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Mechanistic information on ligand-substitution reactions of europium(III) in aqueous solution from high-pressure stopped-flow experiments†

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Substitution reactions of arsenazo III [3,6-bis(*o*-arsonophenylazo)-4,5-dihydroxynaphthalene-2,7-disulfonic acid] complexes of Eu^{III} with the polyaminecarboxylates dtpa (diethylenetriaminepentaacetate) and edta (ethylenediaminetetraacetate) were studied as a function of polyaminecarboxylate concentration, pH, temperature, pressure and ionic strength by stopped-flow spectrophotometry within the acidity range $3.61 < pH < 5.56$ and between 17.5 and 40 °C. Under all experimental conditions two consecutive steps (k_1 and k_2) were observed over different time-scales. For the fast step (k_1) the substitution rate of $Eu^{III}L_2(H_2O)$ (L = arsenazo III) by dtpa and edta (L′) increases with increasing acidity of the medium, $k_1 = k_a + k_b[H^+]$, and depends on the L′ concentration, *i.e.* $k_1 = k_c + k_d[L']$. For the slow step (k_2) plots of k_2 *versus* $[H^+]$ are linear and exhibit no intercept and k_2 is independent of L′ concentration. Ionic strength studies indicated no significant dependence of k_1 and k_2 on $[NaClO_4]$. Rate constant k_1 increases with increasing pressure, and there is a very good linear relationship between ln k_1 and pressure at any temperature, ligand concentration, pH and ionic strength. In contrast, k_2 exhibits almost no pressure dependence for any temperature, pH and ligand concentration. It is suggested that this latter step involves acid-catalysed dechelation of arsenazo III accompanied by chelation of L′. In terms of intrinsic volume changes, bond formation and breakage contributions seem to cancel in order to account for the zero $\Delta V_2^‡$ values. The substitution of arsenazo III by dtpa on Eu^{III} is much faster than the same process on Gd^{III}.

There has been considerable interest in thermodynamic[1,2] and kinetic studies[3–23] of lanthanide (Ln) complexes because of their co-ordination chemistry and their use as contrast-enhancing agents in magnetic resonance imaging (MRI),[24] as ion-selective reagents in analytical chemistry[25] and in lanthanide separation.[25b] Also europium(III) complexes display an intense luminescence which is useful for spectroscopic probes.[26] An important characteristic of the lanthanide elements is the small spatial extension of the 4f shell. Thus, even in the complexes, the 4f electrons, which belong to inner orbitals, are shielded from ligand interactions. This results in the similarities in the ionic radii and chemical properties of the various lanthanide ions. However, it is interesting that the substitution reactivity of lanthanide(III) complexes varies strongly within the series and reaches a maximum between Sm^{3+} and Gd^{3+}.[5–7,21,22] This is believed to be related to a changeover in co-ordination number from nine for the earlier, lighter members to eight for the later, heavier members of the series in aqueous solution.[5–7,21,22]

High-pressure kinetic techniques have been particularly useful in the elucidation of solvent-exchange and ligand-substitution mechanisms for transition-metal complexes, but little has been reported concerning lanthanide complexes.[6,27–29] In a previous study we used a high-pressure stopped-flow spectrophotometer to investigate ligand substitution reactions of Gd^{III} in an effort to resolve the intimate details of the underlying mechanism.[30] No comparisons were made among different lanthanide complexes. Merbach and co-workers[6,21,22] studied the kinetics of water exchange on the lanthanide(III) aqua ions and complexes by oxygen-17 NMR spectroscopy and discussed the phenomenon of the changeover of co-ordination number. Unsuccessful attempts were made to study the water exchange on Eu^{3+}.[21,22]

In the present study we used high-pressure stopped-flow spectrophotometry to investigate the ligand substitution of arsenazo III [3,6-bis(*o*-arsonophenylazo)-4,5-dihydroxy-naphthalene-2,7-disulfonic acid] by linear polyaminecarboxylate ligands on Eu^{III} with the following goals: (*i*) to elucidate the important mechanistic role of Eu^{III} in the changeover of co-ordination number of lanthanide(III) complexes; (*ii*) to clarify the nature of the non-symmetrical ligand-substitution behaviour; (*iii*) to investigate the possible involvement of protonated complex species in the acid-assisted substitution of lanthanide complexes and (*iv*) to improve our understanding of the influence of high pressure on the kinetics and mechanism of the ligand substitution of lanthanide complexes.

Experimental

Materials

A stock solution of Eu^{III} was prepared by dissolving $EuCl_3$ (Strem, 2×10^{-4} mol) and arsenazo III (Aldrich, 5×10^{-4} mol) in aqueous acetate buffer solution (pH 4.8, 50 cm^3) over a period of 20 h at 50 °C. Ethylenediaminetetraacetate (edta) and diethylenetriaminepentaacetate (dpta) solutions were also prepared in acetate buffer. pH Adjustments were made with $HClO_4$ and NaOH. Substitution reactions of the Eu^{III}–arsenazo III complexes were monitored spectrophotometrically at λ = 670 nm, where such reactions exhibit characteristic spectral changes.[17,18]

Kinetic measurements

These were made on a laboratory-made high pressure stopped-flow system[31] at pressures up to 1000 bar. A tungsten-filament light source, Edmund Scientific f/3.9 monochromator and photomultiplier tube provided the analysing detection beam. Light intensity *versus* time signals were recorded on a storage oscilloscope (LeCroy 9400) and transferred to a personal computer, on which the data were fitted with the KINFIT set of programs.[32] A number of test experiments were performed with

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† *Non-SI unit employed:* bar = 10^5 Pa.

this apparatus in order to determine the dead-time of the instrument, *ca.* 10 ms.

The substitution of arsenazo III by dtpa or edta on Eu^{III} was studied at temperatures between 17.5 and 40.2 °C. Constant temperature was maintained by an external water circulation bath (± 0.1 °C). All data were measured after 1 h of temperature equilibration at a new pressure. All reactions were carried out under pseudo-first-order conditions.

Results and Discussion

The compound arsenazo III is an azo-dye often used in spectrophotometry, especially for the determination of lanthanide and actinide ions. A large number of studies on its stereochemistry, complex-ion stability and complexation kinetics have been reported.[33–36] Earlier kinetic investigations were carried out at high acidity and low reactant concentrations, such that the kinetics only covered the first complexation step. No subsequent ring-closure steps were observed because arsenazo III existed in the protonated form under such acidic conditions. Arsenazo III can co-ordinate *via* four oxygen-donor atoms to Ln^{3+} at higher pH values,[36] and can form 1 : 1 and 1 : 2, *i.e.* LnL_2, complexes in solution.

The distribution of the 1 : 1 and 1 : 2 complexes depends on the $[Eu^{3+}]$: [arsenazo III] ratio. Based on the available stability constants K_1 and K_2 (see below) for the 1 : 1 and 1 : 2 complexes,[37] we calculated by using the SEQS program[38] that more than 99% of the combined 1 : 1, 1 : 2 complexes and free Eu^{3+} exists as the 1 : 2 complex when the ratio of $[Eu^{3+}]$: [arsenazo III] is 1 : 2.5 [equations (1)–(4)].

