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# Kinetics and mechanisms of formation of the lanthanide(III)-*trans*-1,2-diaminocyclohexane-*N*,*N*,*N′*,*N′*-tetraacetate complexes†

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The rates of formation of the DCTA complexes of $Ce^{3+}$, $Eu^{3+}$ and $Yb^{3+}$ are significantly lower than expected on the basis of the water-exchange rates of $Ln^{3+}$(aq). The kinetics of formation of these complexes were studied by means of a stopped-flow method. The reactions were found to be first order in the reactants, and the formation of monoprotonated and diprotonated intermediates was detected. The reactions occur through the deprotonation and rearrangement of the monoprotonated intermediates, which are in equilibrium with the diprotonated ones. The rate constants obtained for this pathway are $15 \pm 0.2\ s^{-1}$, $28 \pm 1.3\ s^{-1}$ and $144 \pm 3\ s^{-1}$ for the formation of $Ce(DCTA)^-$, $Eu(DCTA)^-$ and $Yb(DCTA)^-$, respectively. General base catalysis is not valid for the reactions, indicating a fast deprotonation of the intermediate. The rate-determining step is presumably the rearrangement of the monoprotonated intermediate, when $Ln^{3+}$ enters into the coordination cage and displaces the proton from the $NH^+$ group. Another reaction pathway is the $OH^-$-assisted deprotonation of the monoprotonated intermediate, followed by the rate-controlling rearrangement of the deprotonated intermediate. The rate constants obtained for the formation of $Ce(DCTA)^-$ and $Eu(DCTA)^-$ are $(6.6 \pm 0.1) \times 10^8\ M^{-1}\ s^{-1}$ and $(2.2 \pm 0.12) \times 10^9\ M^{-1}\ s^{-1}$, respectively. The activation parameters for the reactions of $Ce^{3+}$ and $Eu^{3+}$, involving the transformation of the monoprotonated intermediates, proved to be practically equal, indicating the formation of similar transition states. The rate constants characterizing the formation of the complexes exhibit an increasing trend with increase in the atomic number of the lanthanide.

## Introduction

The formation reactions of the complexes of lanthanides ($Ln^{3+}$) with monodentate and flexible multidentate ligands are very fast and can be studied by relaxation techniques. The rates of formation of the complexes of $Ln^{3+}$ with sulfate ion are determined by the water-exchange rates of the ions $Ln^{3+}$(aq).[1,2] The complexes with certain bidentate ligands, such as murexide, anthranilate and oxalate, are formed 10–100 times more slowly than expected on the basis of the water-exchange rates. These findings were explained by assuming the ring closure to be the rate-controlling step of the reactions.[2–5]

The complexes of $Ln^{3+}$ with flexible polyaminopolycarboxylate ligands are also formed in very fast reactions. For the rates of formation of the complexes $Ln(NTA)_2$ ($H_3NTA$ = nitrilotriacetic acid) in the reaction $Ln(NTA) + H_xNTA = Ln(NTA)_2 + xH^+$, the rate constants were obtained by studying the ligand-exchange reactions by means of $^1H$-NMR spectroscopy.[6] The rates of formation of some complexes $Ln(EDTA)^-$ ($H_4EDTA$ = ethylenediamine-*N*,*N*,*N′*,*N′*-tetraacetic acid, Ln = Nd, Gd, Er and Y) were determined by an indirect method, by studying the exchange reactions between $Ce(EDTA)^-$ and $Ln^{3+}$ as reversible reactions.[7] In these formation reactions, the rate-determining step is presumably the ring closure, the coordination of the first iminodiacetate (imda) group of the ligand.[7]

The first experimental data which indicated that the rigid structure of the ligand may slow down the formation of the complexes of $Ln^{3+}$ were presented by Nyssen and Margerum. They found that the formation of $La(DCTA)^-$ ($H_4DCTA$ = *trans*-1,2-diaminocyclohexane-*N*,*N*,*N′*,*N′*-tetraacetic acid) was slow enough to be studied by a stopped-flow method.[8] Nyssen and Margerum assumed the fast formation of a monoprotonated intermediate, La(HDCTA), which deprotonates in a rate-controlling step and rearranges to the product.[8] The results on the formation of $La(DCTA)^-$ became interesting when it was found that the reactions of $Ln^{3+}$ with the macrocyclic ligand DOTA and its derivatives occur along similar pathways[9–12] ($H_4DOTA$ = 1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid). The complexes of $Ln^{3+}$ with DOTA and DOTA derivatives are very important, because of their use in medical diagnosis and therapy.[13–16]

