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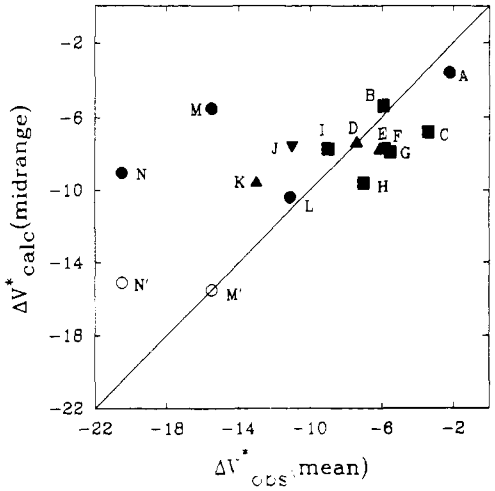

Figure 12. Calculated and observed ΔV^* values at midrange of pressure (100 MPa, except 70 MPa for $Fe(H_2O)_6^{3+/2+}$) for adiabatic (filled symbols) and nonadiabatic (open circles) self-exchange in couples with rigid ligands. Solvents: (○, ●) water; (■) CD_3CN; (▲) $(CD_3)_2CO$; (▼) CD_3OD. Key: (A, B) $Fe(phen)_3^{3+/2+}$; (C, D) $Cu(dmp)_2^{2+/+}$; (E–G) $Ru(hfac)_3^{0/-}$; (H) $Fe(C_5H_5)_2^{+/0}$; (I–K) $Mn(CN\text{-}t\text{-}Bu)_6^{2+/+}$; (L) $Fe(H_2O)_6^{3+/2+}$; (M, M') $Co(en)_3^{3+/2+}$; (N, N') $MnO_4^{2-/-}$. Experimental data were taken from refs 4–12. The straight line represents exact agreement between theory and experiment.

Figures 1–11 and Supplementary Figures S1–S7 show that correspondence between calculated ln (k/k_0) vs P plots and the experimental data is good only in a limited number of cases. For nonaqueous solvents in particular, the theoretical plots tend to be too sharply curved at the lower end of the pressure range, although the slopes around the middle of the range and above generally match the trend of the measurements. The discrepancies between theory and experiment cannot be ascribed to inadequacies in the treatment of interactions of highly charged ions with the medium and with other ions, since systems involving a neutral redox partner are among those most poorly described. There is no obvious pattern of successes and failures, and it may be that each couple has special features, such as nonadiabatic behavior or possibilities for interpenetration of the ligands, that would preclude application of any general theory of redox rates.

The comparison of plots of ln (k/k_0) vs P is cumbersome and may be too severe a test of theory; one might wish for a simpler, if less rigorous, criterion of the adequacy of the models. As a compromise, one can calculate ΔV^* from theory for the *midpoint* of the experimental pressure range and compare it with a *mean* ΔV^* value obtained by linearizing the experimental ln k vs P plot (often, this is in any case the only statistically significant way to represent the measurements). This is done in Figure 12 for self-exchange reactions of some rigid complexes in relatively polar solvents—reactions in solvents of low D such as chloroform have been omitted because of the instability of the theoretical calculations. If the aqueous $Co(en)_3^{3+/2+}$ and $MnO_4^{-/2-}$ cases are either excluded or, as justified above, taken as non-adiabatic (points M' and N'), it can be seen that there is at least *qualitative* agreement between theory and experiment—all the ΔV^* values are negative, those $|\Delta V^*|$ values predicted to be relatively small are indeed small, etc. The number of points falling on or close to the plotted line of exact correspondence, however, is disappointingly small.

Acknowledgment. I thank Profs. H. G. Drickamer and John P. Hunt for making available unpublished data, Drs. E. D. German, R. G. Gilbert, and S. Wherland for discussions, and the Natural Sciences and Engineering Research Council of Canada for financial assistance.

Supplementary Material Available: Plots of ln (k/k_0) vs P for $Ru(hfac)_3^{0/-}$ in acetone, $Cu(dmp)_2^{2+/+}$ in acetone and in acetonitrile, and $Mn(CNR)_6^{2+/+}$ and $Fe(C_5H_5)_2^{+/0}$ in acetonitrile (Supplementary Figures S1–S7) (7 pages). Ordering information is given on any current masthead page.

