Preparation of (2*R*,4*R*,6*R*,8*R*)-1,9-Dihydroxy-3,5,7-trioxanonane-2,4,6,8-tetracarboxylic Acid and Its Complexation with Lanthanide(III) Cations, As Studied by Multinuclear Magnetic Resonance Spectroscopy

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(2*R*,4*R*,6*R*,8*R*)-1,9-Dihydroxy-3,5,7-trioxanonane-2,4,6,8-tetracarboxylic acid (H_4TT) has been prepared via a catalytic oxidation of D-trehalose with molecular oxygen and via a two-step oxidation with periodate and chlorite. The lanthanide complexes have 1:1 and 1:2 metal−ligand stoichiometries. Ln(III)-induced effects on chemical shifts, relaxation rates, and vicinal proton−proton coupling constants yielded information on the geometries of these complexes. The complexes with Ln(TT) stoichiometry have 2 water molecules in the first coordination sphere of Ln(III), and the remaining 6−7 positions are occupied by carboxylate, ether, and $-CH_2OH$ oxygens of the two oxidized sugar units of TT. The $-CH_2OH$ oxygens are coordinated for about 85% of the time. The $Ln(TT)_2$ complexes have one TT ligand that is bound in a hexadentate fashion via the two terminal oxydiacetate units (each in a tridentate fashion), whereas the second TT ligand has only one oxydiacetate unit coordinated. The exchange between bound and free oxydiacetate moieties in $Ln(TT)_2$ is rapid on the NMR time scale. In about 20% of the TT ligands of this complex one of the coordinated carboxylate groups is substituted by a $-CH_2OH$ group.

Introduction

Oxydiacetate and its derivatives are promising compounds for use as metal sequestrants, for example, as builder and cobuilder in detergent formulations. They have excellent complexing abilities[1−4] and are in general readily biodegradable,[1] whereas their toxicity is low.[5] The lanthanides (Ln(III)) constitute a series of hard Lewis acids with similar chemical behavior.[6] Interactions between these ions and ligand donor sites are largely electrostatic resulting in nondirectional bonds. Both the ionic size and the binding character of the Ln(III) ions are similar to those of Ca(II). These ions usually coordinate with the same donor sites of a particular ligand. However, the stability constants of the Ca(II) complexes are at least 1 order of magnitude smaller because of the lower charge density.[7,8] The similarity with Ca(II) makes Ln(III) a substitute for the NMR silent Ca(II) in coordination studies. The diversity of the magnetic properties of the lanthanides can be exploited for the structure elucidation of complexes, especially by multinuclear magnetic resonance.[9]

In this paper we report a study on the coordination of Ln(III) by (2*R*,4*R*,6*R*,8*R*)-1,9-dihydroxy-3,5,7-trioxanonane-2,4,6,8-tetracarboxylate (TT; see Scheme 1), obtained from oxidative cleavage of the carbohydrate trehalose. A multinuclear magnetic resonance study was performed to elucidate the structure of the complexes involved. The TT ligand is interesting from a coordination chemistry point of view, because of the presence of several coordinating groups (four carboxylic groups, two hydroxyl functions, and three acetal oxygen atoms) that cannot be involved in coordination simultaneously.

Experimental Section

Materials. D-Trehalose was obtained as the dihydrate from Acros Chimica (Geel, Belgium). All other chemicals were purchased from Aldrich Chemical Co. and were used without further purification. The lanthanide content of the hydrated lanthanide chlorides was determined by chelatrometric titration with EDTA and xylenol orange as the indicator. Water used was demineralized.