The kinetics and mechanisms of the formation of the $Ln^{3+}$ complexes of DOTA and DOTA derivatives have been studied in detail.[9–12,17–19] In the pH range 4–6, a diprotonated intermediate was detected, but the rate-controlling step is the deprotonation of the monoprotonated intermediate. The formation of the diprotonated intermediate $Ln(H_2DOTA)^+$ was explained by the large values of the first two protonation constants of DOTA ($\log K^H_L = 12.6$, $\log K^H_{HL} = 9.70$ and $\log K^H_{H_2L} = 4.50$).[19] The first protonation constant of DCTA is also large ($\log K^H_L = 11.76$), but the second one is significantly lower ($\log K^H_{HL} = 6.12$[20]) which might result in a monoprotonated intermediate being formed in the reaction of DCTA and $La^{3+}$ in the pH range 5–6.[8] Thus, a comparative study of the kinetics of formation of the complexes $Ln(DCTA)^-$ may provide new information concerning the role of the protonation constants of the ligands in the composition of the reaction intermediate formed in the reactions of rigid ligands. Accordingly, we considered it interesting to study the kinetics of formation of the DCTA complexes of $Ce^{3+}$, $Eu^{3+}$ and $Yb^{3+}$ (a larger, a medium and a smaller $Ln^{3+}$) in a broad $H^+$ concentration range, at different temperatures and buffer concentrations, with the aim

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† Electronic supplementary information (ESI) available: first-order rate constants obtained for the formation of $Ce(DCTA)^-$, $Eu(DCTA)^-$ and $Yb(DCTA)^-$ at 25 °C and the temperature dependence of the first-order rate constants for $Ce(DCTA)^-$ and $Eu(DCTA)^-$. See http://www.rsc.org/suppdata/dt/b0/b003143g/

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of acquiring new information on the kinetics and mechanisms of the formation reactions.

## Experimental

Chemicals of the highest purity available were obtained and used without further purification. The concentration of the DCTA (Fluka) stock solution (pH = 5.2) was determined by complexometric titration of $Ce^{3+}$ solution with xylenol orange as indicator. The $LnCl_3$ solutions were prepared as described previously.[19]

The rates of complex formation were studied by a stopped-flow method, with an Applied Photophysics DX-17MV instrument.[19] The formation of $Ce(DCTA)^-$ was studied at 284 nm, where the absorbance of the intermediate was higher than that of the product. In a number of other experiments, the wavelength used was 303 nm, where the absorbance of the product, $Ce(DCTA)^-$, was higher. The formation of $Eu(DCTA)^-$ was followed at 280 nm, where $Eu^{3+}$(aq) does not absorb and the absorbance of $Eu(DCTA)^-$ is significantly larger than that of the intermediate.

The rate of formation of $Yb(DCTA)^-$ was studied by the "indicator method".[19,21] The indicators used were $1.5 \times 10^{-5}$ M bromophenol blue (591 nm, pH: 3.0–4.6) or bromocresol green (616 nm, pH: 4.0–5.4). The buffers used are as follows: *N*-methylpiperazine (0.05–0.1 M, pH: 3.5–5.2), MES (2-morpholinoethanesulfonic acid, 0.085 M, pH: 5.3–6.2) and HEPES (*N′*-(2-hydroxyethyl)piperazine-*N*-ethanesulfonic acid, 0.085 M, pH: 6.2–7.2).

The kinetic studies were carried out in the presence of a DCTA excess. The concentration of DCTA was varied in several experiments, which revealed that the rates of the formation reactions reached a saturation value at about a 10–20-fold ligand excess. In a number of experiments, these saturation rate values were determined with the use of a 25-fold excess of DCTA. The rate data presented were calculated as the average values of the results of 5 parallel stopped-flow measurements.

