid errors introduced by the different linewidths of the resonances in the EXSY series of complex **1** in methanol solution, the heights of the two exchange signals and the geometric average of the heights of the diagonal signals, $(h_A h_B)^{1/2}$, were fitted to the two-site exchange model with the constraints that $M_0(A) = M_0(B)$ and $R_1(A) = R_1(B)$. Thus, the three parameters k_{BA} , $M_0(A)$ and $R_1(A)$ were estimated from 24 signal heights for each EXSY series.

The uncertainties in the signal heights were estimated as $[\sum \{h_i(\text{exp}) - h_i(\text{calc})\}^2 / (n - n_p)]^{1/2}$, where $h_i(\text{exp})$ and $h_i(\text{calc})$ are the i th experimental and calculated signal height, respectively. The sum goes over all signal heights ($n = 32$ in acetonitrile and $n = 24$ in methanol), and n_p is the number of estimated parameters in the least-squares calculation ($n_p = 5$ in acetonitrile and $n_p = 3$ in methanol). The uncertainties of the estimated parameters were subsequently calculated from the covariance matrix. The least-squares calculations showed good convergence, and the results were insensitive to the selection of initial parameters.

Other physical measurements. Optical absorption spectra were recorded on a Cary 5E UV-VIS-NIR spectrophotometer.

Results and discussion

Synthesis and optical absorption spectra. Complex **1** was prepared by the method reported earlier.² The optical absorption spectrum of complex **1** in acetonitrile was very similar to the spectrum in methanol and to the spectra of the europium(III) and gadolinium(III) complexes of **L** in methanol.²

Assignment of the NMR spectra. The resonance assignment for the complex in acetonitrile solution at 298 K is summarized in Table 1 and the labeling of the protons in **L** is shown in Fig. 1. For the spectra recorded in acetonitrile solution (Fig. 2), the four pyridine groups exist in two chemically distinct environments with two pyridine groups in each environment. This is evident in the spectra where the protons H^d , H^e , H^f and H^g on the pyridine groups give rise to two sets of signals of equal intensity (Fig. 2). The four pyridine groups are accordingly pairwise chemically equivalent. However, the aromatic part of the spectrum does not indicate which of the pyridine groups are chemically equivalent. The two pyridine rings of the bipyridine group are symmetry related, as the symmetric protons on the rings are chemically equivalent. The aromatic protons were assigned on the basis of the one-dimensional spectra by analysis of the spin-spin coupling multiplets and by comparison with chemical shift values for other pyridine compounds. The assignment was confirmed by inspection of the COSY spectrum (Fig. 2).

The six methylene groups give rise to three AX spin systems of equal intensity, and the methylene groups must consequently be pairwise symmetric. Furthermore,

Table 1. Chemical shift (δ) assignment of the ^1H NMR spectrum of **1** in acetonitrile at 298 K.^{a,b}

Nuclei	δ (ppm)
H ^{a1} , H ^{a2}	7.58
H ^{b1} , H ^{b2}	7.88
H ^{c1} , H ^{c2}	7.74
H ^{d1} , H ^{d3}	7.58
H ^{d2} , H ^{d4}	6.84
H ^{e1} , H ^{e3}	7.90
H ^{e2} , H ^{e4}	7.40
H ^{f1} , H ^{f3}	7.11
H ^{f2} , H ^{f4}	6.77
H ^{g1} , H ^{g3}	8.59
H ^{g2} , H ^{g4}	8.34
H ^{α1} , H ^{α2}	4.16
H ^{α1'} , H ^{α2'}	5.94
H ^{β1} , H ^{β3} (or H ^{β2} , H ^{β4})	3.90
H ^{β1'} , H ^{β3'} (or H ^{β2'} , H ^{β4'})	4.12
H ^{β2} , H ^{β4} (or H ^{β1} , H ^{β3})	4.13
H ^{β2'} , H ^{β4'} (or H ^{β1'} , H ^{β3'})	5.86

^aThe chemical shifts are referenced to TMS relative to the residual ^1H signal in acetonitrile at 1.95 ppm. ^bThe unprimed and primed methylene protons refer to chemically (and magnetically) inequivalent protons bound to the same carbon atom and do not refer to a particular stereo-specific assignment.