Oxidation of D-Trehalose with Molecular Oxygen. In a typical oxidation, 1−2 g (2.5−5 mmol) of D-trehalose was dissolved in 100 mL of water in a 300 mL Hastalloy C stainless steel Parr autoclave; 4.0 g (71 mmol) of KOH was added and dissolved. Then, ruthenium bismuth pyrochlore oxide (0.5 g) catalyst was added and, after flushing with oxygen, the mixture was pressurized to 20 bar of O_2. The reaction mixtures were stirred with a propeller fan at 1500 rpm. The temperature was brought to 70 °C in about 10 min. At suitable time intervals aliquots of 2 mL were taken for HPLC analysis. After about 2 h the reaction mixture was brought to pH 8 and unwanted salts were removed by membrane ultra filtration. Lyophilization yielded 60% tetracarboxylate, which was about 70% pure according to ^{13}C NMR, the impurities being mainly products from overoxidation, such as penta- and hexacarboxylates.

Oxidation of Trehalose with Sodium Periodate. In a typical oxidation, 4.0 g (11.7 mmol) of trehalose was suspended in 50 mL of water. Sodium periodate ($NaIO_4$) (15 g, 70 mmol) was dissolved in 25 mL of water and in 25 min added to the trehalose suspension at 0 °C. After the mixture was stirred in the dark for 2 h, the trehalose

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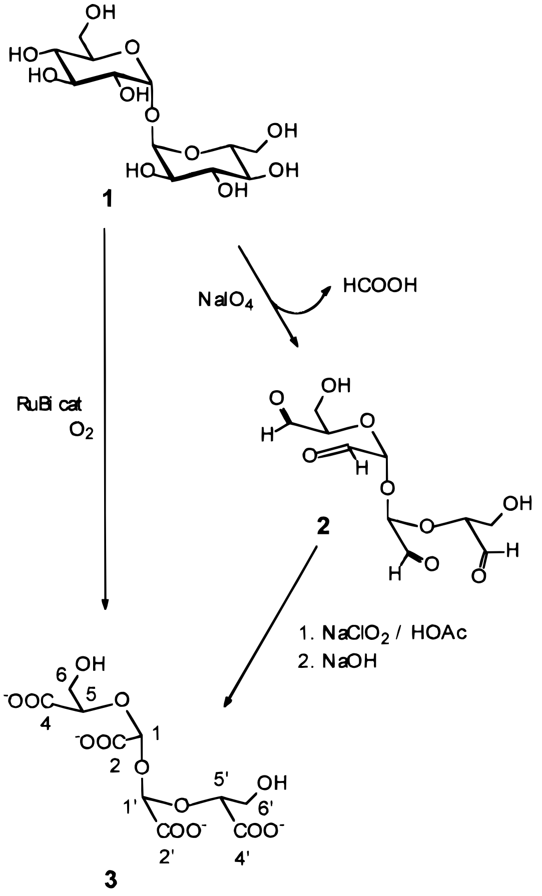
Scheme 1. Synthesis of the TT Ligand



was fully dissolved. The solution was stirred for 16 h at 5 °C in the dark, after which the precipitate formed was filtered off (sodium iodate, 9.4 g). The trehalose tetraldehyde formed was not further isolated but oxidized in situ with sodium chlorite.

The trehalose tetraldehyde solution was diluted with water to 100 mL. Acetic acid (7.0 g) was added to a solution of 40 g (0.44 mol) of $NaClO_2$ in 50 mL of water. After being stirred for 30 min the yellow solution (*poisonous ClO_2 fumes*) was added dropwise in 1 h to the trehalose tetraldehyde solution. After this solution was stirred for 5 h at 20 °C, the ClO_2 was removed by bubbling the solution with air for 1 h. The pH of the colorless solution obtained was raised to 8 with a 2 M NaOH solution, and after concentration to 75 mL, 5 g of precipitated inorganic salts was removed. The filtrate was diluted with water to 150 mL, and the amount of inorganic salts was further reduced by membrane ultrafiltration. After lyophilization, 4.0 g of the product was obtained. ^1H NMR using a weighted amount of *tert*-butyl alcohol showed the Na_4TT content to be to be 3.2 g (7.4 mmol, 63%), the remainder being water and inorganic salts.