To keep the ionic strength constant, the experiments were carried out in 1.0 M KCl. The rates of formation reactions were determined in general at 25 °C. For establishment of the activation parameters characterizing the formation of $Ce(DCTA)^-$ and $Eu(DCTA)^-$, the rate constants were determined in the pH range 3.6–5.0 at 10, 15, 20, 25, 30 and 35 °C.

The composition of the protonated intermediate was determined by measuring the decrease in pH that occurred in weakly buffered solutions at the start of the reaction (on mixing of the reactants) and during the reaction, *i.e.* by determining the amounts of protons released from the intermediate. The pH changes were measured with the acid–base indicators bromophenol blue (591 nm, pH: 3.0–4.5) and chlorophenol red (575 nm, pH: 4.8–6.4). The experiments were carried out with the stopped-flow instrument under similar conditions as in the kinetic studies. The pH values were obtained from the pH–absorbance calibration curves.

The measurements of pH and the calculation of $H^+$ concentration were made as described before.[19,22]

## Results and discussion

### Kinetics of complex formation

The formation of the complexes is described by eqn (1):

$$Ln^{3+} + H_nDCTA \rightleftharpoons Ln(DCTA)^- + nH^+ \qquad (1)$$

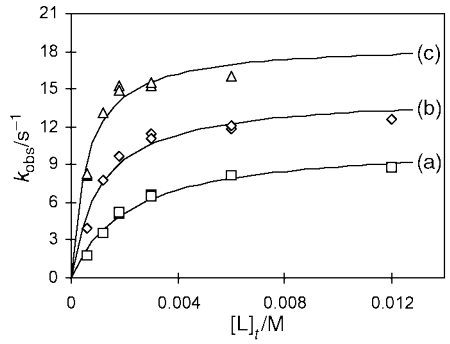

**Fig. 1** First-order rate constants characterizing the formation of $Ce(DCTA)^-$ at pH = 4.04 (a), pH = 4.60 (b) and pH = 5.08 (c) ($[Ce^{3+}] = 6 \times 10^{-4}$ M, 25 °C).

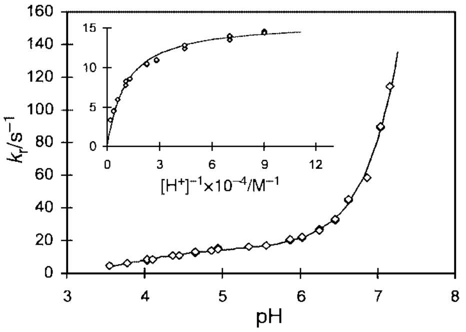

**Fig. 2** Rates of formation of $Ce(DCTA)^-$ ($[Ce^{3+}] = 5 \times 10^{-4}$ M, $[DCTA] = 1.25 \times 10^{-2}$ M, 25 °C).

In the pH range where the rates of complexation were studied, the ligand is present in different protonated forms: $HDCTA^{3-}$, $H_2DCTA^{2-}$ and $H_3DCTA^-$.[20] The experimental data reported by Nyssen and Margerum on the formation of $La(DCTA)^-$,[8] and also our own preliminary results, indicated that the complex formation occurs in a first-order reaction. In the presence of a ligand excess, the rate of complexation is:

$$\frac{d[LnL]}{dt} = k_{obs}[Ln]_t \qquad (2)$$

where $k_{obs}$ is a pseudo-first-order rate constant which depends on the ligand and $H^+$ concentrations, and $[Ln]_t$ is the total concentration of $Ln^{3+}$-containing species after mixing the reactants. The dependence of the $k_{obs}$ values on $[L]_t$ ($H_4L = H_4DCTA$) in the reaction between $Ce^{3+}$ and DCTA is illustrated in Fig. 1. The experimental data indicated the formation of the complexes in first-order reactions, even at comparable concentrations of the reactants, and the "saturation curves" obtained by plotting the $k_{obs}$ values against the ligand concentration (Fig. 1), can be interpreted in terms of the fast formation of a reaction intermediate which slowly rearranges to the product. The reaction scheme is:

$$Ln^{3+} + H_nDCTA^{(4-n)-} \rightleftharpoons (n-x)\,H^+ + Ln(H_xDCTA)^{(x-1)+} \xrightarrow{k_r} Ln(DCTA)^- + xH^+ \qquad (3)$$