Contribution from the Laboratory of Organic Chemistry, Delft University of Technology,
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Synthesis of Polyhydroxy Carboxylates. 5. Metal Ion Catalyzed O-Alkylation of Ethylene Glycol with Maleate. A Multinuclear NMR Study of the Lanthanide(III) Complexes Present in the Reaction Mixture of the Lanthanide(III)-Catalyzed Reaction

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The structures and stabilities of Ln^{III} complexes occurring in the reaction mixture of a Ln^{III}-catalyzed O-alkylation of ethylene glycol (EG) with maleate (MAL) have been investigated with the use of ^{139}La, ^{17}O, and ^{13}C NMR shift and relaxation measurements and with potentiometry. In EG the Ln^{III} ion appears to be coordinated by nine oxygen atoms; chloride counterions are not present in the first coordination sphere. The Ln^{III} ions have some preference for coordination of EG over that of water. MAL is able to coordinate with the Ln^{III} ions in EG medium. The mono-O-alkylation product of EG (EGMS) forms 1:1 and 1:2 Ln^{III} complexes, in which the ligand is bound in a tetradentate fashion via the two carboxylate groups and the two oxygens of the EG residue. The Ln^{III} coordination of the di-O,O'-alkylation product (EGDS) is analogous; all carboxylate groups and ether oxygens are coordinated.

Introduction

Polyfunctional carboxylates containing an α-(hydr)oxy function are known to be good sequestering agents for metal ions.[1] Recently, we have reported on the synthesis of some compounds of this class by a metal ion catalyzed O-alkylation reaction of di- and polyhydroxy compounds with maleate (MAL).[2] For instance, O-alkylation of ethylene glycol (EG) with MAL, in the presence of multivalent metal cations as catalysts, yields ethylene glycol monosuccinate (EGMS). In a consecutive step, another O-alkylation with MAL can give ethylene glycol disuccinate (EGDS) (see Scheme I). The metal ion probably functions as a template, and it may activate a hydroxyl group of EG and EGMS via ionization upon coordination.

This paper reports on the characterization of metal ion complexes in the reaction mixture of the lanthanide(III)-catalyzed O-alkylation reaction of EG with MAL, using multinuclear NMR

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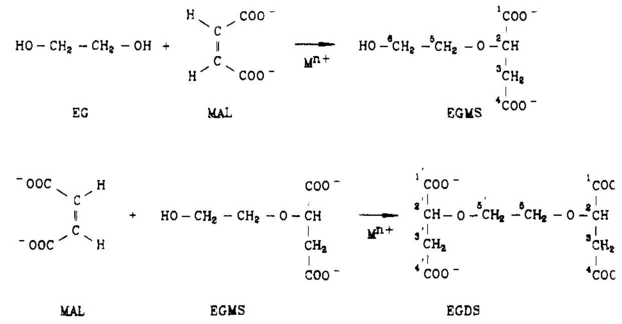
Scheme I



spectroscopy and potentiometry.

Since Ln^{III}–ligand bonds are predominantly of an electrostatic nature,[3] the geometry of the complexes is determined by the steric requirements of the ligands. Usually, complexes of the various Ln^{III} ions with a particular ligand are isostructural and often are similar to the corresponding complexes with alkaline-earth-metal ions.[4]

La^{III} and Lu^{III} are diamagnetic, whereas the other Ln^{III} ions are paramagnetic. The differences among these ions with regard to NMR spectroscopic properties are quite large, which is useful in the structural analysis of Ln^{III} complexes and which make them attractive probes for "NMR-silent" metal ions, such as Ca^{II}.[5,6]

Experimental Section

Abbreviations. EG = ethylene glycol; H_2MAL = maleic acid; H_2EGMS = ethylene glycol monosuccinic acid (2-(hydroxyethoxy)butanedioic acid); H_4EGDS = ethylene glycol disuccinic acid ((ethylenedioxy)dibutanedioic acid).

