^{139}La NMR Kinetic Study of Lanthanum(III) Complexation with Acetohydroxamic Acid

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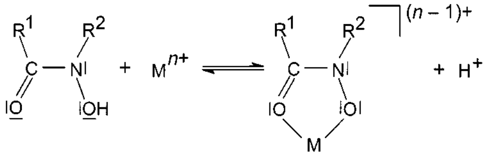
Keywords: Lanthanum / NMR spectroscopy / Kinetics / Reaction mechanisms

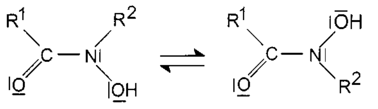
The application of ^{139}La NMR spectroscopy to kinetic and equilibrium studies of the substitution of coordinated water by acetohydroxamic acid (HA) is described. The reaction of La^{3+} with HA can be represented by the following equation (with equilibrium constant K_1): $La^{3+} + HA \rightleftarrows La(A)^{2+} + H^+$ (1). The following equilibrium parameters were calculated from the ^{139}La NMR chemical shift of the equimolar reactants measured as a function of acidity and temperature: $K_1(298) = 2.36(8) \cdot 10^{-4}$, $\Delta_r H_1 = -28(1)$ kJ·mol^{-1}, $\Delta_r S_1 = -162(4)$ J·K^{-1}·mol^{-1}. The kinetics of the reaction between La^{3+} and HA can be represented by the following equations: $La^{3+} + HA \rightleftarrows La(A)^{2+} + H^+$ (11) and $La^{3+} + A^- \rightleftarrows La(A)^{2+}$ (12). The complexation rate constants were calculated from the line widths of the corresponding signals as a function of acidity and temperature: $k_{11}(298\,K) = 1.54(4) \cdot 10^6$ M^{-1}·s^{-1}, $\Delta H^{\ddagger}_{11} = 70(14)$ kJ·mol^{-1} and $\Delta S^{\ddagger}_{11} = +108(47)$ J·K^{-1}·mol^{-1}, k_{12} (298 K) = 1.6 10^{10} M^{-1}·s^{-1}, $\Delta H^{\ddagger}_{12} = 35(6)$ kJ·mol^{-1} and $\Delta S^{\ddagger}_{12} = +68(20)$ J·K^{-1}·mol^{-1}. The spin-spin relaxation times of La^{III} in the aqua ion and the hydroxamato complex are 4.36(4) ms and 54(1) µs at 298 K, respectively.

Introduction

The rare earth metal cations are widely used in industry[1] and medicine.[2] Due to the "hard" character of the lanthanum(III) ion, it is capable of forming stable complexes with "hard" ligands that contain oxygen electron-donor atom(s) within their functional groups. It also forms stable complexes with hydroxamic acids [$R^1C(=O)N(OH)R^2$], coordinating in a bidentate manner through the two oxygen atoms of the hydroxamate group.[3] Hydroxamic acids are weak organic acids with p$K_a \approx 9$, which release one proton per coordinated hydroxamato group as shown in the following reaction.

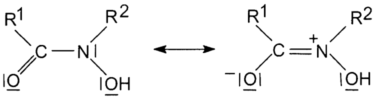


Hydroxamic acids are believed to exist in the two forms shown below, evidence for the presence of these forms and their isomerization is confirmed by NMR spectroscopic data.[4–6]



cis *trans*

The room-temperature isomerization of *N*-methylacetohydroxamic acid (≡ NMHA; $R^1 = R^2 = CH_3$) from the *trans* to the (chelation kinetically appropriate) *cis* form is characterized by a rate constant of ca. 3 s^{-1}. The magnitude of this rate constant indicates a partial double bond character of the hydroxamate C−N bonds, which can be explained by the two extreme resonance structures of the hydroxamic acids shown by structures **Ia** and **Ib**.[7–9]



Ia **Ib**

As the electron-donor capability of R^2 increases, the form **Ib** predominates. This form bears a partial negative charge on the carbonyl oxygen atom, which results in an increased stability of the formed metal complex. The crystallographic data show that the more stable the ferric hydroxamate complex, the shorter the Fe−O(C) bond in the complex, probably due to the emerging negative charge on the carbonyl oxygen atom.[10]