where $k_r$ is a rate constant characterizing the rate of rearrangement of the intermediate $Ln(H_xDCTA)^{(x-1)+}$ to the product. The relationship between the first-order rate constants $k_{obs}$ and the ligand concentration shown in Fig. 1 can be expressed as follows:[23]

$$k_{obs} = \frac{k_r K_c^*[L]}{1 + K_c^*[L]} \qquad (4)$$

In eqn. (4), $K_c^*$ is the conditional stability constant of the intermediate, $Ln(H_xDCTA)^{(x-1)+}$.[24] As is to be seen in eqn. (4), at higher ligand concentrations, if $K_c^*[L] \gg 1$, then $k_{obs} = k_r$, *i.e.* $k_r$ is the "saturation value" of the rate constant $k_{obs}$ obtained when the formation of the intermediate is complete. Rate constants $k_r$ determined in a broad range of pH in the formation of $Ce(DCTA)^-$ are presented in Fig. 2. The rate constants obtained for the formation of Eu(DCTA)$^-$ are somewhat higher and show a very similar trend. These data, together with all the rate constants, obtained in the study are deposited in Tables S2–S4 (ESI).† The rates of formation of Yb(DCTA)$^-$ were significantly higher, and to obtain reliable rate data with the indirect "indicator" method, the rates of formation were studied in a narrower pH range.

In order to know the composition of the intermediate Ln(H$_x$DCTA)$^{(x-1)+}$, the value of $x$ was determined from the pH decrease measured during the deprotonation of the intermediate in the stopped-flow instrument. When the pH of the solution of the reactants ($5 \times 10^{-4}$ M Ce$^{3+}$ and $1.25 \times 10^{-2}$ M DCTA) was 3.90, the pH of the reaction mixture instantaneously dropped to 3.43 and then slowly decreased to an equilibrium value of 3.34. By producing similar pH changes in a $1.25 \times 10^{-2}$ M DCTA solution (in these studies, the excess DCTA weakly buffered the system) with a dilute HCl solution of known concentration, the value $x = 1.62$ was obtained. This $x$ value means that the intermediates formed in the reaction mixture at around pH = 3.5 are the monoprotonated species Ln(HDCTA) and the diprotonated species Ln(H$_2$DCTA). When the pH values of the reactants at the start of the reactions were 4.20, 5.30 or 5.81, the numbers of protons released from the intermediates, obtained through the use of similar procedures, were $x = 1.39$, $x = 1.04$ and $x = 1.05$, respectively. The decrease in the $x$ values means that the concentration of the diprotonated intermediate decreases with increasing pH, and at about pH > 5 the monoprotonated intermediate predominates. Nyssen and Margerum found a similar intermediate, La(HDCTA), in the formation of La(DCTA)$^-$, but the conditions of their experiment were not specified.[8]

As regards the structure of the monoprotonated intermediate Ln(HDCTA), Nyssen and Margerum assumed that the La$^{3+}$ is outside the coordination cage determined by the two nitrogen and four carboxylate oxygen atoms. The proton is on a nitrogen atom and only three carboxylate oxygens are coordinated to the La$^{3+}$.[8] In the diprotonated intermediate, the two protons are attached to the two nitrogens and presumably three (or four) carboxylates are coordinated to the Ln$^{3+}$. The structures of the monoprotonated and diprotonated intermediates are different. The spectra obtained in the Ce$^{3+}$–DCTA system at the start of the reactions (the first spectrum was obtained 5 ms after mixing the reactants) at different pH values differ considerably. The maxima of the absorption bands observed at the longest wavelengths for the monoprotonated intermediate Ce(HDCTA) and the product Ce(DCTA)$^-$ are at 299 nm and 303 nm, respectively. At about pH > 5, only these two species are present, which is indicated by the appearance of isosbestic points in the spectra. At lower pH values, diprotonated intermediates are also present, but the maximum of the absorption band of the species Ce(H$_2$DCTA)$^+$ cannot be determined. The small difference in the positions of the band maxima of Ce(DCTA)$^-$ and Ce(HDCTA) indicates that in both species presumably four carboxylate groups are coordinated to the Ce$^{3+}$. (It was found that the shift in this band in the direction of longer wavelengths is proportional to the number of coordinated donor atoms of the ligand.)[25]

## Mechanistic aspects of complex formation

The rate constants $k_r$ obtained for the formation of Ce(DCTA)$^-$ and Eu(DCTA)$^-$ (Fig. 2 and Fig. S1)† indicate that in the pH range about 4.5–6 the dependence of $k_r$ values on [OH$^-$] is very week, a 30-fold increase in [OH$^-$] results in about a 3-fold increase in $k_r$.