Materials. Perchlorate solutions of the lanthanides were prepared by dissolution of the reagent grade oxides into perchloric acid. The lanthanide content was determined by titration with EDTA using xylenol orange as the indicator. The lanthanide chlorides were obtained from Alfa Products. Na_2EGMS and Na_4EGDS were prepared as described previously.[2] ^{17}O-enrichment of the carboxylate groups was achieved as described previously for other carboxylates.[7]

NMR Measurements. The ^{139}La and ^{35}Cl NMR spectra were recorded with a Nicolet NT-200 WB spectrometer at 28.3 and 19.6 MHz, respectively, using 12-mm sample tubes. The chemical shifts were measured with respect to a 0.1 M solution of $LaCl_3$ in D_2O as external standard. The chemical shifts and the line widths were determined by fitting the experimental peaks with Lorentzian curves. The ^{17}O NMR spectra were recorded with a Nicolet NT-200 WB or with a Varian VXR-400 S spectrometer at 27.3 or 54.2 MHz, respectively. The deuterium signal of D_2O was used for internal lock, when possible. The Dy^{III}-induced shifts (DyIS) of samples in EG as the single solvent were measured with a coaxial inner tube with acetone-d_6 for internal lock. The ^{17}O signal of acetone was then used as standard for the chemical shifts. Chemical shifts obtained in these measurements were corrected for bulk magnetic susceptibility effects.[8]

All ^1H and ^{13}C NMR measurements were obtained with the Varian VXR-400 S spectrometer at 100.1 MHz. The methyl group of *tert*-butyl alcohol was used as internal standard (1.2 and 31.2 ppm for ^1H and ^{13}C NMR measurements, respectively). Longitudinal relaxation times were measured with the use of a $[(90°_x180°_y90°_x)-\tau-90°-acq]$ inversion recovery pulse sequence. The relaxation times were calculated by using a three-parameter fit of the experimental data.[9] Some of the ^{13}C NMR signals of EGDS almost coincided. In these cases a deconvolution program was used for the determination of the peak intensities.

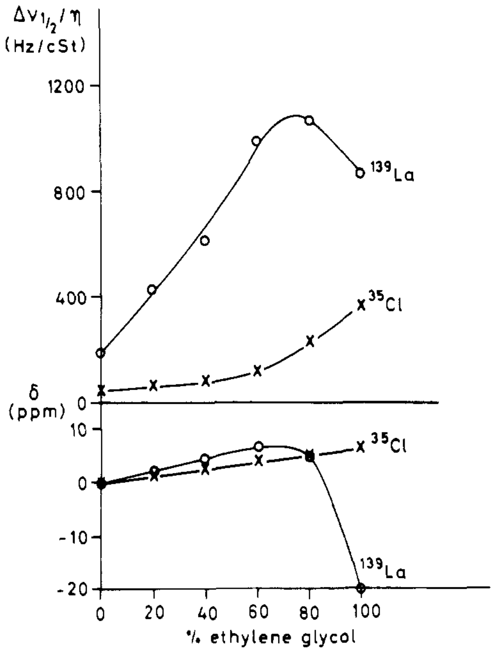


Figure 1. Line width:viscosity ratios and chemical shifts of ^{139}La and ^{35}Cl versus % EG (v/v) in EG–D_2O solutions containing 0.1 M $LaCl_3$ at 77 °C. The viscosities were 0.386, 0.552, 0.827, 1.240, 1.989, and 3.226 cSt for 0%, 20%, 40%, 60%, 80%, and 100% EG, respectively.

pH values quoted are direct meter readings.

Viscosity Measurements. The viscosities of the solutions of $LaCl_3$ in EG–water mixtures were determined with the use of an Ubbelohde viscometer.

Potentiometry. These measurements were performed as described previously.[10] The pK_a's of H_2EGMS (I = 1.0 M ($NaClO_4$)) were determined in duplicate by titrating a solution of H_2EGMS (0.002 M), which was obtained by passing the disodium salt through a Dowex 50W (H^+) cation-exchange column, with NaOH (0.04 M). For determination of the pK_a's of H_4EGDS, a solution of H_4EGDS (0.0036 M) and NaOH (0.145 M) was used. The stabilities of the 1:1 and 1:2 complexes of EGMS were determined by titration of a $Ln(ClO_4)_3$ solution at I = 1.0 M ($NaClO_4$) with a solution containing ligand (0.03 M) and 0.015 M H^+. For determination of β_{101} of EGDS, a ligand solution containing 0.02 M EGDS and 0.01 M H^+ was used. The computation of the stability constants from the titration curves obtained was performed as described previously.[10]

Results and Discussion

Solvation of $LnCl_3$ in EG. The O-alkylation reactions of EG with MAL were performed with the former compound as solvent and with the hydrated lanthanide chlorides as catalyst.[2] It is well-known that in dilute aqueous solutions of $LnCl_3$ (<1 M) the Ln^{III} ion is completely solvated with water,[11-15] whereas in organic solvents, such as methanol, acetonitrile, and *N*,*N*-dimethylformamide, Cl^- forms inner-sphere complexes with Ln^{III} ions.[16] Therefore, the solvation of the Ln^{III} ions in EG was investigated by ^{139}La, ^{35}Cl, and ^{17}O NMR techniques.