For desalination, a laboratory ultrafiltration apparatus was used suitable for filtration of 180 mL of liquid at a nitrogen pressure of a maximum of 25 bar. The salts with low molecular weights were removed from the trehalose reaction mixtures at 12 bar and pH 7−8 using a UTC-60 membrane from Toray Industries, Tokyo, Japan (separation limit: molecular weight of 300−500, depending on the pressure applied). ^1H NMR (400 MHz, D_2O, for labeling of nuclei, see Scheme 1): δ 5.20 (s, 2H, H-1), 4.13 (dd, 2H, H-5, $J_{5,6a} = 2.9$, $J_{5,6b} = 5.5$ Hz), 3.82 (dd, 2H, H-6a, $J_{6a,6b} = -12.1$ Hz), 3.75 (dd, 2H, H-6b). ^{13}C NMR (50.3 MHz, D_2O): δ 178.7 (C-2), 175.2 (C-4), 102.0 (C-1), 81.6 (C-5), 63.7 (C-6), 55.2 (OMe).

Isotopic enrichment of the oxygen atoms of the COO^- groups was achieved by exchange in $H_2{}^{17}O$-enriched water (10% ^{17}O) at pH 1 followed by neutralization with aqueous NaOH and removal of the enriched water and NaCl by ultrafiltration.

HPLC Measurements. Trehalose samples were analyzed by HPLC on a Waters 625 LC system equipped with a Dionex Carbopac PA1 column in combination with a Dionex PED 1 pulsed electrochemical detector and a Spectra-Physics SP4270 integrator. A Waters pump and controller were used to apply the desired solvent gradient. The solvents used for the mobile phase were as follows: A, 0.1 M aqueous NaOH; B, 0.1 M aqueous NaOH, 0.5 M sodium acetate. Gradient program: $t = 0$ min, 100% A; $t = 35$ min, 50% A, 50% B; $t = 40$ min, 20% A, 80% B; $t = 45$ min, 100% B; $t = 55$ min, 100% A. Times and voltages for the electrochemical cell of the detector: measuring period T_1 0−0.50 s, U_1 0.05 V; oxidation period T_2 0.51−0.60 s, U_2 0.80 V; reduction period T_3 0.61−0.70 s, U_3−0.60 V.

NMR Measurements. NMR analyses were performed on a Varian VXR-400 S spectrometer, a Varian Inova 300 spectrometer, and on a Nicolet NT-200 WB spectrometer. The ^1H and ^{13}C chemical shifts were determined with respect to *tert*-butyl alcohol as internal reference (Me at 1.2 and 31.2 ppm, ^1H and ^{13}C, respectively). Dy-induced ^{17}O water shift measurements were conducted at 27.1 MHz, 349 K and at 54.22 MHz, 353 K. The ^{17}O chemical shifts were measured with respect to D_2O as external standard (substitution method); the chemical shifts were determined by fitting the observed signals with Lorenzian line functions. Samples were prepared by stepwise addition of 0−0.9 equiv of $DyCl_3$ to a solution of 0.1 M TT in D_2O. The pH of the samples was adjusted to 6.5 using diluted NaOH. The calibration was obtained by stepwise addition of $DyCl_3$ to D_2O. The ^{13}C relaxation time measurements were performed at 100.6 MHz using the inversion recovery pulse sequence. The molecular models used for the evaluation of the Gd(III)-induced relaxation rate enhancements were constructed with the use of the HyperChem program (version 3, MM+ force field, HyperCube Inc., Gainsville, FL).

Results and Discussion

Synthesis. Trehalose (**1**) was oxidized with a previously developed environmentally clean oxidation method using molecular oxygen[10] and ruthenium bismuth pyrochlore oxide as the catalyst (Scheme 1).[11] The main product was the desired trehalosetetracarboxylate TT (**3**), which was about 70% pure according to ^{13}C NMR. The impurities were mainly products from overoxidation, such as penta- and hexacarboxylates. For calcium complexation in detergent formulations this would not be a problem, but this product is not suitable for accurate complexation studies.