The rate constants obtained for the formation of La(DCTA)$^-$ and Am(DCTA)$^-$ in the pH range 4.25–6 also show such a "plateau", but this unusual phenomenon was not interpreted by the authors.[8,26] However, in the formation reactions of Ce(DCTA)$^-$ and Eu(DCTA)$^-$ the order of reaction for OH$^-$ is approximately one at about pH < 4, where the diprotonated intermediate predominates. The order of reaction is also one at about pH > 6.5, where the intermediate formed is a monoprotonated one. These experiences are similar to those found for the formation reactions of Ln(DOTA)$^-$ complexes,[19] which suggests that the mechanisms of the formation reactions can be also similar. In the formation of complexes Ln(DOTA)$^-$ the rate-controlling step is the deprotonation of the intermediate Ln(HDOTA). The concentration of this species is directly proportional to [OH$^-$] (or [H$^+$]$^{-1}$) up to about pH 7.5, because of the protonation equilibrium between the intermediates, Ln(H$_2$DOTA)$^+$ and Ln(HDOTA), which is characterized by the protonation constant $K^{\mathrm{H}}_{\mathrm{LnHL}}$.[19]

**Table 1** Rate constants and activation parameters characterizing the formation of the complexes Ln(DCTA)$^-$ and Ln(DOTA)$^-$, the protonation constants and enthalpies of protonation of the monoprotonated intermediates (25 °C, 1.0 M KCl)

| Complex | $k_{\mathrm{LnHL}}$/s$^{-1}$ | $k^{\mathrm{OH}}_{\mathrm{LnHL}}$/M$^{-1}$ s$^{-1}$ | log $K^{\mathrm{H}}_{\mathrm{LnHL}}$ |
|---|---|---|---|
| Ce(DCTA)$^-$ | 15 ± 0.2 | (6.6 ± 0.11) × 10$^8$ | 3.96 ± 0.02 |
| Eu(DCTA)$^-$ | 28 ± 1.3 | (2.2 ± 0.12) × 10$^9$ | 4.2 ± 0.03 |
| Yb(DCTA)$^-$ | 144 ± 3 | — | 3.84 ± 0.03 |
| Ce(DOTA)$^{-\,a}$ | 18.5 ± 2.8 | (1.9 ± 0.1) × 10$^7$ | 8.64 ± 0.05 |
| Yb(DOTA)$^{-\,a}$ | 245 ± 131 | — | — |
| | $\Delta H^‡$/ kJ mol$^{-1}$ | $\Delta S^‡$/ J mol$^{-1}$ K$^{-1}$ | $\Delta H_2$/ kJ mol$^{-1}$ |
| Ce(DCTA)$^-$ | 65 ± 1.2 | −4.3 ± 0.1 | −48 ± 1.3 |
| Eu(DCTA)$^-$ | 64 ± 1.1 | −3.7 ± 0.1 | −41 ± 2.4 |

[a] Ref. 19.

The difference in the kinetics of formation of the complexes Ln(DCTA)$^-$ and Ln(DOTA)$^-$ is the existence of a "plateau" for the formation rates of Ln(DCTA)$^-$. This difference can be interpreted by considering the protonation constants of ligands, which strongly influence the composition of the intermediates. The first two protonation constants of DCTA and DOTA are 11.76 and 6.12 and 12.6 and 9.70, respectively.[19,20] Because of the lower value of the second protonation constant of DCTA, the concentration of the monoprotonated ligand, HDCTA$^{3-}$ is significant at about pH > 4 and in the presence of excess DCTA, the intermediate, Ln(HDCTA) predominates at about pH > 4.5. If the concentration of Ln(HDCTA) is large, then it is either weakly or uninfluenced by the protonation equilibrium between Ln(H$_2$DCTA)$^+$ and Ln(HDCTA), and thus the rate of complex formation depends slightly on the [OH$^-$] or [H$^+$]$^{-1}$, which explains the existence of the "plateau". In the case of DOTA the second protonation constant is higher and the species HDOTA$^{3-}$ and Ln(HDOTA) are formed in significant concentration only at about pH > 7.5 (log $K^{\mathrm{H}}_{\mathrm{LnHL}} \approx 8.5$) where the OH$^-$ assisted deprotonation becomes important.[19]

