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An Exploratory Scandium-45 NMR Study into the Complexation of Alanine and Oligopeptides

DIETER REHDER* and MARTINA SPEH

Institut für Anorganische Chemie der Universität, Martin-Luther-King-Platz 6, D-2000 Hamburg 13, F.R.G.

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Abstract

The 87.5 MHz ^{45}Sc NMR spectrum of 0.025 M aqueous $Sc(NO_3)_3$ exhibits two resonance signals, separated by *ca.* 25 ppm, attributable to $[Sc(H_2O)_6]^{3+}$ and $[Sc(H_2O)_5OH]^{2+}$. Acidification leads to a single, comparatively sharp line ($W_{1/2}$ = 160 Hz) for the hexaqua complex, the temperature dependence (temperature gradient = 0.076 ppm/deg) of which indicates that relaxation is dominated by the quadrupole mechanism. Addition of α-alanine gives rise to an additional broad signal at *ca.* +70 ppm (relative to $[Sc(H_2O)_6]^{3+}$), which is assigned to a carboxylato complex $[Sc(H_2O)_{6-n}(ala)_n]^{3+}$ or $[Sc(H_2O)_{5-n}OH(ala)_n]^{2+}$ ($1 < n < 2$). At ambient temperatures, these species are in slow exchange with the hexaqua and pentaqua-hydroxo complex, progressing through medium towards fast exchange as the temperature increases, and giving rise to an exchange contribution to relaxation. $W_{1/2}$ becomes a measure for the stability of the complexes, which increases in the order ala < $(ala)_4 \sim (ala)_2$ < ala-val-leu. The pronounced stability of the latter is due to the formation of a chelate-five ring structure (participation of the NH-function of the peptide bond in coordination to Sc^{3+}). 1 M aqueous $ScCl_3$ probably contains the two species $[Sc(H_2O)_6]^{3+}$ and $[Sc(H_2O)_5Cl]^{2+}$, separated by 33 ppm.

Introduction

Sc^{3+}, according to the present state of knowledge, does not belong to the metal ions which play an essential role in living organisms. Its ionic radius is, however, very close to that of Mg^{2+} (75 and 72 pm, respectively, in complexes with the coordination number 6), for which the importance as a regulatory metal ion and activating centre in enzymes (such as ATPase) has long been recognized [1]. The similar ionic radii of Sc^{3+} and Mg^{2+} suggest that the chemistry of these two metal ions is also comparable in some respect under physiological conditions despite of their different ionic charges. The direct investigation of the *in vivo* role of Mg^{2+} by spectroscopic methods is cumbersome since this ion is a closed-shell (d^0) diamagnetic system. For this reason, Mg^{2+} has been replaced by ions which can be studied by ESR and electron absorption spectroscopy (Mn^{2+}, Co^{2+}, Cr^{3+} [2]). Only recently, ^{25}Mg NMR spectroscopy, in conjunction with ^{43}Ca NMR, has been employed to study the binding of Mg^{2+} to functional proteins [3, 4].

The nucleus ^{25}Mg is, however, a difficult one to study. It is evident from the NMR properties given in Table I that ^{45}Sc is a much more suitable NMR probe. While both are quadrupolar nuclei ($I > ½$), which is an advantage in terms of the availability of the line width parameter in the investigation of complex systems containing Mg^{2+} or Sc^{3+}, ^{45}Sc clearly has the more favourable relative receptitivity and resonance frequency, a fact which has prompted the present exploratory study. This is the first ^{45}Sc NMR investigation into systems containing ligands of biological relevance. The few ^{45}Sc NMR studies on inorganic scandium compounds which have been carried out to date have been reviewed [5].

Background

Scandium salts ScX_3 with X = Cl^-, Br^-, I^-, NO_3^-, ClO_4^- and $½SO_4^{2-}$ all exhibit, in aqueous solution and at concentrations <*ca.* 0.1 M, practically the same ^{45}Sc chemical shift which has been assigned to $[Sc(H_2O)_6]^{3+}/[Sc(H_2O)_5OH]^{2+}$ [6, 7]. Replacement of H_2O by other ligands coordinating via oxygen ($OC(NH_2)_2$ [6], $OP(OR)_3$ [8]) results in changes in the chemical shift $\delta(^{45}Sc)$ of less than 30 ppm. In the pH range 3–5, where amino acid complexes of Sc^{3+} are stable towards hydrolysis to $Sc(OH)_3$ (solubility product 10^{-28}), the species present is $^+NH_3CH(R)CO_2^-$ and the function available for coordination is the carboxylato group of the amino

*Author to whom correspondence should be addressed.