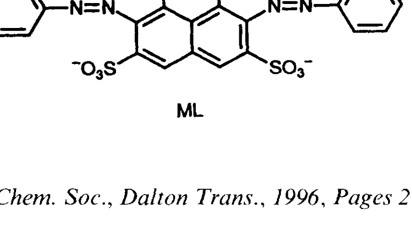
$$Eu^{3+} + L \rightleftharpoons EuL \qquad (1)$$

$$EuL + L \rightleftharpoons EuL_2 \qquad (2)$$

$$K_1 = [EuL]/[Eu^{3+}][L] = 1.86 \times 10^4 \text{ dm}^3 \text{ mol}^{-1} \qquad (3)$$

$$K_2 = [EuL_2]/[EuL][L] = 1.99 \times 10^6 \text{ dm}^3 \text{ mol}^{-1} \qquad (4)$$

In order to investigate the influence of the 1 : 1 and 1 : 2 complexes on the observed kinetics we first fixed the concentration of Eu^{3+} at 5×10^{-5} mol dm^{-3} and changed [arsenazo III] successively from 2.5×10^{-5}, to 5×10^{-5}, to 7.5×10^{-5}, to 1×10^{-4} and finally to 1.25×10^{-4} mol dm^{-3} (pH 4.81). In this way, the ratio $[Eu^{3+}]$: [arsenazo III] was varied in steps from 1 : 0.5 to 1 : 1, 1 : 1.5, 1 : 2 and finally to 1 : 2.5. The solution changed continuously from dark blue to dark purple. We then investigated the kinetic behaviour for different $[Eu^{3+}]$: [arsenazo III] ratios. Two consecutive steps (fast and slow) were observed in all cases. From the kinetic data it followed that the rate of the fast step increased with decreasing $[Eu^{3+}]$: [arsenazo III] ratio from 1 : 0.5 to 1 : 2.0, below which it reached a maximum value. No large changes in rate were observed for the slow step. Kinetically no change occurred in the range $[Eu^{3+}]$: [arsenazo III] = 0.5–1.0 : 1, the rate increased from 0.0406 s^{-1} at 1 : 1 ratio to 0.0597 s^{-1} at 1 : 2.0, and finally no change occurred from 1 : 2.0 to 1 : 2.5. These observations indicate that as the proportion of the 1 : 2 complex present increases with decreasing $[Eu^{3+}]$: [arsenazo III] ratio the 1 : 2 complex becomes predominant.



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We therefore used a $[Eu^{3+}]$: [arsenazo III] ratio of 1 : 2.5 in order to form the 1 : 2 complex as the predominant species. The exact charges on the 1 : 2 complex and its reacting intermediates are unknown because of the influence of the acidity of the medium, but arsenazo III carries a highly negative charge within the range $3.60 < \text{pH} < 5.6$. Thus, the 1 : 2 complex and its reacting intermediates are anions carrying multiple negative charges.

Addition of an excess of a polyaminecarboxylate to a solution of the 1 : 2 complex results in complete substitution of arsenazo III by the polyaminecarboxylate (dtpa or edta). In this way information on the reactivity of the multidentate lanthanide–arsenazo III complexes can be obtained *via* a kinetic study of the non-symmetrical ligand-substitution reactions. The rate of the substitution is such that it can be monitored conveniently on a conventional spectrophotometer at ambient pressure and on a stopped-flow instrument at elevated pressure.

A detailed analysis of the kinetic traces indicated that all absorbance *vs.* time plots for both the consecutive fast and slow steps consist of single exponential decays. The half-lives are in the range 100–500 ms and 5–50 s for the fast and slow steps, respectively. So the kinetic traces of the two steps could be recorded on different time-scales. Some typical kinetic traces for the two steps recorded under different experimental conditions are shown in Fig. 1. In general, the fit of the traces by KINFIT is good, and k_1 and k_2 can be resolved to within an error limit of ± 10%. At this point we assume on the basis of a thermodynamic analysis[37] and the following kinetic studies that the fast reaction step (k_1) involves the leaving of the first arsenazo III and the entering of the polyaminecarboxylate L′ (dtpa or edta), and the slow reaction step (k_2) involves a subsequent reaction, which may be further dechelation of arsenazo III or chelation of L′.

Fast step of the substitution reaction of the 1 : 2 complex $Eu^{III}L_2(H_2O)$

pH Dependence. The rate constants for the substitution of arsenazo III in $Eu^{III}L_2(H_2O)$ by the polyaminecarboxylate L′ (dtpa or edta) are summarized in Tables 1 and 2 for dtpa and edta, respectively, at several different pH values within the range $3.6 < \text{pH} < 5.6$ and at several pressures. The $[H^+]$ dependence at ambient pressure is also shown in Fig. 2, which is the basis for the the following observations: (1) plots of k_1 *vs.* $[H^+]$ are linear and k_1 increases with increasing acid concentration for the substitution by both dtpa and edta with the same positive intercept, *i.e.* $k_1 = k_a + k_b[H^+]$; (2) for the substitution by dtpa a larger slope k_b was observed. The positive intercepts indicate that a parallel reaction pathway, *i.e.* a spontaneous reaction, is followed in addition to that involving acid catalysis. For L′ = dtpa, $k_1 = (7.08 + 1.44 \times 10^5[H^+])$ s^{-1} and for L′ = edta, $k_1 = (6.25 + 7.55 \times 10^4[H^+])$ s^{-1} at 25 °C. The difference between dtpa and edta reflected in the slopes may be due to the difference in pK_a values and the distribution of protonated species, since dtpa is an octadentate chelating ligand with three amine groups and five carboxylate groups and edta is a hexadentate chelating ligand with two amine groups and four carboxylate groups.

Ligand concentration dependence. The dependence on the concentration of L′ was studied at 25.0 °C, ambient pressure and pH 4.81. The results (Fig. 3) indicate that k_1 increases linearly with increasing concentration of both dtpa and edta with a positive intercept, namely $k_1 = k_c + k_d[L']$. When L′ = dtpa $k_1 = (6.41 + 4.47 \times 10^2[L'])$ s^{-1} and when L′ = edta $k_1 = (5.91 + 1.15 \times 10^2[L'])$ s^{-1}. The values of k_c are very close to those found for k_a in the $[H^+]$-dependence study, indicating that k_c represents the contribution from the spontaneous reaction path. These observations again support the two-pathway mechanism which differs from what had