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To date, only two papers (from our laboratories) have been devoted to the kinetics of the complexation of La^{III} with hydroxamic acids.[5,6] We have recently proposed that a slow *trans→cis* isomerization of *N*-alkylhydroxamic acids is the rate-determining step for their chelation to La^{3+} ions. The observed complexation processes were followed on the same time scale as was the isomerization of the free ligands. On the other hand, when R^2 is an H atom, as in HA, the complexation rate was found to be extremely fast, exceeding the limits of the stopped-flow mixing time. In order to investigate the complexation of La^{3+} with HA, it was necessary to utilize a kinetic technique that is not limited to such a long time-scale. ^{139}La NMR has already been successfully used as a tool for determining rate constants in kinetic studies involving complex-formation reactions.[11] In this study, we extend our previous investigations by presenting kinetic and equilibrium studies of the complexation of La^{3+} with HA ($R^1 = CH_3$; $R^2 = H$) in aqueous medium. The study was accomplished by observing ^{139}La NMR line-broadening and the chemical-shift change as a function of temperature, acidity and concentration of the reactants.

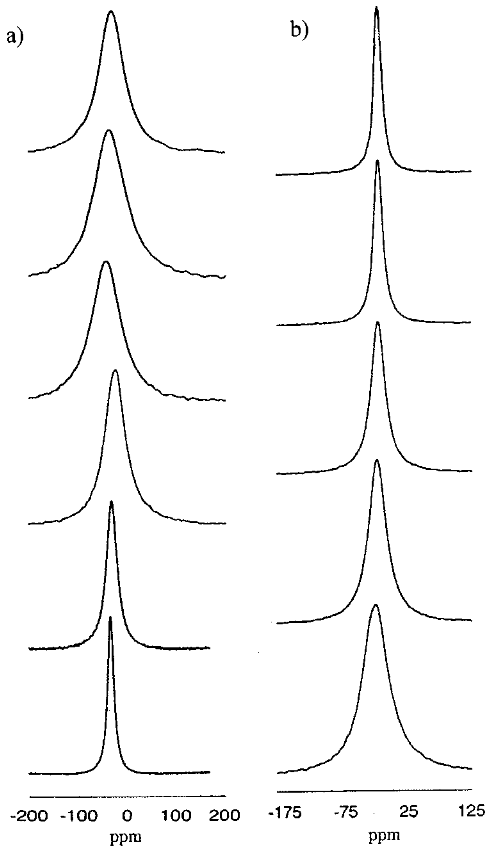

Figure 1. (a) ^{139}La NMR spectra of 0.2 M $La(ClO_4)_3$ and 0.2 M acetohydroxamic acid in 20% (w/w) D_2O at 298 K at $p[H^+] = 2.48$ (bottom), 3.49, 3.99, 4.47, 4.89, and 5.46 (top); (b) ^{139}La NMR spectra of 0.2 M $La(ClO_4)_3$ and 0.2 M acetohydroxamic acid in 20% (w/w) D_2O ($p[H^+] = 3.71$) at 278 K (bottom), 288 K, 298 K, 328 K, and 338 K (top)

Results and Discussion

Figure 1(a) shows the ^{139}La NMR spectra of 0.2 M solutions of $La(ClO_4)_3$ and acetohydroxamic acid at 298 K as a function of $p[H^+]$. The recorded spectra are characterized by a one-resonance peak, which broadens as the $p[H^+]$ increases.[12] The spectra also exhibit a temperature dependence, which is shown for the same reactants at $p[H^+] = 3.71$ in Figure 1(b).

Since the UV-spectroscopic data under the employed conditions indicate a complexation reaction, the occurrence of only one peak in the recorded spectra reveals that lanthanum nuclei exchange fast on the NMR time-scale between two different environments, i.e. the aqualanthanum(III) ion and mono(acetohydroxamato)lanthanum(III) complex. In other words, reaction (1) lies in the so-called "fast-exchange region".

In the acidity range used, neither the hydrated La^{3+} ions nor HA deprotonate considerably in aqueous solutions; for both reactants $pK_a \geq 9$.[13,14] In equimolar solutions of the reactants, the only expected species formed is a monohydroxamato complex in which acetohydroxamate is chelated in a bidentate manner through two oxygen atoms of hydroxamate.[3] The formation of such a complex is represented by Equation (1), which is related to the equilibrium constant, $K_1 = [La(A)^{2+}]\cdot[H^+]\cdot[La^{3+}]^{-1}\cdot[HA]^{-1}$, where the terms in brackets represent the molar concentrations, HA is $CH_3C(=O)N(H)OH$ and $La(A)^{2+}$ is $La[CH_3C(=O)N(H)O]^{2+}$ (coordinated water molecules are omitted for clarity).

$$La^{3+} + HA \rightleftarrows La(A)^{2+} + H^+ \tag{1}$$

The modified Bloch equation for a two-site exchange has been solved by Leigh[15], and for the reaction system studied, the relaxation rate ($1/T_2$) is described by Equations (2) to (9).