Figure 1 shows that the ^{35}Cl chemical shift of 0.1 M solutions of $LaCl_3$ in D_2O–EG mixtures increases slightly from D_2O to EG. The increase is, however, much smaller than that observed upon replacement of water by methanol (180 ppm),[17] indicating that in EG the inner-sphere coordination of La^{III} by Cl^- is of minor importance. This is confirmed by the ^{139}La chemical shifts. For

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coordination of each Cl^- ion to La^{III} an induced shift of 100 ppm has to be expected.[14,17] When the EG:D_2O ratio is increased in the system, the ^{139}La chemical shift initially shows a slight increase (see Figure 1), but when the amount of EG becomes larger than 70% (v/v), it declines until it reaches a value of −19 ppm for pure EG. This has to be ascribed to coordination of La^{III} by EG. The rather small effect on the ^{139}La chemical shift of substitution of a D_2O oxygen in the first coordination sphere of La^{III} by an oxygen of EG indicates that under the conditions applied, the ionization of the hydroxy group of coordinated EG is probably negligible; for negatively charged oxygens a high-frequency shift of about 30 ppm per oxygen should be expected.[5,18,19]

The ^{139}La and ^{35}Cl line widths (see Figure 1) confirm the absence of inner-sphere complexes between La^{III} and Cl^-. They are governed by the quadrupolar relaxation, which under extreme narrowing conditions ($\omega_0{}^2\tau_C{}^2 \ll 1$) is given by[20]

$$\frac{1}{T_2} = \frac{3}{10}\pi^2\frac{2I+3}{I^2(2I-1)}\left(\frac{e^2qQ}{h}\right)\left(1+\frac{\eta^2}{3}\right)\tau_c \qquad (1)$$

Here e^2qQ/h is the quadrupole coupling constant, η is the asymmetry parameter, and τ_c is the molecular reorientational correlation time. The latter can be estimated by the Debye–Stokes–Einstein equation (2), if it is assumed that the molecules concerned are

$$\tau_c = 4\pi r^3\eta_s/3kT \qquad (2)$$

spherical. Here η_s is the solution viscosity. Formation of an inner-sphere La^{III}–Cl^- complex would result in an increase of both the asymmetry parameter, η, and τ_c and thus would give rise to an increase of the line width ($\Delta\nu_{1/2}$) of both the ^{139}La and the ^{35}Cl signal. For this complex in methanol, it has been reported that the $\Delta\nu_{1/2}/\eta_s$ values are 1360 and 1780 Hz/cSt for ^{139}La and ^{35}Cl, respectively. Figure 1 shows, however, that the increase of $\Delta\nu_{1/2}/\eta_s$ in the ^{35}Cl signal is relatively small (380 Hz/cSt) from D_2O to EG. The ^{139}La line width initially increases upon replacement of D_2O by EG, but when the amount of EG is more than 70%, it decreases again. This behavior can be attributed to substitution of D_2O by EG in the first coordination sphere of La^{III}, yielding initially relatively asymmetric La^{III}–EG–D_2O complexes and finally a D_2O-free complex La^{III}–EG that has a lower asymmetry parameter η. It should be noted that the maxima in the curves of the ^{139}La line widths and chemical shifts occur at the same concentration of EG.

The increase of the concentration of the La^{III}–EG complexes at high concentrations of EG (>70%), as witnessed by the ^{139}La chemical shifts and line widths, is accompanied by some increase of the viscosity-corrected ^{35}Cl line width (see Figure 1). Probably this is caused by the presence of a solvent-separated (solvent = EG) ion pair of La^{III} and Cl^-. This has a relatively large radius, and consequently τ_c and $\Delta\nu_{1/2}$ for ^{35}Cl of that complex are large in comparison to those of "unbound" Cl^-.

Previously, we have observed that, for Dy^{III}, the induced shift (DyIS) of a bound ^{17}O nucleus is dominated by the contact contribution and is almost independent of the nature of the ligand in question and also of the other ligands coordinated to the Dy^{III} ion.[7,21,22] Therefore, the DyIS can be utilized to establish the oxygen coordination sites of the ligand and to determine the stoichiometry of the complex.