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TABLE I. Nuclear Data

Nucleus	Spin	Natural abundance	Relative receptivity[a]		Quadrupole moment[b]	ν_o[c]
			constant B_o	constant ν_o		
^{25}Mg	5/2	10.13%	2.7×10^{-3}	0.714	0.20	6.12
^{45}Sc	7/2	100%	0.301	5.10	−0.22	24.29

[a]Relative ^{1}H = 1; same number of nuclei per unit volume. B_o = external magnetic field, ν_o = measuring frequency. [b]In units of 10^{-28} m^2. [c]Frequency (in MHz) at B_o = 2.35 T [$\nu(^1H)$ = 100 MHz].

acid. Thus, the coordination sphere of an amino acid complex is still occupied by oxygen donors, and changes in $\delta(^{45}Sc)$ will be moderate.

As in other heavier nuclei, shielding variations of the ^{45}Sc nucleus are governed by the paramagnetic deshielding contribution to the overall shielding $\sigma = A - \sigma(para)$ [5, 9], where A is the diamagnetic term which is practically constant for a given nucleus, and the small non-local contributions arising from nuclei in the coordination sphere are neglected. For $\sigma(para)$, we write

$$\sigma(para) = b(\overline{r^{-3}C^2})_{val}\overline{\Delta E^{-1}} \quad (1)$$

where b is a numerical value, r the distance of the valence electrons from the Sc nucleus, and C the scandium coefficient of the molecular orbitals taking part in electron transitions, the main contribution coming from orbitals with sizable C(3d) coefficients. ΔE is the (averaged) HOMO–LUMO gap.

Partial replacement of H_2O in $[Sc(H_2O)_6]^{3+}$ by other oxygen ligands leads to a decrease in symmetry and a concomittant lifting of the degeneracy of the HOMO and LUMO. As a consequence, ΔE and σ decrease; *i.e.*, the signal shifts to lower field (higher frequency).

The situation is somewhat different as nitrogen donors come in, which can readily be provided by the NH group of the peptide linkages in oligopeptides. Apart from the symmetry effect discussed above, there will be a direct influence of the less electronegative nitrogen ligand upon ^{45}Sc shielding. The expected trend in a d^0 system such as Sc^{3+} is a decrease of shielding with respect to $\{ScO_6\}$ due to an increase of C(3d) and a decrease of ΔE [10], a behaviour which is commonly known as 'inverse electronegativity dependence of metal shielding' [5, 11] and which, in the Sc system, has been verified for thiocyanato and chloro complexes of Sc^{3+} [7, 12, 13]. The increase of C(3d) in $\{ScO_{6-n}N_n\}$ relative to $\{ScO_6\}$ is mediated by the better π-donating ability of the nitrogen ligand (*cf.* ref. [10]).

Since ^{45}Sc is a quadrupolar nucleus, spin-lattice relaxation times T_2 are expected to be governed by the quadrupole relaxation mechanism, and comparatively broad lines should arise in all complexes except those with cubic symmetry. Although broad lines are a disavantage with respect to spectral resolution, the line width parameter can also be considered a valuable additional quantity in evaluating the NMR information. Line widths are usually quoted as widths at half-height, *viz.* $W_{1/2}$. Under extreme narrowing conditions ($\omega\tau_c \ll 1$, ω = Lamor frequency of the nucleus, τ_c = molecular correlation (reorientation) time) [9, 14], and provided there is no chemical exchange,

$$W_{1/2} = (\pi T_2)^{-1} = 3\pi/10\, f_I(NQC)^2(1 + \eta^2/3)\tau_c \quad (2)$$