$$1/T_2 = A_2 \pm \{[G + (G^2 + H^2)^{1/2}]/2\}^{1/2} \tag{2}$$

$$A_2 = (1/\tau_{2a} + 1/\tau_{2b})/2 \tag{3}$$

$$G = (1/\tau_{2a} - 1/\tau_{2b})^2/4 + 1/\tau_A\tau_B - (\Delta\omega_{AB}/2)^2 \tag{4}$$

$$H = 0.5\cdot(1/\tau_{2a} - 1/\tau_{2b})\,\Delta\omega_{AB} \tag{5}$$

$$1/\tau_{2a} = 1/T_{2A} + 1/\tau_A \tag{6}$$

$$1/\tau_{2b} = 1/T_{2B} + 1/\tau_B \tag{7}$$

$$\Delta\omega_{AB} = \Delta\nu_{La^{3+}} - \Delta\nu_{La(A)^{2+}} \tag{8}$$

$$p_A = \tau_A/(\tau_A + \tau_B) = p_{La^{3+}};\ p_B = \tau_B/(\tau_A + \tau_B) = p_{La(A)^{2+}} \tag{9}$$

In these equations, A and B are the above-mentioned two different environments, $1/T_{2A}$ and $1/T_{2B}$ are the intrinsic relaxation rates in the absence of the exchange, τ_A and τ_B are the residence times and p_A and p_B are the molar fractions of lanthanum in the sites A and B, respectively; $\Delta\omega_{AB}$ is the difference in chemical shift of the two sites in the absence of exchange, i.e. $\Delta\nu_A - \Delta\nu_B$. Since the observed relaxation rate ($1/T_2$) was found to depend linearly on the "free" ligand concentration, as shown in Figure 2, Equation (6) had to be modified to include the first-order term with respect to the concentration of HA, $\tau_A^{-1} = k$ [HA].

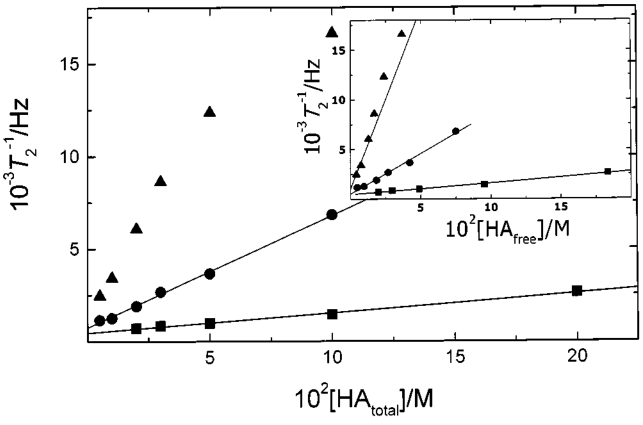

Figure 2. The observed ($1/T_2$) as a function of the total HA concentration at: − solid squares − p[H$^+$] = 3.74(2), − solid circles − p[H$^+$] = 4.85(2), − solid triangles − p[H$^+$] = 5.74(1); conditions: temperature 298 K, ionic strength 1.2 M (perchlorate), equimolar [La(ClO$_4$)$_3$]$_{total}$ and [HA]$_{total}$ = 0.005−0.2 M; the inset shows the observed ($1/T_2$) as a function of the calculated "free" HA concentration, under the same experimental conditions

The above equations show that in order to calculate the kinetic parameters for the La^{III} complexation reaction, it is necessary to accurately estimate p_A, p_B, and the concentration of free HA under the experimental conditions employed. The estimates were made using the equilibrium parameters for reaction (1) obtained from the experimentally determined temperature and p[H$^+$] dependent ^{139}La chemical shift, seen in Figure 3. The chemical shift of the ^{139}La NMR resonance for equimolar solutions containing lanthanum perchlorate and acetohydroxamic acid is mainly determined by temperature and by the composition of the La^{III} inner coordination sphere, which depends on p[H$^+$]. The observed chemical shift in the reaction mixture can be regarded as a weighted average of the shifts related to the La^{3+} and La(A)$^{2+}$ species, using the mol fractions as a weighting factor for each species.

$$\Delta\nu_{obs.} = \Delta\nu_{La^{3+}} \cdot p_{La^{3+}} + \Delta\nu_{La(A)^{2+}} \cdot p_{La(A)^{2+}} \quad (10)$$