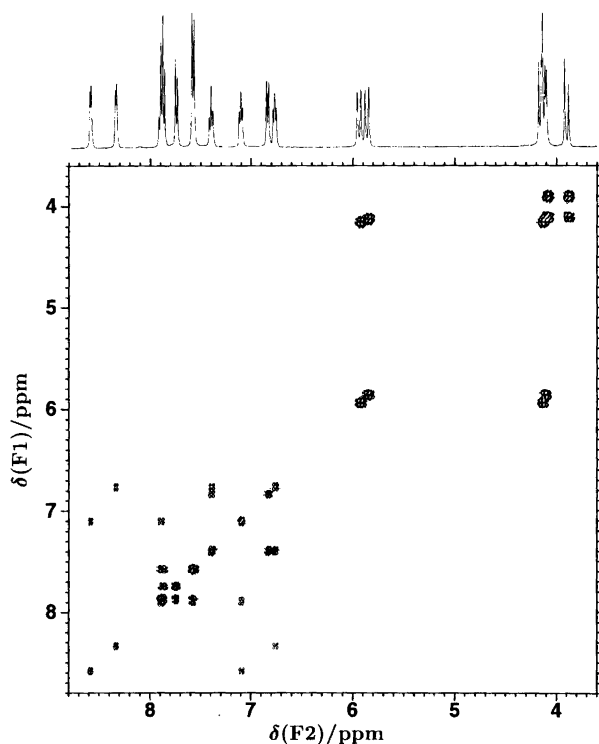


Fig. 2. One-dimensional ^1H NMR and COSY spectrum of complex **1** in acetonitrile solution at 298 K.

the pairs of symmetric methylene groups must comprise ($\alpha 1$, $\alpha 2$), ($\beta 1$, $\beta 3$) and ($\beta 2$, $\beta 4$), and they thereby resolve the symmetry relationship of the pyridine groups which must correspond to the methylene groups (Fig. 1). Thus,

pyridine groups 1 and 3 must be symmetry-related, and so must pyridine groups 2 and 4.

At 323 K, the signals in the one-dimensional spectrum corresponding to the protons on the four pyridine groups and the six methylene carbons are broadened. This indicates slow exchange between the two pairs of symmetric pyridine groups. The exchange broadening of the H ^{α 1} and H ^{α 1'} protons (and the symmetry-related protons H ^{α 2} and H ^{α 2'}) suggests that the primed and unprimed protons exchange their chemical environment in the exchange process. This is confirmed by the observation of an exchange cross peak in the EXSY spectrum (Fig. 3) between the primed and unprimed protons for one of the methylene groups. The two other pairs of methylene groups display an exchange cross peak connecting the two groups and confirming the assignment of the methylene protons. The absence of exchange broadening of the signals corresponding to the protons on the bipyridine group is consistent with the pairwise chemical equivalence of these protons. In addition to the exchange signals, the EXSY spectra contain several weak negative signals corresponding to inter-proton nuclear Overhauser effects (NOEs). A NOE correlates the H ^{α 1}/H ^{α 2} methylene protons with the H ^{α 1}/H ^{α 2} protons of the bipyridine. All other NOEs are between a vicinal proton within the bipyridine, the pyridine rings and between the geminal protons of the methylene groups. At long exchange delays, exchange-relayed NOE signals are also observed. No NOE correlations are observed between the beta