where f_I is a function of the nuclear spin I (for ^{45}Sc, $f_I = 0.136$), η the asymmetry parameter (= 0 in axially symmetric systems), and NQC the nuclear quadrupole coupling constant e^2qQ/h (Q = quadrupole moment, q = [zz component of the] field gradient [tensor]). τ_c can be described as a quantity interrelated to the solvent–solute interaction. For a given nucleus, $W_{1/2}$ mainly depends upon τ_c and q. q is closely connected to the local symmetry and the electronic interaction between the metal nucleus and the ligand functions. In our complexes, where there is no profound variation of the electronic interaction in the coordination sphere, we can expect $W_{1/2}$ to increase as (i) the local symmetry decreases ($[ScO_6] \rightarrow \{ScO_{6-n}O'_n\}$ or $\{ScO_{6-n}N_n\}$, $0 < n < 6$) and (ii) the size/bulk of the ligands ($H_2O \rightarrow$ peptide) and the viscosity of the solution increase (decreasing temperature; increasing concentration).

If ^{45}Sc relaxation is actually quadrupole dominated (eqn. (2)), then line widths of the ^{45}Sc NMR signal of an individual species present in solution should decrease with increasing temperature according to [15]

$$W_{1/2} = c\sqrt{T}\exp(E_A/RT) \quad (3)$$

where c is a constant and E_A the activation energy for molecular reorientation. If this is not so, a second, superimposed component has to be taken into account.

This component can be spotted in exchange contributions to $W_{1/2}$ [16] arising from equilibria of the kind

$$[Sc(H_2O)_6]^{3+} + nL \rightleftharpoons [Sc(H_2O)_{6-n}L_n]^{(3-n)+} + nH_2O \quad (4)$$

where L is a ligand such as OH, Cl or $^{+}NH_3CH(R)$-CO_2^{-}. We have to consider two limiting cases. Case (i) is the slow exchange between the hexaqua complex and a stable complex containing one or more ligands L. Two separate signals will be observed. Case (ii) prevails if the complex $[Sc(H_2O)_{6-n}L_n]^{(3-n)+}$ is labile and exchange is fast. One signal is observed, the characteristic NMR parameters δ and $W_{1/2}$ of which are the weighted average of the two species in equilibrium. Passing from case (i) to case (ii), e.g. by gradually increasing the temperature, results in a gradual increase of $W_{1/2}$ in the temperature range where intermediate exchange rates dominate the relaxation of the system and in a subsequent decrease of $W_{1/2}$ as the fast exchange domaine is approached. The evaluation of these temperature dependencies has been described by Forsén and co-workers and applied to the binding of ^{25}Mg and ^{43}Ca to calmodulin and troponin [3, 4].

Results and Discussion

Aqueous $ScCl_3$ and $Sc(NO_3)_3$

The standard we have used in this investigation, 1 M $ScCl_3$, gives rise to a strong signal at $\delta = 0$ ppm (by definition), $W_{1/2} = 220$ Hz, and a broad, weak signal at $\delta = +33.1$ ppm. $W_{1/2} = 1300$ Hz (Fig. 1). Only one signal has previously been observed in aqueous scandium chloride solutions; it was attributed to complexes containing up to two chlorine ligands, possibly in fast exchange [6, 7, 13]. This assignment is, however, not consistent with the small shift difference to a 0.025 M $Sc(NO_3)_3$ solution acidified with HNO_3 to a pH = 1 ($\delta = +0.7$ ppm, $W_{1/2} = 160$ Hz), in which the only species present is $[Sc(H_2O)_6]^{3+}$. We therefore assign the two signals of the $ScCl_3$ solution to the hexaqua cation and an aqua-chloro complex (possibly $[Sc(H_2O)_5Cl]^{2+}$ in slow mutual exchange. The broad signal of the latter is shifted to low field, as expected for the inverse electronegativity dependence discussed above.

The temperature dependence of $W_{1/2}$ of an acidified $Sc(NO_3)_3$ solution (Table II) in the temperature range 293 to 363 K clearly illustrates that relaxation here is quadrupole dominated (eqn. (2)) via τ_c; *i.e.*, relaxation times increase with increasing temperature (eqn. (3)). There is also a slight but distinct decrease of ^{45}Sc shielding with increasing temperature (Table II). The average temperature gradient is 0.076 ppm/deg. This deshielding effect is predicted by theory and has been explained by increasing electron populations of excited rovibrational levels (of the electronic ground state) at higher temperatures, which amounts to a decrease of ΔE in eqn. (1) [17, 18]. For the temperature dependencies of δ and $W_{1/2}$ see also the graphical representations in the next section (Fig. 4).