We, therefore, prepared the tetracarboxylate via the classical glycol cleavage route using periodate. The tetraldehyde (**2**) was not isolated but treated in situ with sodium chlorite/acetic acid (Scheme 1). After removal of the inorganic salts and formate by ultrafiltration, the tetracarboxylate (**3**) was obtained.

Dy(III)-Induced ^{17}O Shifts. To obtain information on the number of donor sites of TT in the Ln(III) complexes, studies with the paramagnetic lanthanide ion Dy(III) were performed. In aqueous solution Dy(III) is surrounded by eight H_2O molecules in its inner coordination sphere.[12] In the presence of organic ligands, the water is (partially) replaced by donor groups of the ligand. The effect of replacing bound water by ligands can be measured by observing the ^{17}O water NMR signal.[9] Upon addition of Dy(III) to a 0.1 M solution of TT in D_2O at 75 °C and 4.7 T, a single ^{17}O water resonance was observed, the chemical shift of which was dependent on the molar ratio Dy(III)/TT (ρ_L; see Figure 1). This indicates that the exchange of water between the inner coordination sphere and the bulk solution is rapid on the NMR time scale. The detected chemical shift is a weighted average of the chemical shifts of bound and bulk water molecules.

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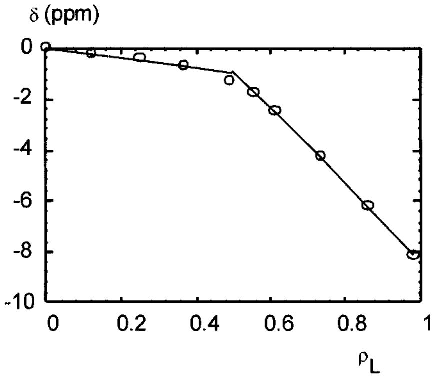

Figure 1. Plot of the Dy(III)-induced water ^{17}O shift versus the molar ratio Dy(III)/TT (ρ_L) for 0.1 M TT in D_2O at 353 K, pH 6.5, and 40.7 MHz.

It has previously been shown that the Dy(III)-induced shifts of ^{17}O nuclei coordinated to Dy(III) are mainly of contact origin and that the magnitude of these shifts always lies in a narrow range irrespective of other ligands coordinated to the Dy(III) ion.[9,13] This means that the observed shift in the ^{17}O water signal can be directly related to the number of bound water molecules.

In Figure 1, a change in slope is observed at $\rho_L = 0.5$. This corresponds with a change in stoichiometry from a 1:2 complex Dy(TT)$_2$ to a 1:1 complex Dy(TT). For each point of the curve the average number of Dy(III) bound waters, N_w, can be determined from the Dy(III)-induced ^{17}O water shift in the presence (Δ_L) and in the absence of TT (Δ_0) with the use of eq 1.

$$N_w = 8(\Delta_L/\Delta_0) \tag{1}$$

The slope of a plot of the ^{17}O water shift versus [Dy(III)]$_{tot}$/[D_2O] obtained for the addition of Dy(III) to D_2O in the absence of an organic ligand is $-18\,500$ ppm. The initial slope of a plot of the ^{17}O water shift versus ρ_w is -1100 ppm, which corresponds to $(-1100/-18\,500) \times 8 = 0.5$ waters bound per Dy(III) in the Dy(TT)$_2$ complex. Similarly, it can be calculated from a comparison of the Dy(III) induced shift at $\rho_L = 1$ with the shift measured in the absence of TT that the Dy(TT) complex has 2.0 Dy(III) bound waters. Since the most common coordination numbers of Dy(III) in this type of complexes are 8 and 9, it can be concluded that 8−9 coordination sites are occupied by the tetracarboxylate in the Dy(TT)$_2$ complex and 6−7 sites are occupied by the tetracarboxylate in the Dy(TT) complex. Therefore, the TT ligand is most likely bound in a tetradentate fashion to the metal ion in the Dy(TT)$_2$ complex and hexa- or heptadentate in the Dy(TT) complex. The measurements could not be extended to $\rho_L > 1$, because of precipitation at these high Dy(III) concentrations.