The exchange of the ^{17}O nuclei of bound and free ligands was fast on the NMR time scale. Straight lines were obtained in plots of the DyIS versus the Dy^{III}:ligand molar ratio (ρ, $\rho < 0.1$, correlation coefficients > 0.999). The slopes of these lines (Table I) correspond to $n\Delta$, where n is the number of bound oxygens of the concerned ligand per Dy^{III} and Δ is the bound shift of that ^{17}O nucleus.

Table I. Solvation of Dy^{III} as Deduced from Dy^{III}-Induced ^{17}O NMR Shifts

system[a]	temp, °C	Dy^{III}-induced shift,[b] ppm		bound O atoms[c]	
		D_2O	alcohol–O	D_2O	alcohol
D_2O	80	−17 458		9.0	
EG	80		−8 408		8.7
D_2O–EG (37:63)	80	−5 814	−6 581	3.0	6.8
D_2O–EG (44:56)	80	−6 322	−4 589	3.3	4.7
D_2O–EG (67:33)	80	−9 902	−3 537	5.1	3.6
D_2O	25	−20 401		9.0	
CD_3OD	25		−12 182		5.4
D_2O–CD_3OD (1:1)	25	−19 248	−2 636	8.5	1.2
CD_3OD–EG (1:1)	25		−8 307 (EG)		7.3
			−973 (CD_3OD)		0.4

[a] Molar ratios in parentheses. [b] Extrapolated to $\rho = 1$, where ρ is the molar ratio of Dy^{III} added as $DyCl_3{\cdot}6H_2O$ and the concerned ligand. [c] Average number per Dy^{III} ion. For calculation, see text.

We assume that, for the very low Dy^{III} concentrations we have used, Dy^{III} is hydrated by nine D_2O molecules.[15,23] Then from the DyIS of D_2O extrapolated to $\rho = 1$ (−17 458 ppm; see Table I), it can be calculated that the bound shift of an ^{17}O donor site is −17 458/9 = −1940 ppm.

Upon addition of Dy^{III} to EG, a single EG ^{17}O signal was observed, which is in agreement with the fast exchange between the complex and the bulk. From the DyIS extrapolated to ρ = 1 (−8408 ppm, Table I), the average number of bound EG oxygens per Dy^{III} can be calculated to be −8408 × 2/−1940 = 9. The multiplication by 2 is needed because each EG ligand has two indistinguishable oxygens. No conclusions concerning the denticity of EG can be made on the basis of these data; mono- and bidentately bound EG would give rise to the same DyIS extrapolated to ρ = 1, if it is assumed that the coordination number of Dy^{III} for monodentately bound EG is twice that of bidentately bound EG and that the DyIS of a noncoordinated oxygen is negligible. Anyway, these data confirm that Dy^{III} is completely solvated by EG and that Cl^- is not able to substitute EG in the first coordination sphere of Dy^{III}.

For comparison, we have also performed measurements on the system $DyCl_3$–methanol. From the DyIS extrapolated to $\rho = 1$ (Table I), it can be deduced that Dy^{III} is coordinated by 5.4 methanol ligands. The first coordination sphere is then completed by three Cl^- ligands, which is in good agreement with conclusions in the literature, based on other techniques.[16,17] Apparently the affinity of Ln^{III} ions for methanol is less than for water and EG, which are both able to expel Cl^- from the first coordination sphere of the Ln^{III} ions. This is confirmed by the results of competition experiments with 1:1 mixtures of methanol with D_2O and EG, respectively (see Table I), showing that in the former experiment D_2O is bound preferentially, whereas in the latter coordination of EG to Dy^{III} is predominant.

The strong preference of Dy^{III} for EG in the competition experiment with EG and methanol suggests that at least some bidentate coordination of the former occurs. Steric effects may account for the difference in stability of the Dy^{III}–methanol and Dy^{III}–D_2O complexes. Likewise, the average number of coordinated D_2O and EG oxygens per Dy^{III} was determined from the DyIS in mixtures of D_2O and EG (see Table I). It appears that the ratio of coordinated EG oxygens to coordinated waters is always somewhat larger than the molar ratio of EG and D_2O. From these data it may be concluded that the order of affinity of Ln^{III} is EG > D_2O > Cl^- > methanol.