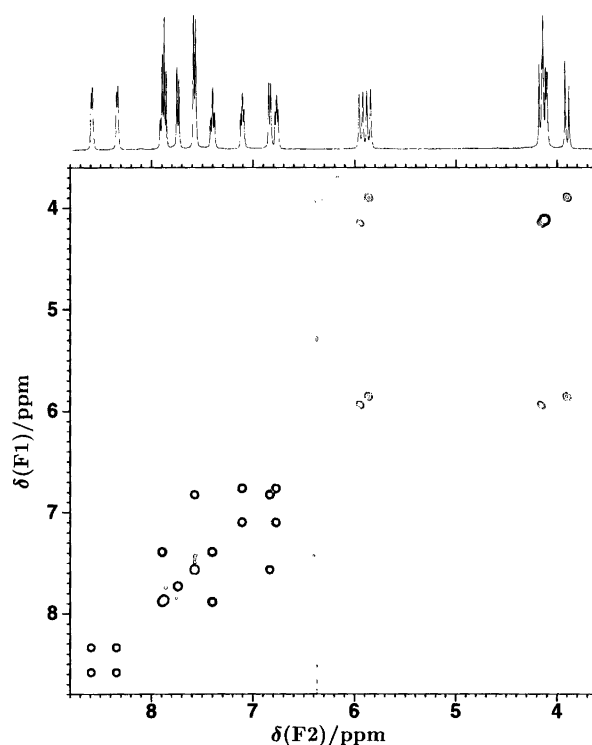


Fig. 3. The EXSY spectrum recorded of the complex **1** in acetonitrile solution at 300 K with an exchange delay of 1.0 s.

methylene protons and the protons on either the bipyridine or the pyridine rings.

The one-dimensional spectrum recorded of the complex in methanol solution is very similar to the spectrum recorded in acetonitrile solution except for a number of weak and broadened signals superimposed on the aromatic region. The EXSY spectra reveal that these signals correspond to at least four different minor forms of the pyridine rings, which are in slow to intermediate exchange with each other and in slow exchange with the two major forms corresponding to the two forms present in acetonitrile solution. As a consequence, these EXSY spectra display a complex network of exchanging signals.

Exchange rates in acetonitrile. For the spectra (Figs. 2 and 3) recorded in acetonitrile solution, the signals corresponding to the two pairs of protons H^{g1} , H^{g3} and H^{g2} , H^{g4} are particularly well resolved within the examined temperature range and have been chosen for the estimation of the exchange rate between the two forms of the pyridine groups. An example of a least-squares fit is shown in Fig. 4, and Table 2 summarizes the results of

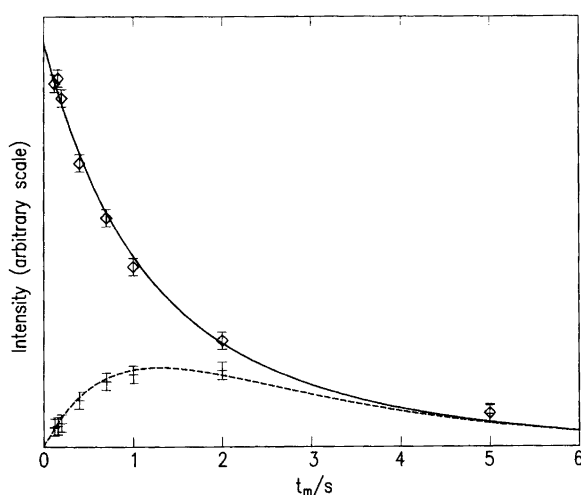


Fig. 4. Signal heights for one of the diagonal signals (\diamond) and one of the exchange signals (+) vs. the exchange delay (t_m) for the EXSY spectrum recorded of the complex in acetonitrile solution at 315 K. The error bars represent the estimated uncertainty (see text) and the curves are calculated from the estimated parameters.