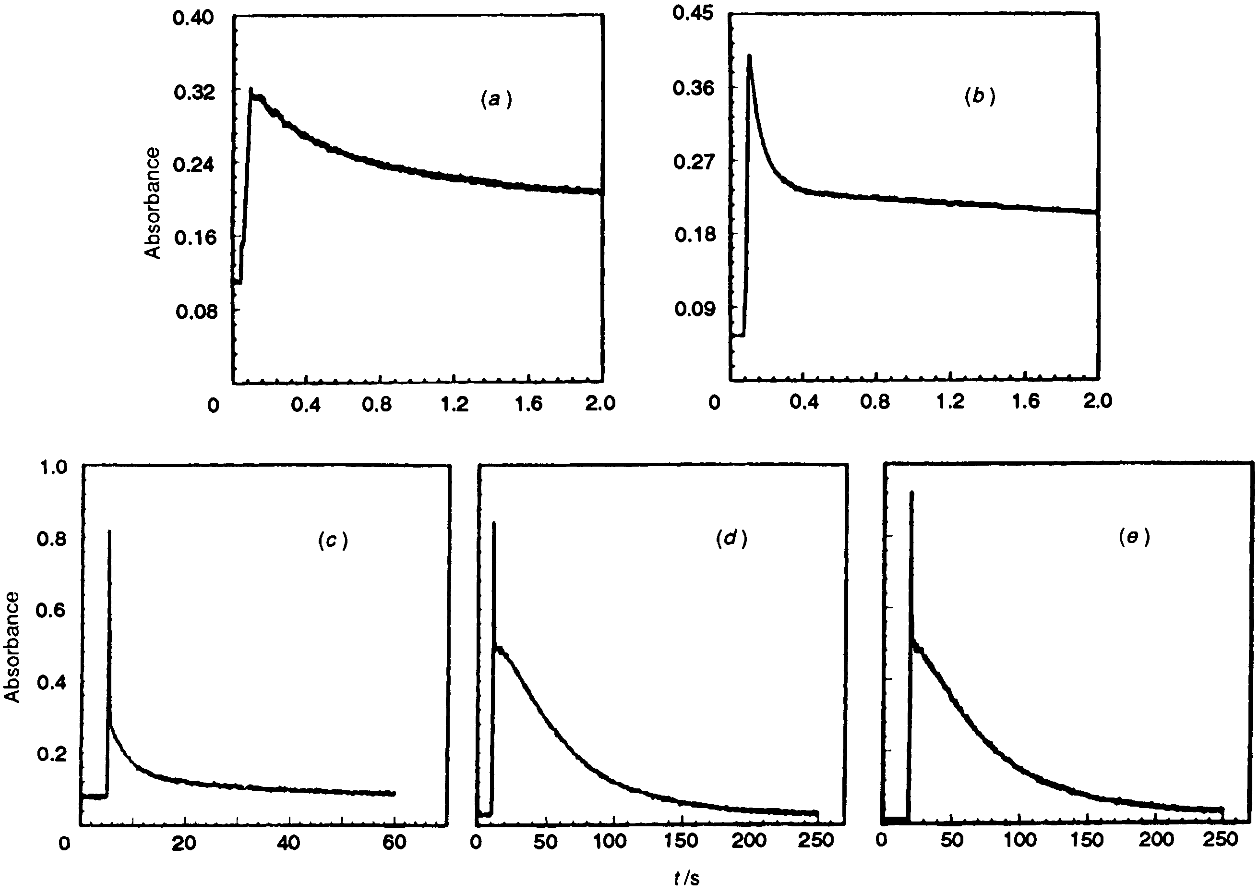


Fig. 1 Typical kinetic traces recorded for the substitution of arsenazo III by edta on aqueous Eu^{III} at 25 °C and (for experimental conditions see Table 2): (*a*) $P = 1$ bar, pH 5.55 (fast step); (*b*) $P = 1000$ bar, pH 5.55 (fast step); (*c*) $P = 1$ bar, pH 3.61 (slow step); (*d*) $P = 1$ bar, pH 5.55 (slow step); (*e*) $P = 500$ bar, pH 5.55 (slow step)

Table 1 Rate constants as a function of pH and pressure and $\Delta V^\ddagger$ values for the substitution of arsenazo III by dtpa on Eu^{III}[a]

pH	P/bar	$k_1{}^b/s^{-1}$	$\Delta V_1{}^\ddagger/cm^3\ mol^{-1}$	$10^2\ k_2{}^b/s^{-1}$	$\Delta V_2{}^\ddagger/cm^3\ mol^{-1}$
3.61	1	42.1 ± 0.40	−20.3 ± 0.3	32.0 ± 1.80	+2.4 ± 2.3
	250	52.3 ± 0.05		28.3 ± 0.90	
	500	64.8 ± 0.06		30.2 ± 0.50	
	750	80.0 ± 0.08		26.0 ± 1.20	
	1000	96.2 ± 0.71		29.3 ± 0.80	
4.08	1	18.2 ± 0.21	−20.1 ± 0.9	13.5 ± 0.13	−0.5 ± 0.5
	250	21.6 ± 1.10		13.0 ± 0.20	
	500	26.6 ± 0.80		13.3 ± 0.30	
	750	31.4 ± 0.78		13.5 ± 0.30	
	1000	41.7 ± 0.71		13.6 ± 0.40	
4.81	1	9.04 ± 0.23	−19.3 ± 1.0	4.56 ± 0.04	−0.9 ± 1.4
	250	11.1 ± 0.10		5.06 ± 0.02	
	500	13.5 ± 0.10		4.62 ± 0.01	
	750	16.2 ± 0.10		4.71 ± 0.02	
	1000	20.1 ± 0.10		4.96 ± 0.01	
5.2	1	7.78 ± 0.70	−24.9 ± 0.5	2.92 ± 0.01	+0.3 ± 3.2
	50	8.16 ± 0.03		3.75 ± 0.01	
	100	8.58 ± 0.04		3.19 ± 0.02	
	150	9.06 ± 0.05		3.08 ± 0.00	
5.55	1	6.60 ± 0.08	−18.8 ± 0.5	2.28 ± 0.02	+3.4 ± 6.3
	250	7.80 ± 0.05		2.85 ± 0.03	
	500	9.43 ± 0.07		2.49 ± 0.03	
	750	11.8 ± 0.06		1.88 ± 0.03	
	1000	14.0 ± 0.05		1.85 ± 0.02	

[a] Experimental conditions: $[Eu^{III}] = 5 \times 10^{-5}$ mol dm^{-3}, [dtpa] $= 1 \times 10^{-2}$ mol dm^{-3}, $[MeCO_2H\text{–}NaO_2CMe]_T = 0.1$ mol dm^{-3}, 25.0 °C, wavelength = 670 nm. [b] Mean value of between six and ten kinetic runs.

previously been observed[30] for Gd^{III}. In the latter case k_1 was independent of the polyaminecarboxylate concentration[30] and the observed rate constants were much smaller. The difference may be related to the changeover in co-ordination number on going from Eu^{III} to Gd^{III}.

Ionic strength dependence. The ionic strength dependence is reported in Table 3 and Fig. 4 for the substitution of arsenazo III in $Eu^{III}L_2(H_2O)$ by dtpa. The plot of k_1 *vs.* $[NaClO_4]$ at 25 °C and ambient pressure (Fig. 4) indicates that the change in k_1 is so small that we can consider the substitution rate

Table 2 Rate constants as a function of pH and pressure and $\Delta V^‡$ values for the substitution of arsenezo III by edta on Eu^{III}[a]

pH	P/bar	$k_1{}^b/s^{-1}$	$\Delta V_1{}^‡/cm^3\ mol^{-1}$	$10^2\ k_2{}^b/s^{-1}$	$\Delta V_2{}^‡/cm^3\ mol^{-1}$
3.61	1	24.7 ± 0.30	−15.7 ± 0.5	36.4 ± 0.80	+0.3 ± 1.6
	250	29.0 ± 0.30		34.4 ± 1.10	
	500	34.0 ± 0.50		37.2 ± 4.20	
	750	40.1 ± 3.00		33.3 ± 0.40	
	1000	47.0 ± 2.80		36.4 ± 1.10	
4.08	1	12.4 ± 0.70	−16.9 ± 1.5	15.2 ± 0.80	−0.6 ± 2.6
	250	16.5 ± 0.60		17.8 ± 0.20	
	500	18.6 ± 0.50		16.5 ± 0.08	
	750	22.3 ± 0.10		17.7 ± 0.05	
	1000	25.4 ± 0.11		15.7 ± 0.05	
4.81	1	7.20 ± 0.05	—	5.87 ± 0.22	—
5.20	1	6.98 ± 0.05	−23.2 ± 1.9	4.00 ± 0.05	+0.2 ± 1.5
	250	9.28 ± 0.05		4.45 ± 0.02	
	500	12.7 ± 0.06		4.07 ± 0.02	
	750	14.8 ± 0.08		4.07 ± 0.02	
	1000	18.1 ± 0.09		4.14 ± 0.04	
5.55	1	6.60 ± 0.05	−17.5 ± 0.2	2.19 ± 0.12	+0.3 ± 1.1
	250	8.00 ± 0.05		2.35 ± 0.21	
	500	9.69 ± 0.08		2.19 ± 0.15	
	750	11.8 ± 0.07		2.30 ± 0.12	
	1000	13.3 ± 0.04		2.25 ± 0.06	