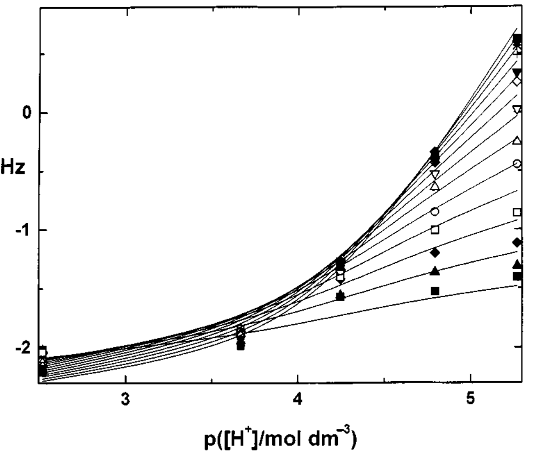

Figure 3. The temperature and p[H$^+$] dependencies of the ^{139}La chemical shift of 0.2 M La(ClO$_4$)$_3$ and 0.2 M acetohydroxamic acid in 20% (w/w) D$_2$O; the lines drawn are the theoretical ones calculated using the optimized parameters of Equation (10); the temperature increment between the experimental series is 5 K, the solid squares corresponding to the lowest temperature, 278 K

For each experimental data point the species concentrations were calculated from the known total concentration of each reactant and the value of K_1 in the temperature range used. A nonlinear least-square fitting procedure[16] was applied for the optimization of the parameters defined in Equation (10) to the experimental data points shown in Figure 3, taking into account the temperature dependent behavior of both the chemical shifts and the equilibrium constant. The following equation $K_1(T) = K_1(298) \times \exp[\Delta_rH_1(T - 298)/298RT]$ describes the relationship between temperature and the equilibrium constant, where Δ_rH_1 is the reaction enthalpy for reaction (1). During the fitting procedure, the distribution of species was calculated simultaneously for each experimental point by a Newton−Raphson algorithm[17] used for solving a set of homogeneous differential equations. The temperature dependence of the chemical shift for the La^{3+} ion was found to be concentration-independent. Within the temperature range used, the experimentally determined $\Delta\nu_{La}{}^{3+}$ is found to be satisfactorily described by the linear relationship $\Delta\nu_{La}{}^{3+}(T)$ Hz = $-2.18(2)\cdot10^3$ Hz − 3.3(3) Hz·K^{-1} × (T − 298) K (see Supporting Information, Figure S1).[18] Under the experimental conditions used, full complexation could not be achieved (see Supporting Information, Figure S2), hence, the experimental determination of the temperature-dependent nature of $\Delta\nu_{La(A)}{}^{2+}$ is impossible.[19] Therefore, the parameters describing the dependence had to be adjusted during the fitting procedure. For the La^{3+} ion, a linear temperature dependence of $\Delta\nu_{La(A)}{}^{2+}$ within the temperature range used, is proposed,. Fitting Equation (10) to 87 data points collected at various temperatures and proton concentrations resulted in the following parameters: $\Delta\nu_{La(A)}{}^{2+}(T)$ Hz = $2.5(3)\cdot10^2$ Hz + $7.9(2)\cdot10^1$·Hz·K^{-1} × (T − 298) K, $K_1(298) = 2.36(8)\cdot10^{-4}$, $\Delta_rH_1 = -28(1)$ kJ·mol^{-1}, and $\Delta_rS_1 = -162(4)$ J·K^{-1}·mol^{-1}.

From these parameters a chemical shift of δ = 44 is calculated for ^{139}La in the La(A)$^{2+}$ complex relative to the aqua ion at 298 K. This is within the range expected for the coordination of the hydroxamate oxygen atoms to the central lanthanum ion.[20] The K_1(298) value obtained, which was confirmed by potentiometric titration under the same experimental conditions, differs from the reported value of $6.17\cdot10^{-5}$ determined at 20 °C and $I = 0.1$.[3] The observed discrepancy can be attributed to the difference between the reactant concentrations and activities used in our and the reported study. For the same reason our calculated values of the thermodynamic functions do not represent the standard values, and possibly a larger negative value of the reaction entropy than expected is calculated. As expected, the K_1 value obtained is slightly smaller than that reported for the complexation of La^{III} with *N*-methylacetohydroxamic acid.[6]