The carboxylate ^{17}O nuclei of TT were observed at 276 ppm for a sample of TT in which the carboxylates were 5% ^{17}O-enriched. Carboxylate groups coordinated by Dy(III) have an induced ^{17}O shift of about 1170 ppm and an extremely large line width, which precludes observation under conditions of slow exchange between the complex and the free ligand.[9] No shift of the carboxylate ^{17}O resonance was observed upon addition of small amounts of Dy(III) to a sample of TT in D_2O. However, the signal broadened strongly and its intensity decreased. This suggests that the exchange of the carboxylate ^{17}O nucleus between the free and Dy-bound state is slow on the ^{17}O NMR time scale. At $\rho_L = 0.2$, the COO$^-$ signal could no longer be observed. These phenomena are consistent with all four carboxylate groups of TT being involved in coordination of Dy(III).

Table 1. Longitudinal ^{13}C Relaxation Rates in Gd(TT)$_2$ (in 10^3 s^{-1}) at 100.6 MHz and 298 K

	C-1	C-2	C-4	C-5	C-6
exptl	5.63	5.63	5.62	4.88	2.13
calcd[a]	5.62	5.76	5.64	4.74	2.13

[a] Calculated with eq 5 for a mixture of 82% of the structure depicted in Figure 2 and 18% of structures in which one of the Gd(III)-bound COO$^-$ groups is substituted by a $-CH_2OH$ group; $c = 9.30 \times 10^6$.

Gadolinium-Induced ^{13}C Relaxation Rate Enhancements. Coordination of a ligand to a paramagnetic Ln(III) ion enhances the relaxation rates. The enhancements are related to the distance between the C-atom studied and the Ln(III) ion.[9,14] Hence the Ln(III)-induced enhancements of the various ligand nuclei provide information on the distances of these nuclei to the Ln(III) cation and thus reveal which functionalities interact with the lanthanide. Gadolinium(III) has the largest enhancing effects among the Ln(III) cations because it has a large magnetic moment and the longest electronic relaxation time. Dipolar interactions bring about a shortening of the relaxation rates of nuclei in proximity to the Gd(III) electrons. The amounts of Gd(III) used for the present enhancement experiments were very small ($\rho_L < 10^{-3}$), and accordingly the data obtained give information on the complex with the highest possible ligand/metal ratio, the Gd(TT)$_2$ complex.

The relaxation rates of the ligand nuclei in the complex ($1/T_{1,c}$) can be derived from the experimental relaxation rates ($1/T_1$) with eq 2, where n is the number of ligands in the Gd(III) complex and $1/T_{1,f}$ is the relaxation rate of the free ligand.

$$\frac{1}{T_1} = \frac{n\rho_L}{T_{1,c} + \tau_M} + \frac{1}{T_{1,f}} \tag{2}$$

On the basis of investigations of similar ligands,[15,16] we make the assumption that for a relatively weak ligand like TT the mean residence time in its Gd(III) complex (τ_M) is short with respect to the relaxation time $1/T_{1,c}$. Equation 2 can now be simplified to eq 3.

$$\frac{1}{T_1} = \frac{n\rho_L}{T_{1,c}} + \frac{1}{T_{1,f}} \tag{3}$$

Plots of the experimental relaxation rates versus ρ_L afforded straight lines (correlation coefficients > 0.999). The slopes of these lines give $n/T_{1,c}$. At low concentrations of Gd(III) we take $n = 2$. The relaxation rate enhancements ($1/T_{1,c}$) obtained are given in Table 1. Since the exchange between Gd(III)-bound and free TT ligands is rapid on the NMR time scale, the rate enhancements obtained are averages for corresponding nuclei in the two oxidized monosaccharide moieties of TT.