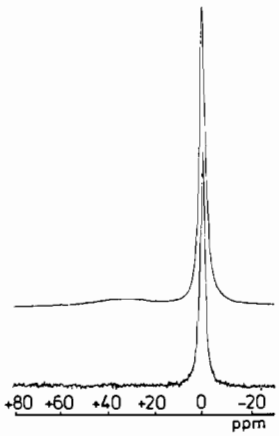

Fig. 1. 87.5 MHz ^{45}Sc NMR spectra of D_2O solutions of 1 M $ScCl_3$ (top; 14 scans) and 0.025 $Sc(NO_3)_3$ (acidified with HNO_3; 1140 scans).

TABLE II. Temperature Dependencies of δ and $W_{1/2}$ of a 0.025 M Aqueous Solution of Scandium Nitrate, Acidified to pH = 1

Temperature (K)	δ (ppm)[a]	$W_{1/2}$ (Hz)
283	+0.06	108
293	+0.74	125
303	+1.51	99
313	+2.39	86
323	+3.24	80
333	+4.08	61
343	+4.80	52
353	+5.50	54
363	+6.14	36

[a]Relative to 1 M $ScCl_3/D_2O$.

If 0.025 M scandium nitrate solutions are left with their intrinsic acidity (pH *ca.* 3.5) based on the equilibrium situation (eqn. (5)) two partly overlapping

$$[Sc(H_2O)_6]^{3+} + H_2O \rightleftharpoons [Sc(H_2O)_5OH]^{2+} + H_3O^{+} \quad (5)$$

signals arise. In Fig. 2, the ^{45}Sc NMR spectra of two samples, prepared in our laboratory (sample 1) and a commercially available one (sample 2) are displayed. We allocate the two signals to the two species of equilibrium (5) [data on sample 1 in brackets]:

$\delta = +16$ [+13] ppm, $W_{1/2} = 1.42$ [1.07] kHz: $[Sc(H_2O)_6]^{3+}$

$\delta = +40$ [+38] ppm, $W_{1/2} = 2.56$ [3.12] kHz: $[Sc(H_2O)_5OH]^{2+}$

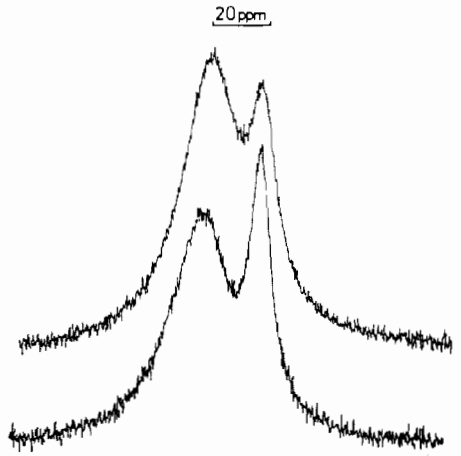

Fig. 2. 87.5 MHz ^{45}Sc NMR spectra (500 scans) of two samples (see text) of 0.025 M aqueous (D_2O) $Sc(NO_3)_3$ at pH *ca.* 3.5. The signal to high field (low frequency; right-hand side) is assigned $[Sc(H_2O)_6]^{3+}$, the broader signal to lower field $[Sc(H_2O)_5OH]^{2+}$. The zero point on the ppm scale corresponds to 1 M $ScCl_3/D_2O$.

The equilibrium is sufficiently slow to allow NMR detection of the two scandium complexes. Nonetheless, there is an obvious exchange contribution both to the positions and the line widths of the signals, which is especially pronounced for the sharper signal at high field assigned to the hexaqua complex which, in sample 1, is shifted to low field by 13 ppm and broadened by a factor of ten with respect to $Sc(NO_3)_3$ at pH = 1. Apparently, the commercial sample 2 contained more 'free HNO_3' than sample 1.