The ^{139}La ($I = {}^7/_2$) nuclear spin-spin relaxation is governed by the quadrupolar interaction, for which it was shown that the extreme narrowing is valid above 278 K.[11] The intrinsic relaxation time in the absence of the exchange for the aqualanthanum(III) ion (T_{2A}) was determined from the NMR spectra of 0.2 M $La(ClO_4)_3$ in 20% D_2O (w/w), collected as a function of concentration and temperature. Figure S3 shows that in the temperature range 278−338 K, the observed relaxation time of the $La(ClO_4)_3$ solution, which was found to be concentration-independent, depends almost linearly on the temperature according to the following equation: $T_{2La^{3+}}(T) = -0.00758$ (s) $+ 3.009 \cdot 10^{-5}$ ($s \cdot K^{-1}$) $\times T$ (K). At 298 K, the spin-spin relaxation time $T_{2La^{3+}} = 4.36(4)$ ms compares reasonably well with the reported values,[11,20] taking into account the slightly different experimental conditions employed in these studies. Since full complexation of La^{3+} was impossible to achieve under our experimental conditions, T_{2B} and its temperature dependence were refined during the fitting procedure (vide infra). The optimized spin-spin relaxation times of lanthanum in the hydroxamato complex at 298 K, $T_{2B}(298) = 54(1)$ μs, is within the range reported for other complexes.[20] For a quadrupolar nucleus such as ^{139}La, besides the exchange broadening effect, the line-width variation should result essentially from two factors, a change in the symmetry of the first coordination shell, and a change in the size of the La^{III} species. The larger the size and the lower the species symmetry, the broader the resonance will be. The substitution of two coordinated water molecules by one acetohydroxamato ligand in the inner sphere of La^{III} should slightly increase the size of the complex, as expected from the reaction molar volume determined for the complexation of iron with HA.[21] This, along with the lower symmetry of the monohydroxamato complex, accounts for a much broader resonance observed for the complex than for the aqua species.

Two essentially different reaction models could be considered as the operative reaction mechanism for the complexation of the lanthanum ion by acetohydroxamic acid. The rate-determining step should be characterized by the energetics of either (*i*) the water exchange on the aquated lanthanum ions, or (*ii*) the ring-closure reaction of the mono-coordinated ligand. For the former process either a dissociative or an associative mode of activation can be proposed, whereas for the latter one the rate-determining step may involve a slow proton transfer from the −NO*H* group or a slow *trans→cis* isomerization of the attached hydroxamato ligand.

Besides the proton, four different reactants can be considered to participate in the complexation kinetics, i.e. La^{3+}, La(OH)$^{2+}$, HA, and A$^-$. Accordingly, the studied reaction can be plausibly represented by Equations (11) to (14).

$$La^{3+} + HA \rightleftarrows La(A)^{2+} + H^+ \qquad (11)$$

$$La^{3+} + A^- \rightleftarrows La(A)^{2+} \qquad (12)$$

$$La(OH)^{2+} + HA \rightleftarrows La(A)^{2+} \qquad (13)$$

$$La(OH)^{2+} + A^- \rightleftarrows La(A)(OH)^+ \qquad (14)$$

Since the pK_a values of both reactants are > 9,[13,22] reaction path (14) results in a calculated microscopic rate constant for the complexation, that would greatly exceed the rate of the diffusion-controlled processes. The reaction paths (12) and (13) are kinetically indistinguishable from each other, but the contribution of the latter path could be excluded for the following reasons. Due to the difference in electric charge of La^{3+} and La(OH)$^{2+}$, the ion−dipole attractive coulombic force between the reactants of path (11) must be more than doubled in comparison with path (13). Furthermore, even at the lowest acidity used, the concentration of La^{3+} was more than 10^3 times that of La(OH)$^{2+}$. Therefore, for a notable contribution of path (13) HA would have to react at least 10^3 times faster with La(OH)$^{2+}$ than with La^{3+}. However, the latter ion exchanges water on a time-scale shorter than 10 ns.[23]

Taking into account the above arguments, Equations (2) to (9) were fitted to the experimental data, but k in Equation (6) was substituted by $k_{11} + k_{12}K_a[H^+]^{-1}$ (the subscripts of the rate constants are related to the equation numbers, whereas K_a stands for the ionization constant of HA). Figure 4 shows the experimentally determined $\Delta\nu_{1/2}$ of 0.2 M reactants plotted as a function of p[H$^+$] at various temperatures. The lines drawn are the theoretical ones calculated using the optimized parameters of Equations (2) to (9), obtained by a non-linear least-squares fit[16] in which