The relaxation rates of the complex ($1/T_{1,c}$) are related to the

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molecular structure via the simplified Solomon−Bloembergen equation (eq 4)[17,18]

$$\frac{1}{T_{1,c}} = \frac{2}{5}\left(\frac{\mu_0}{4\pi}\right)^2\left(\frac{\gamma_I^{\,2}\mu_{eff}^{\;\;2}\beta^2}{r^6}\right)\tau_R \qquad (4)$$

Here r is the distance between the nucleus of the ligand and Gd(III), $\mu_0/4\pi$ is the magnetic permeability in a vacuum, γ_I is the gyromagnetic ratio of the studied nucleus, μ_{eff} is the magnetic moment of the Ln ion, β is the Bohr magneton, and τ_R is the rotational correlation time of the complex. The diamagnetic contribution to the relaxation rates is neglected. Equation 4 can be rewritten as eq 5, in which κ is a constant depending on the metal ion (Gd) and c is a constant for a given Gd(III) complex. Calculation with the use of eq 4 gives $\kappa = 9.7 \times 10^{16}$ Å^6 s^{-2}.

$$\frac{1}{T_{1,c}} = \kappa\frac{\tau_R}{r^6} = \frac{c}{r^6} \qquad (5)$$

The values of $1/T_{1,c}$ (see Table 1) indicate that the average distances between Gd(III) and C-1, C-2, and C-4 are about equal; the distance to C-6 is somewhat larger. It can be concluded that a Gd(TT)$_2$ species predominates, in which the two terminal oxydiacetate (ODA) moieties in each of the TT ligands are involved in the coordination. Coordination of all ODA units simultaneously, however, can be ruled out, since this would lead to a 12-coordinate Gd(III). The prevalent coordination number in this type of complexes is 9, and only a few 10-coordinate complexes have been reported in the literature. The parent system oxydiacetate can form Ln(ODA)$_3$ complexes in solution. For the lighter Ln(III) cations, the coordination number is 9, but for the heavier and smaller Ln(III) cations one of the COO$^-$ groups is detached from the cation.[19]

The Dy(III)-induced ^{17}O water shifts indicated that the Dy(TT)$_2$ complex has on the average less than one water molecule in the first coordination sphere (see above). In combination with the results of the Gd(III)-induced relaxation rate enhancements, this leads to the conclusion that three of the four (terminal) ODA moieties in the predominant Gd(TT)$_2$ complex are coordinated to the Gd(III) ion (in a tridentate fashion).

The Gd(III)−C distances in this complex were estimated from molecular models constructed with the use of molecular mechanics. From these distances and eq 5, relative relaxation rates $1/T_{1,c}$ were calculated. Comparison with the experimental data showed a good agreement for C-1, C-2, C-4, and C-5. However, the calculated value for C-6 is a factor 3 smaller than the experimental one. This suggests that species are present in which one of the carboxylate functions of the structure described above is substituted by its adjacent −CH$_2$OH function. Therefore, the calculations were repeated, taking into account such species. The amount of the latter species was varied until an optimal fit between the observed and calculated $1/T_{1,c}$ values was obtained. The constant c in eq 5 was used as a scaling factor in the comparison of the observed and calculated relaxation rates. A good agreement was obtained for a system containing 82% of the complex described above (see Figure 2) and 18% of species in which a −CH$_2$OH function substituted one of the Gd(III)-bound carboxylate groups. The calculated relaxation rates are included in Table 1.