TABLE III. Temperature Dependencies of δ and $W_{1/2}$ in the System $Sc(NO_3)_3$ (0.025 M)/α-Alanine (Molar Ratio 1/6)

Temperature (K)	Signal number[a]					
	a		b		c	
	δ	$W_{1/2}$	δ	$W_{1/2}$	δ	$W_{1/2}$
283	23	1.47	45	[b]	77	[b]
293	31	1.34	48	2.6	75	3.7
303	28	1.05	46	2.7	74	3.2
313	32	1.40	46	2.6	72	3.0
323	36	1.68	[b]	[b]	70	2.9
333[c]	38	1.82	–	–	69	2.2
343[c]	43	1.86	–	–	67	2.7
353[c]	38	1.30	–	–	–	–
363[c]	35	0.91	–	–	–	–

[a]For the assignment of the three signals see Fig. 3. δ in ppm relative 1 M $ScCl_3/D_2O$; $W_{1/2}$ in kHz. [b]Not sufficiently resolved to allow unambiguous evaluation. [c]The signals at temperatures above 330 K are weighted averages for the species **a** and **b** (and **c**).

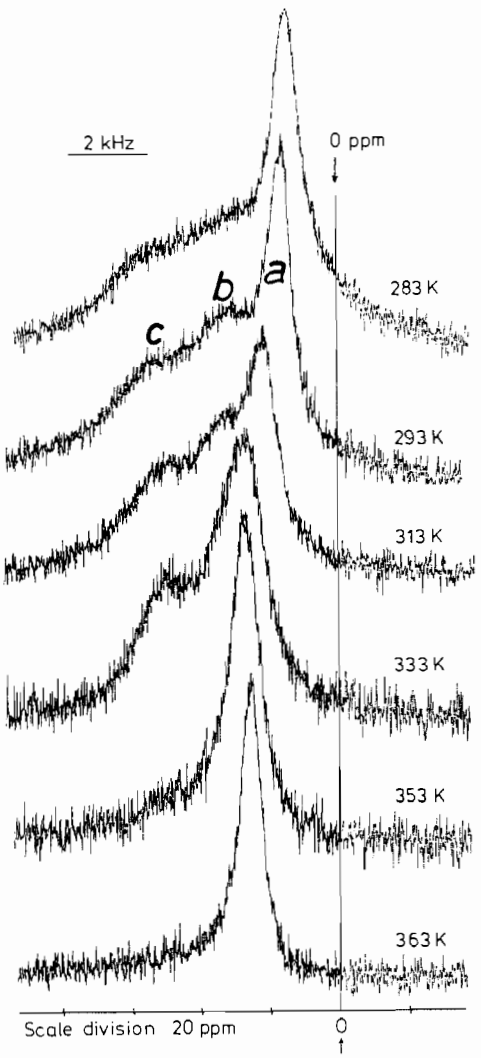

Fig. 3. 87.5 MHz ^{45}Sc NMR spectra (500 scans) of $Sc(NO_3)_3$ (0.025 M)/α-alanine, molar ratio 1/6, pH ~ 4, at variable temperatures. The three signals **a**, **b** and **c** observed at ambient temperatures correspond to at least three species in mutual exchange (*cf.* the equilibrium (6)). With a rise in temperature, the system progresses from slow through intermediate towards fast exchange. For data collection see Table III and Fig. 4.

($Sc(NO_3)_3$ and α-Alanine

Spectra are shown in Fig. 3, the results summarized in Table III and further displayed in Fig. 4.

In the temperature range 283 to 323 K, there are three overlapping signals; *i.e.*, exchange is again sufficiently slow to allow the observation of three distinct species present in slightly acidic (pH *ca.* 4) solution. Comparison with spectra of alanine-free scandium nitrate leads to an assignment of signals **a** and **b** (for the numbering see Fig. 3) to $[Sc(H_2O)_6]^{3+}$ and $[Sc(H_2O)_5OH]^{2+}$. The slightly higher pH of a solution of $Sc(NO_3)_3$ plus alanine accounts for the slight down-field shift of signal **a** with respect