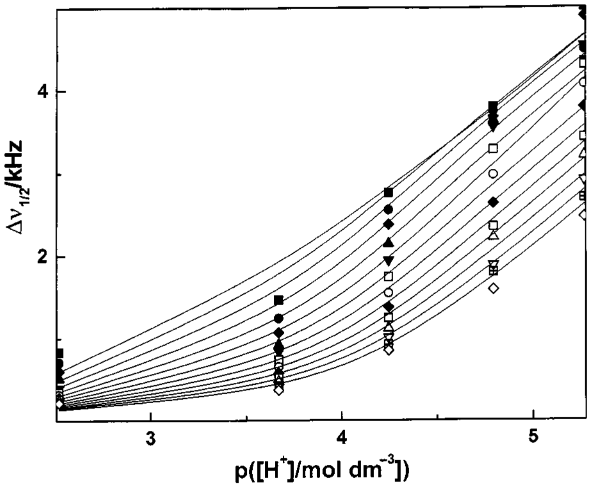

Figure 4. The observed $\Delta\nu_{1/2}$ of 0.2 M $La(ClO_4)_3$ and 0.2 M acetohydroxamic acid in 20% (w/w) D_2O plotted vs. p[H$^+$] at various temperatures; the lines drawn are the theoretical ones calculated using the optimized parameters of Equations (2) to (9); the temperature increment between the experimental series is 5 K, the open diamonds corresponding to lowest temperature, 278 K

τ_B was substituted for $\tau_A p_B/p_A$ in order to reduce the number of variables. The theoretical values follow a general trend delineated by the observed values. A slight disagreement seems acceptable considering the complexity of the expression describing $\Delta\nu_{1/2}$ and the number of parameters that had to be adjusted during the fitting procedure. The necessary equilibrium concentration of free HA for each data point was calculated simultaneously during the iteration procedure, as well as the difference in chemical shift of the two sites in the absence of exchange, $\Delta\omega_{AB}(T) = \Delta\nu_{La}{}^{3+}(T) - \Delta\nu_{La(A)}{}^{2+}(T)$. The values of the kinetic parameters for the formation of $La(A)^{2+}$ are calculated as: $k_{11}(298\ K) = 1.54(4)\cdot10^6\ M^{-1}\cdot s^{-1}$, $\Delta H^{\ddagger}_{11} = 70(14)\ kJ\cdot mol^{-1}$ and $\Delta S^{\ddagger}_{11} = +108(47)\ J\cdot K^{-1}\cdot mol^{-1}$, $k_{12}K_a(298\ K) = 1.5(5)\cdot10^1\ s^{-1}$, $(\Delta H^{\ddagger}_{12} + \Delta_r H_a) = 53(5)\ kJ\cdot mol^{-1}$ and $(\Delta S^{\ddagger}_{12} + \Delta_r S_a) = -45(17)\ J\cdot K^{-1}\cdot mol^{-1}$. From the calculated values and the published thermodynamic parameters for the ionization of HA,[23] the following values can be calculated: $k_{12}(298\ K) = 1.5\cdot10^1/K_a = 1.6\cdot10^{10}\ M^{-1}\cdot s^{-1}$, $\Delta H^{\ddagger}_{12} = 53 - \Delta_r H_a = 35(6)\ kJ\cdot mol^{-1}$ and $\Delta S^{\ddagger}_{12} = -45 - \Delta_r S_a = +68(20)\ J\cdot K^{-1}\cdot mol^{-1}$. The kinetic parameters for the backward reaction are calculated from the forward reaction and the equilibrium parameters: $k_{-11}(298\ K) = 6.75\cdot10^9\ M^{-1}\cdot s^{-1}$, $\Delta H^{\ddagger}_{-11} = 98(14)\ kJ\cdot mol^{-1}$, $\Delta S^{\ddagger}_{-11} = +270(47)\ J\cdot K^{-1}\cdot mol^{-1}$, $k_{-12}(298\ K) = 6.48\cdot10^4\ s^{-1}$, $\Delta H^{\ddagger}_{-12} = 82(8)\ kJ\cdot mol^{-1}$, and $\Delta S^{\ddagger}_{-12} = +121(24)\ J\cdot K^{-1}\cdot mol^{-1}$.