[a] Experimental conditions: $[Eu^{III}] = 5 \times 10^{-5}$ mol dm^{-3}, [edta] = 1×10^{-2} mol dm^{-3}, $[MeCO_2H–NaO_2CMe]_T = 0.1$ mol dm^{-3}, 25.0 °C, wavelength = 670 nm. [b] Mean value of between six and ten kinetic runs.

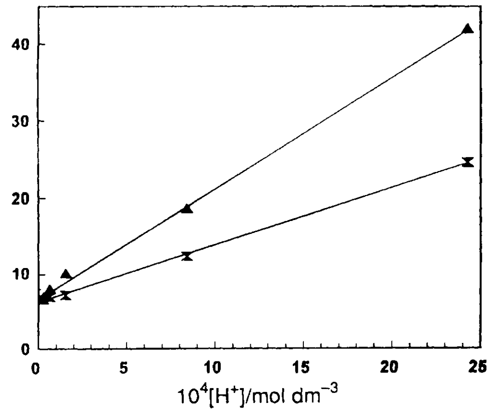


Fig. 2 Acid dependence of pseudo-first-order rate constant k_1 for the fast step of the 1 : 2 complex, undergoing substitution of arsenazo III by dtpa (▲) and edta (⧗) on Eu^{III} at 25.0 °C and 1 bar

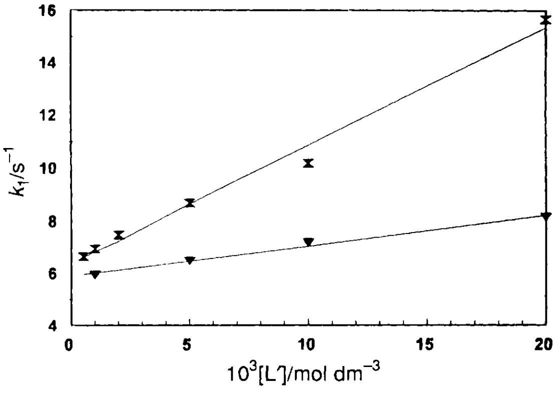


Fig. 3 Plots of k_1 *vs.* [L′] [L′ = dtpa (⧗) and edta (▼)] for the reactions of $Eu^{III}L_2(H_2O)$ with L′ at: $[Eu^{III}] = 5 \times 10^{-5}$ mol dm^{-3}, $[MeCO_2H-NaO_2CMe]_T = 0.1$ mol dm^{-3}, pH = 4.81, 25 °C and ambient pressure, wavelength = 670 nm

to be independent of [$NaClO_4$]. As mentioned above, both $Eu^{III}L_2(H_2O)$ and dtpa or edta are highly charged anionic species, and the mixed arsenazo III–Eu–L′ complex is also negatively charged, though we do not know the exact charges. The reason for the rate being independent of [$NaClO_4$] may be the negative charges on all the reactants, transition states and products. For reactions between ions of like sign, the dependence of the rate constant on ionic strength is not significant.[39]

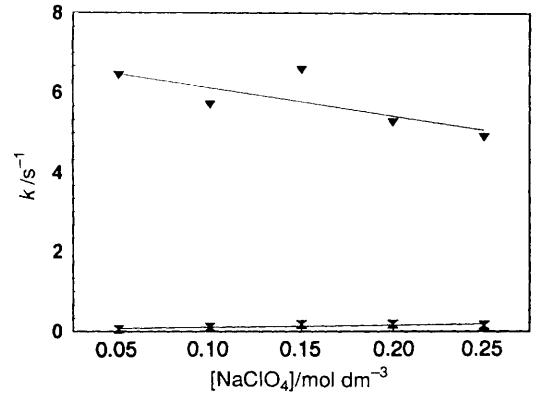


Fig. 4 Plots of the rate constants k_1 (▼) and k_2 (⧗) for the reactions of $Eu^{III}L_2(H_2O)$ with dtpa *versus* [$NaClO_4$] at 1 bar (for experimental conditions see Table 3)

Temperature dependence. The k_1 values at different temperatures are summarized for the substitution by dtpa and edta in Tables 4 and 5, respectively. The activation parameters $\Delta H_1{}^‡$ and $\Delta S_1{}^‡$ at different pH values for dtpa and edta were calculated using Eyring plots and are given in Table 6. We note that at ambient pressure $\Delta S_1{}^‡$ for the substitution of arsenazo III by dtpa is −5 ± 17 J K^{-1} mol^{-1} at pH 5.55 and becomes −66 ± 3 J K^{-1} mol^{-1} at pH 4.81.

Pressure dependence. The pressure dependence was studied at different pH values, temperatures and ionic strengths. The pressure effect for the fast step is obvious in the kinetic traces shown in Fig. 1, which were recorded under the same reaction conditions except for different pressures. The k_1 values at different pH readings and pressures are reported in Tables 1 and 2 for the substitution of arsenazo III by dtpa and edta, respectively. The relationship between k_1 and pressure at different temperatures is shown in Tables 4 (for dtpa) and 5 (for edta). We can see the correlation between k_1 and pressure at various [$NaClO_4$] values at 25.0 °C in Table 3 for the substitution of arsenazo III by dtpa. Plots of ln k_1 *vs.* pressure are perfectly linear at any pH value, temperature and ionic

Table 3 Rate constants as a function of ionic strength, [NaClO$_4$] and pressure and $\Delta V^\ddagger$ values for the substitution of arsenazo III by dtpa on Eu^{III}[a]

[NaClO$_4$]/mol dm^{-3}	P/bar	k_1[b]/s^{-1}	$\Delta V_1^\ddagger$/cm^3 mol^{-1}	$10^2\,k_2$[b]/s^{-1}	$\Delta V_2^\ddagger$/cm^3 mol^{-1}
0.05	1	6.2 ± 0.03	−23.0 ± 2.3	6.10 ± 0.30	+2.3 ± 0.4
	250	8.73 ± 0.04		6.00 ± 0.40	
	500	12.0 ± 0.04		5.90 ± 0.20	
	750	14.7 ± 0.05		5.61 ± 0.30	
	1000	16.0 ± 0.08		5.60 ± 0.20	
0.10	1	5.70 ± 0.04	—	11.4 ± 0.50	—
0.15	1	6.56 ± 0.14	−30.3 ± 1.6	18.1 ± 0.40	+6.3 ± 2.0
	250	9.22 ± 0.23		17.2 ± 0.10	
	500	13.5 ± 1.10		14.5 ± 0.80	
	750	17.4 ± 0.80		13.9 ± 0.90	
	1000	22.5 ± 0.80		14.6 ± 0.50	
0.20	1	5.26 ± 0.11	—	18.6 ± 0.50	—
0.25	1	4.90 ± 0.13	−16.4 ± 0.8	15.7 ± 0.08	−0.7 ± 1.3
	250	5.47 ± 0.10		14.5 ± 1.21	
	500	6.63 ± 0.04		15.9 ± 0.30	
	750	7.92 ± 0.04		15.6 ± 0.30	
	1000	9.42 ± 0.04		15.7 ± 0.50	