The rate of complex formation can be expressed as follows:[19]

$$k_r = \frac{k_{\mathrm{LnHL}}[\mathrm{H}^+] + k^{\mathrm{OH}}_{\mathrm{LnHL}}K_w}{[\mathrm{H}^+] + K^{\mathrm{H}}_{\mathrm{LnHL}}[\mathrm{H}^+]^2} \tag{5}$$

In eqn. (5), $K_w$ is the ionic product of water (p$K_w$ = 13.88), $k_{\mathrm{LnHL}}$ and $k^{\mathrm{OH}}_{\mathrm{LnHL}}$ are the rate constants, characterizing the deprotonation and OH$^-$ assisted deprotonation of the monoprotonated intermediate, which is followed by the rearrangement of the deprotonated intermediate to the product, Ln(DCTA)$^-$. By fitting of the $k_r$ data presented in Fig. 2 and in Fig. S1 and Fig. S2 (ESI)† to eqn. (5), the rate constants $k_{\mathrm{LnHL}}$ and $k^{\mathrm{OH}}_{\mathrm{LnHL}}$ and the protonation constants $K^{\mathrm{H}}_{\mathrm{LnHL}}$ were calculated (for the formation of Yb(DCTA)$^-$, the second term in the numerator of eqn. (5) is negligible). The data obtained are presented in Table 1, where the errors shown are the standard deviation values. For

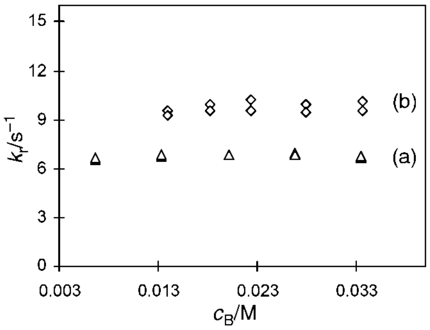

**Fig. 3** Dependence of first-order rate constants on the concentrations of the basic forms of the buffers ($C_B$): (a) formic acid at pH = 4.06 and (b) *N*-methylpiperazine at pH = 4.49 ([$Ce^{3+}$] = 4 × $10^{-4}$ M, [DCTA] = 4 × $10^{-3}$ M, 1.0 M KCl, 25 °C).

comparison, the rate constants characterizing the formation of $Ce(DOTA)^-$ and $Yb(DOTA)^-$ are also given in Table 1.

The rate constants $k_{LnHL}$, characterizing the formation of the complexes $Ln(DCTA)^-$ and $Ln(DOTA)^-$ from the monoprotonated intermediates, are quite similar for the complexes of $Ce^{3+}$ or $Yb^{3+}$ (Table 1). However, the rates of formation of the DCTA complexes are much higher, since the concentrations of the intermediates Ln(HDCTA) in the pH range investigated are much higher than the concentrations of the intermediates Ln(HDOTA). This is a consequence of the significantly lower second protonation constant of the ligand DCTA.

The temperature study of the rates of formation of $Ce(DCTA)^-$ and $Eu(DCTA)^-$ in the pH range 3.6–5, when the second term in the numerator of eqn. (5) ($k^{OH}_{LnHL}K_w$) is negligible, furnished the rate constants $k_r$ (Tables S6 and S7)† and the $K^{H}_{LnHL}$ values at different temperatures. The activation parameters $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ and the enthalpy of protonation of the monoprotonated intermediate, $\Delta H_2$, were calculated and are presented in Table 1.