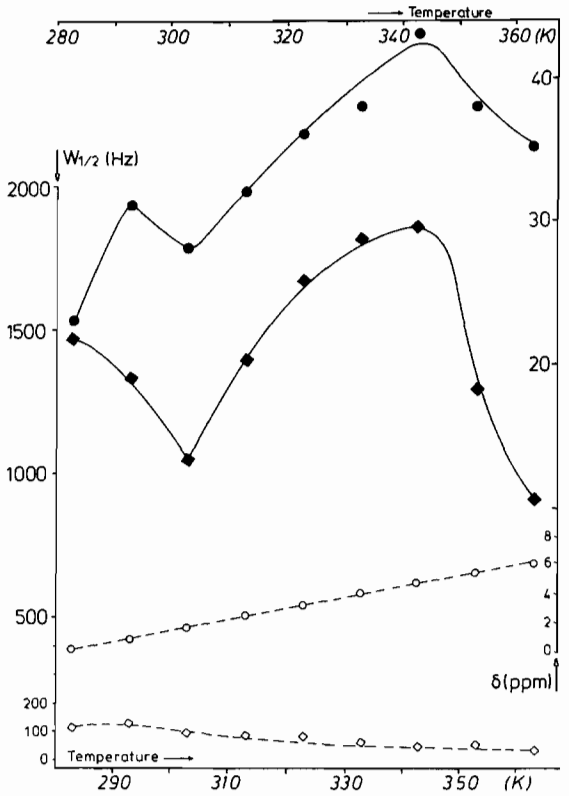

Fig. 4. The temperature dependencies of $\delta(^{45}Sc)$ (squares; right-hand scale) and $W_{1/2}(^{45}Sc)$ (circles; left-hand scale) of 0.025 M $Sc(NO_3)_3$ without alanine (dashed lines, open symbols) and with the addition of a six-fold molar excess of alanine (solid lines, full symbols; signal a (*cf.* Fig. 3) only). In alanine-free, acidified $Sc(NO_3)_3$, $W_{1/2}$ is dominated by the quadrupole relaxation mechanism throughout ($W_{1/2}$ decreases with increasing temperature). For intermediate exchange rates ($Sc(NO_3)_3$/alanine at intermediate temperatures), exchange contributions to the line width become the dominating factor ($W_{1/2}$ increases with increasing temperature).

to the alanine-free sample. The third signal, **c**, around +70 ppm is assigned to a species containing the amino acid coordinated to Sc^{3+}. The overall (pH-dependent) equilibrium situation can be represented by

$$\begin{array}{ccc} [Sc(H_2O)_6]^{3+}\ (\underline{a}) & \rightleftharpoons & [Sc(H_2O)_5OH]^{2+}\ (\underline{b}) \\ \Vert\downarrow & & \Vert\downarrow \\ [Sc(H_2O)_{6-n}(ala)_n]^{3+}\ (\underline{c}) & \rightleftharpoons & [Sc(H_2O)_{5-n}OH(ala)_n]^{2+}\ (\underline{c}) \end{array} \qquad (6)$$

assuming monodentate coordination of the carboxylato group [19] and n values not exceeding 2 in analogy to the $Sc_2(SO_4)_3 \cdot 4ala$ [19] and scandium complexes of carbonic acids [20, 21].

As the temperature rises above 330 K, signals **a** and **b** are replaced by a resonance intermediate between $[Sc(H_2O)_6]^{3+}$ and $[Sc(H_2O)_5OH]^{2+}$. The increase of $W_{1/2}$ is typical for intermediate exchange rates; the concomittant increase of δ illustrates that there are also increasing contributions of the hydroxo complex to the shift and line width. As shown by the decrease of $W_{1/2}$ for signal **c**, relaxation of the alanine complex is still quadrupole dominated. The signal steadily shifts towards higher field due to increasing exchange with the aquahydroxo complex and vanishes above 350 K, *i.e.*, in the fast exchange range, where the alanine complex becomes labile (large off-rate constant for the complex).