[a] Experimental conditions: [Eu^{III}] = 5×10^{-5} mol dm^{-3}, [dtpa] = 1×10^{-2} mol dm^{-3}, [MeCO$_2$H–NaO$_2$CMe]$_T$ = 0.1 mol dm^{-3}, pH 4.81, 25.0 °C, wavelength = 670 nm. [b] Mean value of between six and ten kinetic runs.

Table 4 Rate constants as a function of pH, temperature and pressure and $\Delta V^\ddagger$ values for the substitution of arsenazo III by dtpa on Eu^{III}[a]

T/°C	P/bar	k_1[b]/s^{-1}	$\Delta V_1^\ddagger$/cm^3 mol^{-1}	$10^2\,k_2$[b]/s^{-1}	$\Delta V_2^\ddagger$/cm^3 mol^{-1}
pH 4.81					
17.5	1	5.53 ± 0.40	−20.7 ± 0.1	2.51 ± 0.02	−0.7 ± 3.1
	250	6.50 ± 0.09		2.15 ± 0.01	
	500	8.75 ± 0.08		2.25 ± 0.01	
	750	10.5 ± 0.08		2.15 ± 0.01	
	1000	12.9 ± 0.30		2.61 ± 0.01	
20.5	1	6.96 ± 0.08	—	3.26 ± 0.01	—
25.0	1	9.04 ± 0.23	−19.3 ± 0.4	4.56 ± 0.04	−1.0 ± 1.4
	250	11.1 ± 0.10		5.06 ± 0.02	
	500	13.5 ± 0.10		4.81 ± 0.01	
	750	16.2 ± 0.10		4.71 ± 0.02	
	1000	20.1 ± 0.10		4.96 ± 0.01	
33.2	1	16.6 ± 0.30	−13.0 ± 0.2	7.12 ± 0.02	+4.3 ± 1.1
	250	18.5 ± 0.21		6.71 ± 0.01	
	500	20.4 ± 0.19		6.26 ± 0.01	
	750	23.4 ± 0.40		6.26 ± 0.01	
	1000	28.3 ± 0.40		7.32 ± 0.01	
40.2	1	25.4 ± 0.30	−24.8 ± 0.20	10.4 ± 0.10	+2.6 ± 4.2
	50	28.1 ± 0.03		9.35 ± 0.01	
	250	34.2 ± 0.40		8.75 ± 0.01	
	500	43.4 ± 0.80		9.60 ± 0.01	
pH 5.55					
17.5	1	2.31 ± 0.06	−32.0 ± 0.2	0.86 ± 0.01	+2.3 ± 5.5
	250	3.22 ± 0.08		1.00 ± 0.01	
	500	4.57 ± 0.08		0.64 ± 0.01	
	750	6.29 ± 0.06		0.78 ± 0.01	
	1000	8.84 ± 0.10		0.86 ± 0.01	
20.5	1	3.35 ± 0.03	−24.8 ± 1.2	1.07 ± 0.01	−1.6 ± 4.9
	250	4.13 ± 0.04		1.21 ± 0.01	
	500	5.23 ± 0.05		1.00 ± 0.01	
	750	6.80 ± 0.05		1.43 ± 0.01	
	1000	9.43 ± 0.03		1.07 ± 0.01	
25.0	1	6.43 ± 0.08	−18.8 ± 0.5	2.28 ± 0.02	−0.8 ± 4.0
	250	7.43 ± 0.03		2.85 ± 0.03	
	500	9.42 ± 0.07		2.49 ± 0.03	
	750	11.8 ± 0.05		2.99 ± 0.03	
	1000	14.0 ± 0.05		1.85 ± 0.02	
33.2	1	11.2 ± 0.06	−20.1 ± 1.6	3.21 ± 0.02	+2.5 ± 3.3
	250	13.7 ± 0.14		3.49 ± 0.03	
	500	18.4 ± 0.11		2.92 ± 0.01	
	750	20.2 ± 0.12		2.71 ± 0.01	
	1000	25.1 ± 0.14		3.21 ± 0.01	
40.2	1	22.6 ± 0.30	−18.3 ± 0.7	9.42 ± 0.09	−1.8 ± 2.2
	250	27.4 ± 0.23		9.27 ± 0.03	
	500	31.2 ± 0.03		9.92 ± 0.03	
	750	38.9 ± 0.60		10.9 ± 0.10	
	1000	46.1 ± 1.30		9.49 ± 0.06	

[a] Experimental conditions: [Eu^{III}] = 5×10^{-5} mol dm^{-3}, [dtpa] = 1×10^{-2} mol dm^{-3}, [MeCO$_2$H–NaO$_2$CMe]$_T$ = 0.1 mol dm^{-3}, wavelength = 670 nm. [b] Mean value of between six and ten kinetic runs.

Table 5 Rate constants as a function of pH, temperature and pressure and $\Delta V^{\ddagger}$ values for the substitution of arsenazo III by edta on aqueous Eu^{III}[a]

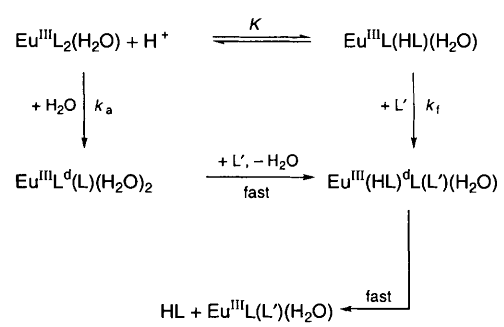
pH	T/°C	P/bar	$k_1{}^b$/s^{-1}	$\Delta V_1{}^{\ddagger}$/cm^3 mol^{-1}	$10^2k_2{}^b$/s^{-1}	$\Delta V_2{}^{\ddagger}$/cm^3 mol^{-1}
4.81	17.5	1	4.20 ± 0.20	—	5.87 ± 0.02	—
	20.5	1	5.15 ± 0.13	—	7.04 ± 0.03	—
	25	1	7.84 ± 0.05	—	9.24 ± 0.03	—
	33.2	1	12.4 ± 0.06	−27.6 ± 1.8	12.6 ± 0.01	+2.5 ± 5.0
		50	13.3 ± 0.09		11.6 ± 0.10	
		100	14.1 ± 0.08		11.3 ± 0.11	
		200	15.5 ± 0.16		12.2 ± 0.10	
	40.2	1	21.2 ± 0.19	−23.7 ± 4.1	19.4 ± 0.40	+4.4 ± 5.4
		50	23.4 ± 0.14		19.4 ± 0.20	
		150	25.4 ± 0.14		20.1 ± 0.20	
		250	27.0 ± 0.30		18.3 ± 0.20	
5.55	25	1	6.60 ± 0.05	−17.7 ± 6.4	3.37 ± 0.01	−0.5 ± 3.2
		250	7.85 ± 0.05		2.93 ± 0.01	
		500	9.69 ± 0.08		3.22 ± 0.01	
		750	11.8 ± 0.08		3.08 ± 0.01	
		1000	13.3 ± 0.04		3.37 ± 0.02	

[a] Experimental conditions: $[Eu^{III}] = 5 \times 10^{-5}$ mol dm^{-3}, [edta] $= 1 \times 10^{-2}$ mol dm^{-3}, $[MeCO_2H-NaO_2CMe]_T = 0.1$ mol dm^{-3}, wavelength = 670 nm. [b] Mean value of between six and ten kinetic runs.