The activation parameters obtained for the formation of $Ce(DCTA)^-$ and $Eu(DCTA)^-$ are very similar which indicates that the transition states in the formation reactions are also similar. The $\Delta H_2$ values connected with the protonation of the monoprotonated intermediate are more negative than the enthalpy of protonation of the monoprotonated ligand $HDCTA^{3-}$, for which $\Delta H^{H}_{HL} = -8.8$ kJ $mol^{-1}$.[20] The great difference in the $\Delta H_2$ and $\Delta H^{H}_{HL}$ values indicates that protonation may lead to some other structural changes in the intermediates. In the diprotonated intermediate $Ln(H_2DCTA)^+$ (where the second proton very probably protonates the other nitrogen), $Ln^{3+}$ may be more remote from the coordination cage than in the monoprotonated species Ln(HDCTA). In this case, the number of water molecules coordinated to $Ln^{3+}$ is probably higher in the diprotonated intermediate. Thus, the attachment of the second proton to the nitrogen atom and the increase in the number of the water molecules coordinated to $Ln^{3+}$ may result in the larger $\Delta H_2$ values presented in Table 1.

In the transformation of the intermediate, Ln(HDCTA), the deprotonation or the rearrangement of the deprotonated intermediate is the rate-controlling process. In the formation of $Ln(DOTA)^-$, general base catalysis is valid, which suggests that the rate-controlling step is the deprotonation of the monoprotonated intermediate.[19] For the formation of $Ce(DCTA)^-$ the rate constants $k_r$ are seen to be independent of the concentration of the basic form of the buffer (Fig. 3), which means that general base catalysis is not valid in the formation of $Ln(DCTA)^-$. To interpret this result, it may be assumed that the transformation of the monoprotonated intermediate may occur *via* two differrent pathways: (i) the deprotonation is rapid and the deprotonated intermediate rearranges to the product slowly, (ii) $Ln^{3+}$ enters slowly the coordination cage from the outside position by displacing the proton from the nitrogen atom. The existence of this latter pathway is more probable, since the rearrangement of the deprotonated intermediate which follows the $OH^-$-assisted deprotonation is very fast.

The rates of formation of $Ln(DCTA)^-$ increase from $Ce^{3+}$ to $Yb^{3+}$. Similar results were found for the formation of $Ln(DOTA)^-$.[19] The interpretation of these findings is difficult, since we have little information regarding the structures of the reaction intermediates.

## Conclusions

The complexation reactions of $Ln^{3+}$ with rigid multidentate ligands such as DCTA occur more slowly than expected on the basis of the rates of water-exchange of $Ln^{3+}$(aq).

The kinetics of formation of the $Ln^{3+}$ complexes with the open-chain DCTA and the macrocyclic DOTA are similar. In the reactions, diprotonated and monoprotonated intermediates are formed in equilibrium. The product is formed through the deprotonation and rearrangement of the monoprotonated intermediates, Ln(HDCTA) or Ln(HDOTA), in which the proton is on a nitrogen atom and the carboxylate groups are coordinated to the $Ln^{3+}$ outside the coordination cage.

The rate constants characterizing the formation of the complexes $Ln(DCTA)^-$ and $Ln(DOTA)^-$ from the intermediates Ln(HDCTA) and Ln(HDOTA), are similar. The protonation constants of the ligands have a significant influence on the rates of formation of the complexes, since the concentrations of the monoprotonated intermediates depend strongly on the value of the second protonation constant, $K^{H}_{HL}$. In the pH range 4–7 the rates of formation observed for $Ln(DCTA)^-$ ($K^{H}_{HL} = 6.12$) are much higher than those for $Ln(DOTA)^-$ ($K^{H}_{HL} = 9.70$), because in this range the intermediates Ln(HDCTA) predominate, while the concentration of the intermediates Ln(HDOTA) is very low. The rate-controlling step in the formation of $Ln(DCTA)^-$ is presumably the entrance of $Ln^{3+}$ into the coordination cage, with displacement of the proton, while in the formation of $Ln(DOTA)^-$ the deprotonation is the slowest step.

The formation of $Ln(DCTA)^-$, similarly to that of $Ln(DOTA)^-$, also occurs with the assistance of $OH^-$, when the rate-controlling step is the rearrangement of the deprotonated intermediate. The rates of formation of the complexes of $Ln^{3+}$ with both the acyclic DCTA and the macrocyclic DOTA increase with decreasing size of $Ln^{3+}$.

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