$Sc(NO_3)_3$ and Small Peptides

According to the above treatment, generation of a new broad resonance line on addition of alanine to an aqueous scandium nitrate solution can be accounted for in terms of complexation of the amino acid to Sc^{3+}. Further, the decrease of the width of the resonance signal at elevated temperatures can be traced back to an increasing labilization of the complex. Line width studies may therefore be used to qualitatively compare the stability of Sc^{3+} complexes. Inspection of Fig. 3 shows, however, that the sufficiently exact determination of $W_{1/2}$ values is a problem even if line fitting procedures are employed. In order to minimize this problem, we have applied a magnetic field B_o of *ca.* 1.55 T (as compared to $B_o = 8.46$ T for the data collated in the previous sections), where there is only one unresolved signal, the line width of which is governed by the broadest component.

The results are listed in Table IV. In non-buffered solutions, $W_{1/2}$ values for complexes formed with oligopeptides are larger than for the alanine complex,

TABLE IV. Line Widths of Scandium Complexes[a]

Ligand	Concentration (M)	Buffer[b]	pH[c]	$W_{1/2}$[d] (kHz)
[e]	0.03	–	3.5	0.52
[e]	0.02	NH_3/NH_4^+	5.0	2.21
α-ala	0.035	–	3.5	0.83
α-ala	0.02	imidazole	4.5	1.38
α-ala	0.03	NH_3/NH_4^+	5.5	1.66
$(ala)_2$	0.03	–	3.5	1.15
$(ala)_2$	0.03	NH_3/NH_4^+	5.5	1.93
$(ala)_4$	0.05	–	3.5	1.02
$(ala)_4$	0.025	NH_3/NH_4^+	5.0	1.75
ala-val-leu	0.03	–	4.0	1.38
ala-val-leu	0.03	NH_3/NH_4^+	5.0	2.40

[a]Obtained on a wide-line instrument at 16.0 MHz and a central magnetic field $B_o = 1.548$ T. Measuring temperature 300(2) K. [b]For details see experimental section. [c]±0.5. [d]±10%. [e]Neat, aqueous (H_2O) $Sc(NO_3)_3$.

with the tripeptide ala-val-leu producing the broadest line. Although the increase of $W_{1/2}$ may also be caused by an increase of τ_c (*cf.* eqn. 2) for complexes with the larger ligands, comparison of $W_{1/2}$ for the compounds formed with $(ala)_2$ and $(ala)_4$ indicates that variations of τ_c are a minor effect. The larger line widths then represent complexes of a more pronounced stability*. The same trend is observed in the buffered systems. Here, the lines are larger throughout, and this fact can be accounted for by increasing participation of hydroxo species (see equilibrium 6) at higher pH. Quite interestingly, the line width of ligand-free scandium nitrate in buffered solution (where the predominent species are $[Sc(H_2O)_{6-n}(OH)_n]^{(3-n)+}$, $n = 1$ and 2) decreases as the ligand is added. We explain this observation on the basis of (partial) displacement of OH^- by the carboxylato ligand {O}, *viz.* the formation of less stable carboxylato ($[Sc(H_2O)_4OH\{O\}]^{2+}$) from a rather stable hydroxo complex ($[Sc(H_2O)_4(OH)_2]^+$).

The greater stability of Sc^{3+} complexes of oligopeptides relative to that of the alanine complex can be traced back to the availability of an additional ligand function, namely the NH group of the peptide linkage, and formation of a comparatively stable chelate-five ring structure (Fig. 5). A strong argument for the participation of nitrogen functions in the coordination to Sc^{3+} is the appearance of Sc–N stretching modes in the IR spectrum (see Experimental). The IR spectrum also suggests a bidentate function of the carboxylato group [$\nu(ScO_2) = 631$ cm^{-1}].

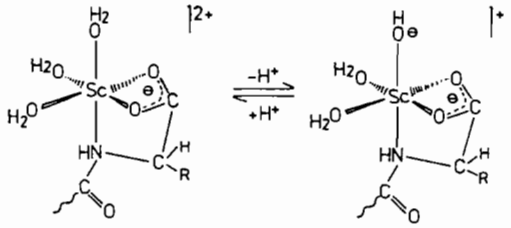

Fig. 5. Proposed (on the basis of NMR and IR results) structures for Sc^{3+}/peptide complexes in solution.