Table 6 Summary of activation parameters $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ for the substitution of arsenazo III by dtpa and edta on Eu^{III}

P/bar	$\Delta H_1{}^{\ddagger}$/kJ mol^{-1}	$\Delta S_1{}^{\ddagger}$/J K^{-1} mol^{-1}	$\Delta H_2{}^{\ddagger}$/kJ mol^{-1}	$\Delta S_2{}^{\ddagger}$/J K^{-1} mol^{-1}
pH 4.81 dtpa				
1	48 ± 1	−66 ± 3	42 ± 2	−124 ± 7
250	51 ± 4	−53 ± 12	42 ± 9	−130 ± 31
500	48 ± 8	−62 ± 25	43 ± 7	−127 ± 22
750	34 ± 3	−107 ± 7	48 ± 14	−112 ± 47
1000	34 ± 4	−108 ± 12	46 ± 7	−117 ± 25
pH 4.81 edta				
1	50 ± 2	−61 ± 8	40 ± 1	−134 ± 3
pH 5.55 dtpa				
1	70 ± 5	−5 ± 17	73 ± 9	−32 ± 29
250	67 ± 3	−3 ± 11	67 ± 11	−53 ± 33
500	63 ± 3	−16 ± 10	80 ± 13	−9 ± 42
750	58 ± 4	−29 ± 14	74 ± 13	−28 ± 44
1000	53 ± 4	−45 ± 12	74 ± 7	−28 ± 24

* For experimental conditions see Tables 4 and 5.



Scheme 1 d = Dechelated

strength and yield the activation parameter $\Delta V_1{}^{\ddagger}$ (calculated from the slope).

Mechanistic interpretation. The pH and ligand-concentration dependences reported above for the substitution of Eu^{III}-$L_2(H_2O)$ by L′ (dtpa and edta) suggest that k_1 can be expressed by $k_1 = k_a + k_b[H^+]$ at constant [L′] and by $k_1 = k_c + k_d[L']$ at constant $[H^+]$. The values of k_a and k_c are indeed very similar, and the values of k_b and k_d are such that the rate laws can be combined to give $k_1 = k_a + k_e[H^+][L']$, where $k_e = 2.17 \times 10^7$ dm^6 mol^{-2} s^{-1} for L′ = dtpa and 7.49×10^6 dm^6 mol^{-2} s^{-1} for L′ = edta. This two-term rate law indicates that the substitution process follows two parallel reaction routes, a spontaneous reaction independent of [L′] and an acid-catalysed reaction dependent on [L′]. A mechanism based on these findings is proposed in Scheme 1. It consists of a protonation equilibrium, during which one of the co-ordinated arsenazo III ligands is protonated to facilitate dechelation, and two rate-determining steps, one a spontaneous slow dechelation followed by rapid attack by L′ and another involving rate-determining attack of L′ on the protonated complex. Both reaction paths lead to the formation of the mixed-ligand species which then experiences rapid departure of the dechelated arsenazo III.

The proposed mechanism is characterized by the rate equation $k_1 = k_a + k_fK[H^+][L']$, which is consistent with the empirical rate equation where $k_e = k_fK$. We now turn to a discussion of the reported activation parameters $\Delta H_1{}^{\ddagger}$, $\Delta S_1{}^{\ddagger}$ and $\Delta V_1{}^{\ddagger}$ to get further insight into the intimate nature of the reaction steps. The values of $\Delta H_1{}^{\ddagger}$ are typical for ligand-substitution reactions involving the formation and breakage of bonds. The values of $\Delta S_1{}^{\ddagger}$ are small and negative at high pH and are significantly negative at low pH for both dtpa and edta, whereas the values of $\Delta V_1{}^{\ddagger}$ are negative under all conditions. This suggests that significant bond formation must occur during the spontaneous (k_a) reaction path, which presumably involves water-assisted dechelation of the $Eu^{III}L_2(H_2O)$ complex. Such a dechelation will involve several volume contributions: a volume collapse due to co-ordination of additional solvent molecules, a volume increase due to the ring-opening process and a volume decrease due to an increase in electrostriction which will accompany the ring-opening process. The overall effect is a negative $\Delta V_1{}^{\ddagger}$ value. Thus the spontaneous (k_a) reaction path can be visualized as a water-assisted dechelation of the arsenazo III ligand accompanied by an overall volume decrease due to binding of an additional solvent molecule and an increase in electrostriction surrounding the dechelated ligand. At lower pH the acid-catalysed pathway will involve protonation of arsenazo III to assist dechelation, accompanied by chelation of L′ (dtpa or edta). It must be particularly the latter contribution that will account for the negative $\Delta V_1^\ddagger$ values observed for the k_fK term of the rate law at low pH, *i.e.* high [H$^+$].

Slow step of the substitution reaction of the 1:2 complex $Eu^{III}L_2(H_2O)$

pH Dependence. The pH dependence of the slow step of the substitution of arsenazo III in $Eu^{III}L_2(H_2O)$ by the polyaminecarboxylate L′ (dtpa or edta) is reported as a function of pressure in Tables 1 and 2 for dtpa and edta, respectively, and in Fig. 5 for ambient pressure. The plots of k_2 *vs.* [H$^+$] are linear and go almost through the origin. They are very similar for both dtpa and edta, *i.e.* $k_2 \approx k_g[H^+]$. Absence of a significant intercept implies that the reaction involves only the acid-catalysed pathway.

Ligand concentration dependence. The dependence on the concentration of dtpa or edta was studied at 25 °C, ambient pressure and pH 4.81. The results are summarized in Fig. 6; k_2 is seen to be independent of concentration for both dtpa and edta. A similar independence of k_2 on ligand concentration was found for the corresponding substitution of aqueous Gd^{III}.[30]

Ionic strength dependence. The k_2 values at different [NaClO$_4$] and at a series of pressures are recorded in Table 3 and Fig. 4. As shown in Fig. 4, the plot of k_2 *vs.* [NaClO$_4$] at 25 °C and ambient pressure indicates that the change in k_2 is also so small (similar to k_1 as discussed above) that we can consider the substitution rate to be independent of [NaClO$_4$] within the range $0.1 \leqslant [NaClO_4] \leqslant 0.25$ mol dm^{-3}. The plots of ln k_2 *vs.* pressure show that the rates of substitution of arsenazo III in $Eu^{III}L_2(H_2O)$ by dtpa are independent of [NaClO$_4$].