From the calculated values of k_{11} and k_{12}, and the estimated outer-sphere association constants for $\{La^{3+}\cdots AH\}$ and $\{La^{3+}\cdots A^-\}$ with concentrations of ca. $10^{-1}\ M^{-1}$ and ca. $5\cdot10^2\ M^{-1}$,[24] respectively, the inner-sphere reorganization rate constants for reactions (11) and (12) can be calculated as $1.5\cdot10^7\ s^{-1}$ (= $1.54\cdot10^6\ M^{-1}\cdot s^{-1}/10^{-1}\ M^{-1}$) and $3\cdot10^7\ s^{-1}$ (= $1.6\cdot10^{10}\ M^{-1}\cdot s^{-1}/5\cdot10^2\ M^{-1}$), respectively. Both constants appear to be an order of magnitude smaller than the water exchange rate constants for the La^{3+} and $La(OH)^{2+}$ ions.[25] However, two factors could easily increase these rate constants to values similar to that of the water exchange rate constant. Participation of the *trans* isomer in free HA increases their values, as well as the inner-sphere reorganization rate constants by a factor of ca. 10, as a statistical correction for the outer-sphere water molecules.

A value of k_{-11} that is larger than the estimated water exchange rate constant by an order of magnitude indicates that this rate constant is not strictly related to the inner-sphere reorganization of the complex, but possibly encompasses protonation of the coordinated hydroxamate according to Equations (15) and (16).[26]

$$La(CH_3C(=O)N(H)O)^{2+} + H^+ \underset{k_{-2}}{\overset{k_2}{\rightleftarrows}} La(CH_3C(=O)N(H)OH)^{3+} \quad K_2 \tag{15}$$

$$La(CH_3C(=O)N(H)OH)^{3+} \xrightarrow{k_{-HA}} La^{3+} + CH_3C(=O)N(H)OH \tag{16}$$

A lack of spectroscopic evidence for $La(AH)^{3+}$, even at the highest proton concentration used (0.003 M), indicates that $K_2 \leq 3\cdot10^1\ M^{-1}$. This results in a decreased protonation constant of $La(A)^{2+}$, by ca. 7 orders of magnitude, in comparison with free A^-. This favorably compares with a decreased protonation constant of the hydroxo ligand coordinated to La^{3+} by ca. $6^1/_2$ orders of magnitude compared with free OH^-. Assuming that $La(AH)^{3+}$ is formed by a fast pre-equilibrium protonation of $La(A)^{2+}$, the inverse of the mean residence time of lanthanum in the mono complexes can be expressed by Equation (17).

$$1/\tau_B = k_{-11}[H^+] + k_{-12} = \frac{k_{-HA}K_2[H^+]}{1+K_2[H^+]} + k_{-12} \tag{17}$$

For $K_2[H^+] << 1$, the equation reduces to a simpler form: $\tau_B{}^{-1} = k_{-HA}K_2[H^+] + k_{-12}$ (the plots of calculated $\tau_B{}^{-1}$ vs. $[H^+]$ at various temperatures show linearity with significant intercepts, Figure S4). Therefore, k_{-11} could be considered as a product of the equilibrium constant for the protonation of $La(A)^{2+}$ and the first order dissociation rate constant of HA from the $La(AH)^{3+}$ complex, and a minimum value of k_{-HA} can be estimated as $7\cdot10^8\ s^{-1}$. The closeness of this value to the water-exchange rate constant seems reasonable considering that both ligands are uncharged, i.e. H_2O and HA molecules, and considering the electrostatic nature of the ligand$-La^{III}$ bond,[27] which also accounts for a much smaller value calculated for k_{-12} than k_{-11}.

Despite the uncertainty in its determination from a far-removed intercept in the Eyring plot, the activation entropy has frequently been used as a useful criterion for distinction between possible mechanisms. The value $\Delta S^{\ddagger} = -100\ J\cdot K^{-1}\cdot mol^{-1}$ reported for the second-order complexation of Fe^{3+} with HA[7] was taken as evidence for an associative mechanism for this reaction. Similarly, the negative activation entropies determined for water exchange on a series of lanthanide ions were interpreted in terms of an associative mechanism.[23] Therefore, considering an associative mechanism for the studied reaction, negative activation entropies would be expected. The reliability of the activation entropies is made more dubious when obtained by such a complex iterative procedure as presented in this study, since mutual compensations between the activation parameters and the natural line broadening for the observed temperature effects are possible. Nevertheless, we believe that for the deduction of the reaction mechanism at least the signs of calculated entropies could be used. Therefore, the positive signs obtained could be indicative of a dissociative mode of activation for the studied reaction. The activation entropies for the backward reactions show that the dechelation of $La(A)^{2+}$ is also accompanied by a large increase in disorder. The proton assisted aquation exhibits an additional 149 $J\cdot K^{-1}\cdot mol^{-1}$ increase in entropy compared with the spontaneous aquation. The additional increase in activation entropy is very similar to the reaction entropy for the proton dehydration in water, viz. $\Delta S = +130\ J\cdot K^{-1}\ mol^{-1}$.[28]

All the above arguments speak in favor of a dissociative reaction mechanism and indeed no other mechanism is necessary to be invoked to rationalize the results obtained.