Experimental

Commercial samples of scandium salts were worked up in the following manner: from an aqueous solution, containing *ca.* 1.3 g Sc per 100 ml, the scandium contents were precipitated with oxalic acid, the scandium oxalate filtered off, dried, and calcinated at *ca.* 800 °C in an open crucible. The Sc_2O_3 thus obtained was dissolved in hot, concentrated HNO_3 (*ca.* 1 g Sc_2O_3 per 15 ml HNO_3) and the nitric acid removed on a water bath; the mixture was stirred until a pale yellow crystalline product was obtained. This was ground up to a coarse powder and dried for 2 h at 80 °C to yield almost white $Sc(NO_3)_3 \cdot 9H_2O$. Total acidity (by potentiometric titration): 47.3 mg HNO_3/1 g $Sc(NO_3)_3 \cdot 9H_2O$; a 0.025 M scandium nitrate solution (the concentration which has commonly been used in this work) therefore is 0.0074 M in H_3O^+.

A Sc^{3+}-alanine complex prepared from scandium nitrate and alanine in analogy to the corresponding reaction with scandium sulfate [19] had the composition, by elemental analysis, $Sc(NO_3)(ala)_2(Hala)_2 \cdot 2H_2O$ [ala = $CH_3CH(NH_2)CO_2^-$, Hala = $CH_3CH(NH_3^+)CO_2^-$]. Characteristic IR bands (KBr mull) *ca.* 1630 [very broad, $\nu_{asym}(CO_2^-) + \delta(NH_3^+)$], 1388s [$\nu_{sym}$(coordin. CO_2^-)], 770s [$\nu(NO_3^-) + \delta(CO_2^-)$], 608m cm^{-1} [$\nu(ScO_2)$]. The complex obtained with ala-val-leu lacked bands belonging to the nitrato ligand. Apart of the $\nu(CO_2^-)$ (see above), several strong, unassigned bands (1225, 1083, 913 cm^{-1}), and $\nu(ScO_2)$ (631 cm^{-1}), there are two absorptions (472s, 400w cm^{-1}) corresponding to the ν(ScN) mode. For assignments see [22–24].

^{45}Sc NMR data have been obtained under the following conditions: $Sc(NO_3)_3$ (Table II), $Sc(NO_3)_3$/ala (Table III), $ScCl_3$: Bruker AM 360, 87.49 MHz, 10 ml vials, D_2O solutions; sweep width 50 K, memory size 8 K, pulse angle 30°, relaxation delay 2 s; digital resolution 12 Hz/point. $Sc(NO_3)_3$/peptides (data in Table IV): Bruker SWL 3-100, 16.00016 MHz, central magnetic field 1.548 T; 14 mm sample tubes; r.f. field strength 10–25 dB, modulation amplitude 20 μT.

The following buffer solutions were employed: 0.2 M NH_3/NH_4Cl of pH 8.6; 0.2 M imidazole/HCl of pH 6.6. 1.5 ml of the buffer solution were added to 2 ml of $Sc(NO_3)_3$ (*ca.* 0.05 M)/ligand (molar ratio 1/4); the resulting pH was 5.0 ± 0.5. In several cases, small amounts of $Sc(OH)_3$ precipitated in the course of the measuring procedure.

*See 'Note Added in Proof'.

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Note Added in Proof

The greater stability of the peptide complexes is also evident from the 87.5 MHz ^{45}Sc NMR spectra of Sc^{3+}/ala-val-leu in D_2O: while a 0.03 M solution containing the two components in equimolar amounts imparts a picture similar to the situation encountered with Sc^{3+}/ala 1/6 (Fig. 3) (the $\delta/W_{1/2}$ parameters for the scanium-peptide complex at 295 K are: +18/0.98 (**a**), +37/4.5 (**b**) and +73/3.8 (**c'**) ppm/kHz), signal **b** ($[Sc(H_2O)_5OH]^{2+}$) disappears as the molar ratio Sc/peptide goes down to 1/4 ($\delta/W_{1/2}$ = +23/2.4 (**a**) and +73/4.1 (**c'**) ppm/kHz), with signal **c'** (the peptide complex) covering about two third of the overall intensity. A further interesting feature is that, despite of the fact that the nitrogen function of the peptide linkage is involved in the coordination to Sc, there is no shift difference between **c'** and the alanin complex **c.**