Temperature dependence. Values of k_2 at different temperatures for the substitution by dtpa and edta are shown in Tables 4 and 5, respectively. The activation parameters $\Delta H_2^\ddagger$ and $\Delta S_2^\ddagger$ for dtpa and edta are given in Table 6.

Pressure dependence. The pressure dependence was studied at different pH values, temperatures and ionic strengths. The k_2 values at different pH values and pressures are reported in Tables 1 and 2 for the substitution of arsenazo III by dtpa and edta, respectively. Two typical kinetic traces [(*d*) and (*e*)] are recorded at different pressures in Fig. 1. We see that the slow substitution $Eu^{III}L_2(H_2O)$ by dtpa or edta exhibits almost no pressure dependence under these conditions.

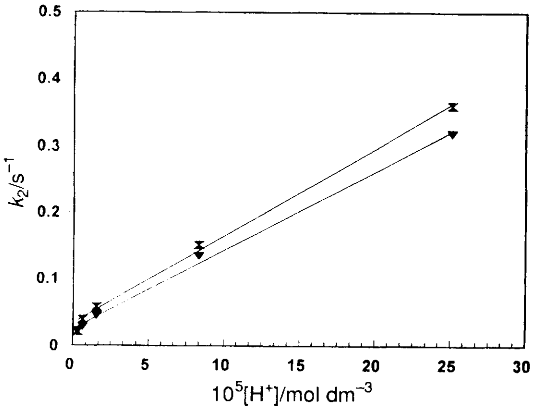


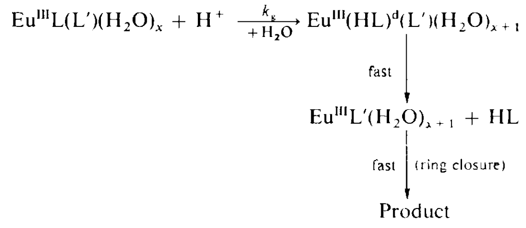
Fig. 5 Effect of pH on the rate of substitution of the arsenazo III ligand in the 1:2 europium(III) complex by dtpa (▼) and edta (⧗) (for experimental conditions see Tables 1 and 2)

Mechanistic interpretation. From the pH and ligand-concentration dependences reported for k_2 it follows that this reaction is acid-catalysed and does not involve the entering ligand in the rate-determining step. Here we should stress that the slow process must be a subsequent dechelation step. The fact that this step is much slower may favour our argument that it is the second arsenazo III that is leaving, starting with acid-catalysed dechelation and followed by rapid further chelation. It is therefore reasonable to suggest that the substitution process is controlled by acid-catalysed dechelation of arsenazo III as suggested in Scheme 2, for which $k_2 \approx k_g[H^+]$. In Scheme 2, the number of co-ordinated H$_2$O molecules is unknown since we do not know how far arsenazo III is dechelated and how far L′ is chelated at the top of the activation-energy barrier.

The reported activation parameters can be interpreted in the following way. The values of $\Delta H_2^\ddagger$ are again typical for a ligand-substitution process; $\Delta S_2^\ddagger$ is close to zero at higher pH, but significantly negative at low pH. The values of $\Delta V_2^\ddagger$ are close to zero under all conditions. This means that the acid-catalysed dechelation step (k_g) must involve co-ordination of an additional solvent molecule to account for the negative $\Delta S_2^\ddagger$ value. In terms of intrinsic volume changes, bond-formation and bond-breakage contributions seem to cancel in order to account for the zero $\Delta V_2^\ddagger$ values. The dechelated complex undergoes a series of fast reactions which involve the release of arsenazo III and the binding of L′.

Comparison between Eu^{III} and Gd^{III}

In Table 7 the data for Eu^{III} are compared with those for the analogous gadolinium(III) species[30] at a pH *ca.* 5.5. In our earlier study[30] it was argued that the two observed reaction steps could be associated with the substitution of arsenazo III by edta and dtpa in the 1:1 and 1:2 complexes, respectively. On the basis of the available stability constant[37] we realize that for all practical purposes only the 1:2 complex is present in solution under the selected experimental conditions. This means that the kinetic data reported for the gadolinium(III) system should be interpreted along the lines outlined in the



Scheme 2 d = Dechelation

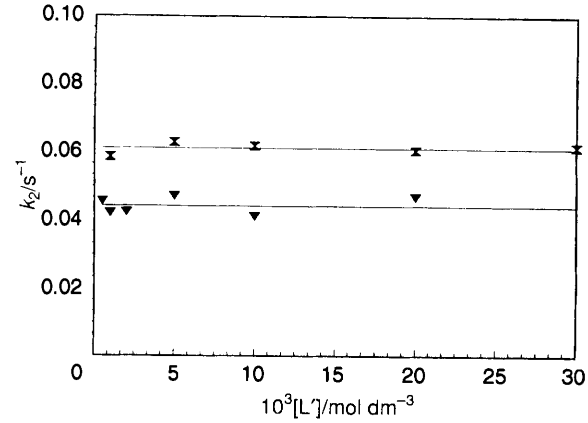


Fig. 6 Plots of k_2 *vs.* [L′] [L′ = dtpa (▼) or edta (⧗)] for the reactions of $Eu^{III}L_2(H_2O)$ with L′. Conditions as in Fig. 3

Table 7 Summary of rate and activation parameters for the substitution of arsenazo III by dtpa on M^{III} (M = Gd or Eu) at 25.0 °C[a]

Parameter	M = Gd[b]	M = Eu[c]
$10^1 k_1$/s^{-1}	0.26 ± 0.01	66.0 ± 0.8
$\Delta H_1^\ddagger$/kJ mol^{-1}	36 ± 2	70 ± 5
$\Delta S_1^\ddagger$/J K^{-1} mol^{-1}	−152 ± 7	−5 ± 17
$\Delta V_1^\ddagger$/cm^3 mol^{-1}	−33.9 ± 0.8	−18.9 ± 0.5
$10^2 k_2$/s^{-1}	0.56 ± 0.05	2.28 ± 0.02
$\Delta H_2^\ddagger$/kJ mol^{-1}	53 ± 2	73 ± 9
$\Delta S_2^\ddagger$/J K^{-1} mol^{-1}	−109 ± 5	−32 ± 29
$\Delta V_2^\ddagger$/cm^3 mol^{-1}	+69.6 ± 3.7	+3.4 ± 6.3

[a] For experimental conditions see ref. 30 (Gd^{III}) and Table 1 (Eu^{III}). [b] pH 5.70 and P = 50 bar. [c] pH 5.5 and P = 1 bar.

present report. In general, the rate of substitution of arsenazo III by dtpa is much faster for Eu^{III} than for Gd^{III} as seen from the values for both k_1 and k_2. This is not an unusual observation since a higher lability has been observed for the europium(III) system before.[21] In this respect it is interesting that k_1 does exhibit a meaningful ligand-concentration dependence in the case of Eu^{III}, but not for Gd^{III}. The higher values of k_1 and k_2 found for Eu^{III} are accompanied by significantly larger values for $\Delta H^\ddagger$ and much more positive values for $\Delta S^\ddagger$, from which it follows that the substitution reaction must be entropy driven. The volume of activation for k_1 is a bit more negative for Eu^{III} than for Gd^{III} and underlines the operation of an associative mechanism. The volume of activation is much smaller for Eu^{III} than for Gd^{III} in the case of k_2. In fact, the $\Delta S_2^\ddagger$ and $\Delta V_2^\ddagger$ values for Eu^{III} are close to zero thus emphasizing the interchange character of the ligand-substitution process. Extremely contrasting $\Delta S_2^\ddagger$ and $\Delta V_2^\ddagger$ values were reported[30] in the case of Gd^{III} and were mainly ascribed to a change in solvation. All in all, the activation parameters reported for the displacement of arsenazo III by dtpa on Eu^{III} clearly indicate that the reactions have a significant associative character and that the substitution mechanism is of the interchange type.