the least-squares calculations. The exchange rates are accurately determined at all four temperatures and span two orders of magnitude over the temperature range. Furthermore, the exchange rates were found to be independent of the concentration of **1** in the range 0.002–0.015 M. The ratio of the equilibrium magnetizations, $M_0(1,3)/M_0(2,4)$, is close to unity, in good agreement with two equally populated sites. Using the rate constants listed in Table 2 the activation parameters ΔH^\ddagger and ΔS^\ddagger for the exchange could be calculated¹³ as 69(1) kJ mol⁻¹ and -9(2) J mol⁻¹ K⁻¹, respectively. The exchange rate for the two pairs of chemically equivalent methylene groups has been estimated from the EXSY spectrum recorded at 315 K to be 6.9(3) s⁻¹. This is identical to the exchange rate of the pyridine rings within the experimental uncertainty. Furthermore, the exchange rate of the two pairs of equivalent α -methylene protons, ($H^{\alpha1}$, $H^{\alpha2}$) and ($H^{\alpha'1}$, $H^{\alpha'2}$), has been estimated from the EXSY spectrum recorded at 315 K to be 7.06(7) s⁻¹, which also is identical to the exchange rate of the pyridine rings within the experimental uncertainty. The very similar exchange rates measured for the different pairs of exchanging protons suggests that the exchange process is a two-site process with a single rate-limiting step.

Exchange rates in methanol. The presence of several minor populations of the pyridine groups, which are in slow exchange with the two major populations of the pyridine groups in methanol solution significantly complicates the analytical description of the exchange processes. For an exact treatment, it is necessary to consider all possible exchange processes as in the relaxation and exchange matrix approaches.¹¹ A further complication arises because the signals corresponding to the different populations display significantly different linewidths and consequently are difficult to quantify accurately. In order to obtain an approximate estimate of the exchange rates between the two major forms of the pyridine groups in methanol solution, the simple two-site exchange model was used to fit the signal heights of the exchange cross-peaks between the two major forms, together with the geometric average of the signal heights of the corresponding diagonal signals, with the constraints that $M_0(A) = M_0(B)$ and $R_1(A) = R_1(B)$. The two constraints are justified by the results obtained from the data set

Table 2. Exchange rates [$k(2,4 \rightarrow 1,3)$], population ratios [$M_0(1,3)/M_0(2,4)$] and longitudinal relaxation rates (R_1) for the proton pairs H^{g1} , H^{g3} , and H^{g2} , H^{g4} in acetonitrile solution and exchange rates and longitudinal relaxation rates for the same proton pairs in methanol solution.^a

T/K	Acetonitrile				Methanol	
	$k(2,4 \rightarrow 1,3)/s^{-1}$	$M_0(1,3)/M_0(2,4)$	$R_1(1,3)/s^{-1}$	$R_1(2,4)/s^{-1}$	$k(2,4 \rightarrow 1,3)/s^{-1}$	$R_1(1,2,3,4)/s^{-1}$
270	0.074(4)	0.99(3)	0.475(9)	0.455(8)	0.170(10)	0.89(3)
285	0.43(2)	0.94(2)	0.40(3)	0.46(3)	0.97(8)	0.74(6)
300	1.78(5)	0.95(2)	0.24(7)	0.45(7)	4.4(1)	0.53(2)
315	7.0(1)	0.99(1)	0.4(2)	0.4(2)	16.1(5)	0.45(1)

^aNumbers in parentheses are estimated standard deviations in the last significant digits.

obtained in acetonitrile solution and serve to reduce the number of parameters one is required to estimate in the least-squares procedure. Together with the symmetric processing of the EXSY spectra in the two dimensions, the fitting of the geometric average of the diagonal signals instead of the explicit diagonal signal heights compensates for the errors otherwise introduced by the different linewidths of the resonances corresponding to the two exchanging forms. The two-site exchange model does not represent an exhaustive model for the description of exchange between the two major forms in methanol, and the estimated exchange rates may contain contributions from spin diffusion. However, the model may serve as a first-order approximation. The estimated exchange rates, summarized in Table 2, give the activation parameters $\Delta H^\ddagger = 71(2) \text{ kJ mol}^{-1}$ and $\Delta S^\ddagger = 4(6) \text{ J mol}^{-1} \text{ K}^{-1}$.

Structural and kinetic models. The two structural models (a) and (b) shown in Fig. 5 are both consistent with the presence of two pairwise equivalent pyridine groups and a symmetric bipyridine. In model (a) the complex is chiral and has a C_2 -axis, whereas the complex has a mirror plane in model (b). In both models solvent and/or chloro ligands may also be bound to the metal centre (in a way that still retains the two-fold symmetry). The data do not allow a distinction between the two models. In Fig. 5 it is suggested that ligand **L** acts as an octadentate ligand. However, the corresponding models in which one of the pyridine pairs is more loosely coordinated to the metal centre, and in the extreme case dangling uncoordinated with **L** acting as a hexadentate ligand, are equally consistent with the presence of two pairwise equivalent pyridine groups and a symmetric bipyridine.