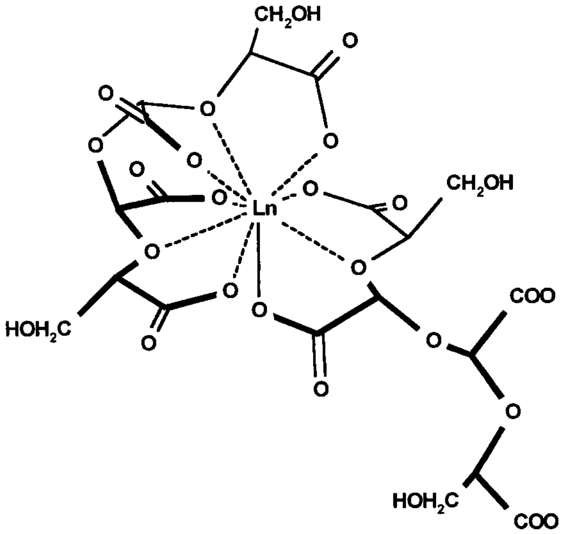

Figure 2. Proposed structure for the major Gd(TT) complex (82%). A minor species (18%) occurs, which is similar but with one of the bound carboxylate functions substituted by a −CH$_2$OH group.

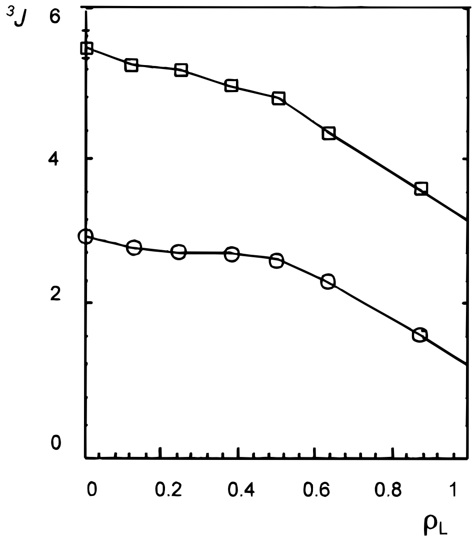

Figure 3. Vicinal proton−proton coupling constants $^3J(5,6)$ (○) and $^3J(5,6')$ (□) as a function of the molar ratio La(III)/TT at 298 K, 400 MHz, measured in a 0.1 M solution of TT in D$_2$O.

The value of c for the optimum was 9.3×10^6 Å^6 s^{-1}. With eq 5 it can then be calculated that $\tau_R = 9.6 \times 10^{11}$ s. The value of τ_R can independently be estimated by the Debye−Stokes−Einstein eq 6 if it is assumed that the complex is spherical with radius a.

$$\tau_R = \frac{4\pi a^3\eta}{3kT} \qquad (6)$$

Here k is the Boltzmann constant and η is the viscosity. From molecular models and literature data on similar Gd(III) complexes,[15] the radius a of the Gd(TT)$_2$ complex is estimated to be 4 Å. For the viscosity of the sample we take the viscosity of water 2×10^{-3} N m^{-2} s. Then the value of τ_R was calculated to be 1×10^{-10} s, which is in good agreement with the value obtained from the fitting of the relaxation rate data.

Vicinal Proton−Proton Coupling Constants. To obtain support for the coordination mode of the primary hydroxyl functions to the Ln(III) proposed above, we investigated the effect of coordination to Ln(III) on the vicinal proton−proton coupling constants of TT (see Figure 3).

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Table 2. Molar Fractions of Conformers (See Chart 1) As Calculated from $^3J(5,6)$ and $^3J(5,6')$[a]

	$^3J(5,6)$ (Hz)	$^3J(5,6')$ (Hz)	f_A	f_B	f_C
free TT	2.9	5.5	0.06	0.34	0.6
La(TT)	1.2	3.2	0.01	0.05	0.94
La(TT)$_2$	2.6	4.8	0.08	0.25	0.67

[a] Calculated with $^3J(5,6) = 10.7$, 5.0, and 0.9 and $^3J(5,6') = 3.1$, 10.7, and 2.8 for A, B, and C, repectively.[21]

Previously it has been reported[20] that rigid ligands do not show a change in vicinal coupling constants upon complexation to Ln(III) ions. However, in flexible ligands such as (2-hydroxyethoxy)butanedioate a dramatic change in the vicinal coupling constants ($^3J(2,3)$ and $^3J(2,3')$) has been observed upon coordination to La(III).[21] This change could be calculated to correspond to a change in conformation.