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References

1 G. R. Choppin, *J. Less-Common Met.*, 1985, **112**, 198.
2 V. Alexander, *Chem. Rev.*, 1995, **95**, 273.
3 C. A. Chang, P. H. L. Chang, V. K. Manchanda and S. Kasprzyk, *Inorg. Chem.*, 1988, **27**, 3786.
4 W. P. Cacheris, S. K. Nickle and A. D. Sherry, *Inorg. Chem.*, 1987, **26**, 958.
5 G. R. Choppin, *J. Alloys Compds.*, 1995, **225**, 242.
6 N. Graeppi, H. Powell, G. Laurenczy, L. Zékány and A. E. Merbach, *Inorg. Chim. Acta*, 1995, **235**, 311.
7 Th. Kowall, F. Foglia, L. L. Helm and A. E. Merbach, *J. Am. Chem. Soc.*, 1995, **117**, 3190.
8 K. Micskei, D. H. Powell, L. Helm, E. Brücher and A. E. Merbach, *Magn. Reson. Chem.*, 1993, **31**, 1011.
9 K. Micskei, L. Helm, E. Brücher and A. E. Merbach, *Inorg. Chem.*, 1993, **32**, 3844.
10 S. Aime, M. Botta, M. Fasano, S. Paolett, P. L. Anell, F. Ugger and M. Virtuani, *Inorg. Chem.*, 1994, **33**, 4707.
11 D. H. González, V. Powell, V. Tissières and A. E. Merbach, *J. Phys. Chem.*, 1994, **98**, 53.
12 F. Maasstani, M. F. Davision, I. C. M. Wehman-Ooyevaar, D. M. Grove, J. J. Smeets, A. L. Spek and G. van Koten, *Inorg. Chim. Acta*, 1995, **235**, 327.
13 E. Brücher and A. D. Sherry, *Inorg. Chem.*, 1990, **29**, 1555.
14 E. Brücher, S. Cortes and A. D. Sherry, *Inorg. Chem.*, 1991, **30**, 2092.
15 K. Kumar, C. A. Chang and M. F. Tweedle, *Inorg. Chem.*, 1993, **32**, 587.
16 S. I. Kang, R. S. Ranganathan, J. E. Emswiler, K. Kumar, J. Z. Gougoutas and M. F. Malley, *Inorg. Chem.*, 1993, **32**, 2912.
17 M. Kodama, T. Koike, A. B. Mahatma and E. Kimura, *Inorg. Chem.*, 1991, **30**, 1270.
18 A. D. Sherry, R. D. Brown, C. F. G. C. Geraldes, S. H. Koenig, K.-T. Kuan and M. Spiller, *Inorg. Chem.*, 1989, **28**, 620.
19 C. A. Chang, L. C. Francesconi, M. F. Malley, K. Kumar, J. Z. Gougoutas and M. F. Tweedle, *Inorg. Chem.*, 1993, **32**, 2912.
20 P. J. Breen, W. D. Horrocks, jun., and K. A. Johnson, *Inorg. Chem.*, 1986, **25**, 1968.
21 C. Cossy, L. Helm and A. E. Merbach, *Inorg. Chem.*, 1989, **28**, 2699.
22 C. Cossy, L. Helm and A. E. Merbach, *Inorg. Chem.*, 1988, **27**, 1973.
23 K. Kumar and M. F. Tweedle, *Inorg. Chem.*, 1993, **32**, 4193.
24 R. B. Lauffer, *Chem. Rev.*, 1987, **87**, 901; S. Jurisson, D. Berning, W. Jia and D. Ma, *Chem. Rev.*, 1993, **93**, 1137; J. F. Desreux and P. P. Barthèlemy, *Nucl. Med. Biol.*, 1988, **15**, 9.
25 (*a*) Y. Marcus and A. S. Kertes, *Ion Exchange and Solvent Extraction of Metal Complexes*, Wiley-Interscience, London, 1969; (*b*) J. Bünzli and D. Wessner, *Coord. Chem. Rev.*, 1984, **60**, 191.
26 M. C. F. Cunha, H. F. Brito, L. B. Zinner and G. Vicentini, *Coord. Chem. Rev.*, 1992, **119**, 1.
27 R. van Eldik, T. Asano and W. J. LeNoble, *Chem. Rev.*, 1989, **89**, 549.
28 A. E. Merbach and J. W. Akitt, *NMR Basic Principles and Progress*, Springer, Berlin, 1990, vol. 24, p. 190.
29 R. van Eldik and A. E. Merbach, *Comments Inorg. Chem.*, 1992, **12**, 341.
30 K. B. Reddy, S. Cao, E. C. Orr, I. Fabian, R. van Eldik and E. M. Eyring, *J. Chem. Soc., Dalton Trans.*, 1994, 2497.
31 R. van Eldik, W. Gaede, S. Wieland, J. Kraft, M. Spitzer and D. A. Palmer, *Rev. Sci. Instrum.*, 1993, **64**, 1355.
32 KINFIT, Olis, Bogert, GA, 1989.
33 S. B. Savvin, *Arsenazo III*, Atomizdat, Moscow, 1966; B. Budĕšínský, *Talanta*, 1969, **16**, 1288; *Collect. Czech. Chem. Commun.*, 1963, **28**, 2902.
34 P. K. Spitsyn, V. S. Shvarev and T. P. Popyvanova, *Russ. J. Inorg. Chem.*, 1972, **17**, 502; N. A. Nepomnyashchaya, A. A. Men'kov and A. S. Lenskii, *Russ. J. Inorg. Chem.*, 1975, **20**, 1010.
35 K. Ogan and E. R. Simons, *Anal. Biochem.*, 1979, **96**, 70; P. Palade and J. Vergara, *Biophys. J.*, 1983, **43**, 355; P. L. Dorogi, *Biochim. Biophys. Acta*, 1984, **799**, 9.
36 K. Inaba, S. Muralidharan and H. Freiser, *Anal. Chem.*, 1993, **65**, 1510; R. Kuroda, M. Kursaki, Y. Hayashibe and S. Ishimaru, *Talanta*, 1990, **37**, 619; D. B. Gladilovich, L. Sommer and V. Kuban, *Talanta*, 1988, **35**, 259; S. Kus, N. Obarski and Z. Marczenko, *Anal. Sci.*, 1992, **8**, 213; V. F. Lukyanov, E. P. Duderova, T. E. Barabanova and E. F. Novak, *J. Anal. Chem. USSR* (*Engl. Transl.*), 1989, **44**, 1793.
37 S. K. Nickle, Ph.D. Dissertation, University of Texas at Dallas, 1986.
38 Simultaneous Equation Solver (SEQS), CET Research Group Ltd., Norman, OK, 1991.
39 R. G. Wilkins, *Kinetics and Mechanism of Reactions of Transition Metal Complexes*, 2nd edn., VCH, Weinheim, 1991, p. 110.

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