The symmetry of the bipyridine and the observation of a single exchange rate for all measured exchange

processes is consistent with a kinetic model in which the two pairs of chemically equivalent pyridine rings simultaneously exchange chemical environment (with the rate constant $1/2k_{\text{obs}}$ for a particular pyridine ring), or where the interchange of two of the pyridine groups (with the rate constant k_{obs}) is followed by a rapid interchange of the two others. This kinetic model can readily be explained within the framework of the two structural models (a) and (b) by a conformational change leading to a change of chirality in the case of model (a) and to a mirror-image conversion through a plane orthogonal to the symmetry plane of the complex in the case of model (b). In the case of an octadentate ligand, neither of the two exchange models requires the breaking or formation of bonds between the ligand, and in the case of a hexadentate ligand two coordination bonds must be broken and reformed. Both models (a) and (b) explain the observation that the primed and unprimed α -methylene protons exchange with the same rate as the pyridine rings. Thus, in the case of model (a), the change in the chirality of the complex will interchange the two inequivalent methylene protons, and in the case of model (b), the mirror-image conversion through a plane orthogonal to the symmetry plane of the complex will have the same effect.

Concluding remarks

This investigation shows that the cation in complex **1** has two-fold symmetry in acetonitrile and methanol solution. The presence of minor amounts of other species in methanol solution may be due to the stronger coordinating ability of the methanol molecules compared to the acetonitrile molecules yielding minor amounts of more or less solvated cations. If the ligand, **L**, coordinates hexadentately the observed interconversion between the two pairs of pyridine groups is thus a substitution of coordinated pyridine groups with uncoordinated pyridine groups. It should be noted that in such case this occurs with a rate several orders of magnitudes lower than the rates usually reported for substitution of unidentate ligands on the lanthanide ions (10^5 – 10^9 s^{-1}).¹⁴ If the ligand is octadentate the observed interconversion could be either a concerted twist of the cation in **1** or it could be associated with a chloro/solvento ligand exchange. The thermodynamic activation parameters of such a bimolecular exchange would, however, be expected to be solvent dependent and the exchange rates would be dependent of the concentration of **1** in contrast to our findings.

With this background, and bearing in mind the previous² luminescence studies of $[\text{Eu}(\text{L})]^{3+}$ in methanol (and aqueous) solution, where the number of solvent molecules coordinated to the metal centre were found to be ~ 0.5 , we suggest that the ligand is octadentately coordinated. Regarding model (a) vs. model (b) it is noteworthy that the cation in the gadolinium(III) complex of **L** was indeed found to be chiral, and that the unit cell contained

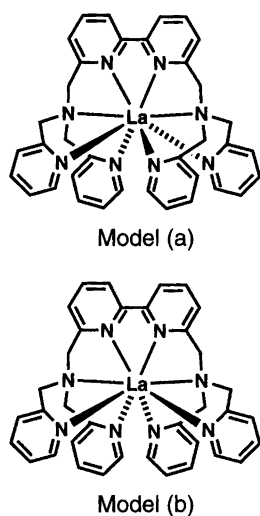


Fig. 5. Suggested structural models for complex **1** in acetonitrile solution having a C_2 -axis [model (a)] or a mirror plane [model (b)]. Possible solvent and/or chloro ligands are not shown.

two cations of opposite chirality.² With the reservation in mind that the structure of the complex in the solid state does not necessarily reflect the structure in solution and that the ionic radius for the lanthanum(III) ion is 0.09 Å larger than for the europium(III) ion,¹⁵ we suggest that an acetonitrile or methanol solution of **1** consists of a racemate of two interconverting enantiomers of which one is shown as model (a) in Fig. 5.

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