The vicinal coupling constants for free TT, La(TT), and La(TT)$_2$, evaluated from these data, are compiled in Table 2. Three staggered conformations (A, B, and C; see Chart 1) may be envisaged for the CH$_2$OH moieties in TT. It should be noted that conformation C is the only one that is able to bind a Ln(III) ion. The coupling constants $^3J(5,6a)$ and $^3J(5,6b)$ for these conformations were calculated with the use of the semiempirical relationship of Altona *et al.*[22] The coupling constants for the conformational equilibrium can be calculated with eq 7, where

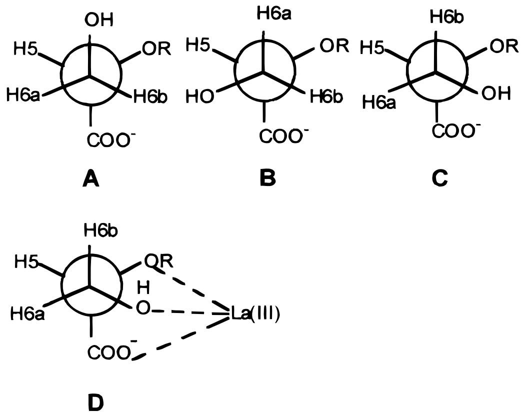
$$J = f_A J_A + f_B J_B + f_C J_C \qquad (7)$$

f_A, f_B, and f_C are the molar fractions of conformers A, B, and C, respectively. From the experimental coupling constants $^3J(5,6a)$ and $^3J(5,6b)$, the distribution of the conformers was calculated (see Table 2). The shift of the conformational equilibrium toward C reflects the extent to which the CH$_2$OH function is bound to the La(III) ion in each complex. From the populations of conformer C, it can be calculated that the CH$_2$OH group is bound to La(III) for about 85% of the time in the La(TT) complex and for about 17% of the time in the La(TT)$_2$ complex. The latter is in excellent agreement with the conclusions from the Gd(III)-induced relaxation rate enhancement data.

Conclusions

This study on the coordination behavior of the complexes provided the stoichiometry and structure of the different binding modes of TT in Ln(III) complexes. The Ln(III) complexes have predominantly 1:1 and 1:2 metal−ligand stoichiometries. Ln$_2$(TT) complexes could not be observed due to precipitation at high molar ratios Ln/TT ($\rho > 0.9$).

Chart 1. Conformations around C-5−C-6 for Free TT (A−C) and Ln(III)-Coordinated TT (D)



The species with Ln(TT)$_2$ stoichiometry are highly fluxional. One TT ligand is bound in a hexacoordinate fashion via the carboxylates and the ether oxygens of its two terminal ODA units, whereas the other TT ligand has a bound and free ODA unit. The exchange between bound and unbound ODA moieties is rapid on the NMR time scale. These species are in equilibrium with others in which one of the bound carboxylates is substituted by the adjacent −CH$_2$OH. The molar ratio of the Ln(TT)$_2$ complexes with bound and unbound −CH$_2$OH functions is about 1:4.

The complexes with a 1:1 metal−ligand stoichiometry have 2 waters in the first coordination sphere. Six of the remaining positions are occupied by the carboxylate and ether oxygens of the two ODA units. The vicinal proton coupling constants indicate additional coordination of the −CH$_2$OH functions for about 85% of the time.

The present investigation clearly shows that the −CH$_2$OH function plays an important role in the coordination of Ln(III).

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