Furthermore, Crumbliss and Garrison[29] have shown that for Fe^{3+} and Al^{3+} ions, the ring-closure step is fast enough not to interfere with the complexation rate, but the water-exchange rate constants for those metal ions are much smaller than for the La^{3+} ion.

Nevertheless, it must also be mentioned that the chelation of HA was indeed proposed as the rate-determining step for its complexation to Fe^{2+}, Co^{2+}, and Ni^{2+}. Ring closure was assumed to be sufficiently retarded by slow proton dissociation from mono-coordinated hydroxamic acid to become the rate-limiting step. However, the value for k_{11} we obtained is more than three orders of magnitude larger than the rate constant for the proton dissociation from free HA in 55 M water at 25 °C, which was estimated as $1.4 \cdot 10^3$ $M^{-1} \cdot s^{-1}$.[30] The metal ion−proton repulsion and the inductive electron flow into the electron-deficient metal ion center could enhance the proton loss from $La(AH)^{3+}$ relative to the free acid, but for the above-mentioned ions the metal ion−proton repulsion was not the dominant factor.

Obviously, the proton exchange limited chelation could not be the rate-determining step for the reaction according to Equation (12) since the entering ligand had already been deprotonated. On the other hand, if the rate-determining chelation step was limited by the *trans→cis* isomerization of mono-coordinated HA, approximately equal rates would be expected for paths (11) and (12), which is not the case based on our results. These arguments indicate that the isomerization rate constant for HA exceeds the reported isomerization rate constant for *N*-alkyl derivatives by at least a factor of ca. 10^5 [$= 1.54 \cdot 10^6\ M^{-1} \cdot s^{-1} \times 0.3\ M\ (HA)/(\approx 3)\ s^{-1}$].

Experimental Section

General Remarks: A stock solution of $La(ClO_4)_3$ was prepared by mixing equivalent amounts of $Ba(ClO_4)_2$ (Merck) and $La_2(SO_4)_3$ (Fluka), dissolved in distilled water, followed by the centrifugation of precipitated $BaSO_4$. The concentration of La^{3+} was determined by titration with EDTA. Acetohydroxamic acid (98%) from Aldrich was used without further purification. Doubly distilled water was used in the preparation of all solutions. The ionic strength was 1.2 M in all the experiments, maintained by the addition of La/Na/H/ClO_4 ions. The pH of the solutions was adjusted with 2 M NaOH. The ^{139}La NMR measurements were performed at 56.52 MHz with a Bruker Avance 400 DRX spectrometer equipped with an 89-mm wide-bore magnet. The temperature was kept constant within ±0.1 K by means of a Bruker BVT 3000 digital temperature control unit, which was tested for the absolute temperature-scale reading. The spectral width of the spectra varied between $\delta = 200$ and 800, according to the changing La linewidth (11.3−45.2 kHz), and 128 up to 8000 data points were collected with a 90° pulse duration of about 18 µs. The half width ($\Delta\nu_{1/2}$), related to the relaxation times T_2 ($= 1/\pi\Delta\nu_{1/2}$), were calculated by fitting a single Lorentzian function to the recorded spectroscopic data. Chemical shifts were measured relative to external 0.2 M $La(ClO_4)_3$ in 20% (w/w) D_2O keeping the frequency of the external lanthanum fixed at 298 K, i.e. $\Delta\nu_{La^{3+}}(298) = -2187$ Hz. The observed temperature dependence of the ^{139}La NMR line widths were within the experimental error limits. A Mettler Toledo MP230 research digital pH meter equipped with a Schott N 6480 combination electrode, containing saturated NaCl solution, was used for pH measurements. The pH readings in $H_2O/D_2O = 4{:}1$ (w/w) solutions were converted into the $p[H^+]$ ($\equiv -\log([H^+]/mol \cdot dm^{-3})$) values by means of a linear function experimentally determined by the titration of $HClO_4$ with NaOH in the same solvent mixture at an ionic strength of 1.2 M (H/Na perchlorate) and at various temperatures. The results revealed that the slope and intercept of the function are temperature-independent within the experimental error limits. In order to exclude hydrolysis of lanthanum ions, experiments were performed in solutions of $p[H^+] < 6$.

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[19] A large fraction of the complex is achievable by increasing p[H^+], but then the bis and tris complexes would form if HA was in excess over La^{III}, whereas the hydrolyzed lanthanum(III) species would interfere if hydroxamic acid was not in a large excess.

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