Ln^{III}–MAL in EG. The DyIS of the ^{17}O nuclei of both MAL (5% ^{17}O-enriched) and EG were determined. In all spectra a single

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Table II. Dy^{III}-Induced ^{17}O Shifts of 0.35 M Solutions of MAL, EGMS, and EGDS in EG or D_2O at 80 °C

		Dy^{III}-induced shift,[a] ppm		Dy^{III}-bound O atoms[b]	
carboxylate	solvent	carboxylate	solvent	carboxylate	solvent
MAL	EG	−496	−7848	1.0	8.1
EGMS	EG	*c*	−870		0.9
EGMS	D_2O	−1531[d]	−2154	3.2[d]	1.1
EGDS	D_2O	*c*	−3773		2.0

[a] Extrapolated to $\rho = 1$. [b] Average number of Dy^{III}-bound O atoms per Dy^{III} ion. [c] Not observable due to excessive line broadening. [d] See text.

carboxylate ^{17}O signal was observed, indicating that the exchange between the two carboxylate oxygens and that between the free and the Dy^{III} bound ligand are fast on the NMR time scale. From the plots of the DyIS versus ρ (Table II), where ρ is the molar ratio of Dy^{III} and the ligand in question (viz. EG or MAL), and with the procedure outlined in the previous section, the average number of oxygens of these ligands attached to Dy^{III} can then be calculated to be 8.1 (−7848/−1940) and 1.0 (4 × −496/−1940), respectively. This shows that MAL is rather weakly bound to Dy^{III}, probably in a monodentate fashion. Previously, we have shown that MAL in D_2O under similar conditions forms Dy(MAL) and Dy(MAL)$_2$ complexes, in which it is proposed to be bound in two fashions: (i) as a seven-membered chelate with two carboxylate groups coordinated and (ii) as a bidentate ligand via a single carboxylate group.[24] This once again demonstrates that the affinity of Ln^{III} ions for EG is larger than for D_2O.

Ln^{III}–EGMS in EG and in D_2O. From the DyIS of the ^{17}O nuclei of the solvent in a 0.35 M solution of EGMS in EG and in D_2O, the average number of coordinated solvent oxygens appeared to be 1 in both cases (see Table II). If it is assumed that the coordination numbers of Dy^{III} in the Dy^{III}–EGMS–EG and Dy^{III}–EGMS–D_2O complexes are the same, it may be concluded that EGMS is coordinated to Dy^{III} in the same fashion in these solvents. Apparently, the stability of the Dy^{III}–EGMS complex is large enough to preclude any competition of the solvent in the coordination. Since EGMS has four functional groups, and the coordination number of Dy^{III} is usually 8–9,[15,23] it is inferred that the stoichiometry of the concerned complexes is Dy^{III}-(EGMS)$_2$(solvent).

Upon addition of Dy^{III} to a sample of EGMS, of which the carboxylate oxygens were 5% ^{17}O-enriched, severe line broadening was observed in the ^{17}O signals for the carboxylate groups. The initially well-separated signals collapsed after a small addition to one broad signal. Further additions of Dy^{III} did not result in any separation; the signals have about the same DyIS, showing that both carboxylate groups of EGMS are attached to the Dy^{III} ion. A calculation, using the procedure described above, of the average number of coordinated carboxylate oxygens per Dy^{III} yields 3.2. This is somewhat low, considering the stoichiometry of the complex and the fact that no separation of the carboxylate signals could be observed at higher ρ values. Probably the exchange of the carboxylate oxygens between the free and the Dy^{III}-coordinated state is not in the fast-exchange region on the NMR time scale. This is supported by the extreme broadening observed and by the smaller DyIS at higher magnetic field.

^{17}O NMR spectroscopy is a very convenient technique to study coordination phenomena in EG solutions. This solvent causes, however, serious problems in ^{13}C and ^{1}H NMR techniques, due to interfering large solvent signals. Because of the similarity of the Dy^{III}–EGMS complexes in EG and D_2O suggested by the results of the experiments described above, we decided to perform further investigations on the structure of these complexes in D_2O or H_2O as the solvent.

The stability constants of the complexes of EGMS and the various Ln^{III} ions in aqueous solution (I = 1.0 M (NaClO$_4$); 25 °C) were determined with the use of potentiometry. The overall stability constants are defined as

$$\beta_{10n} = [\mathrm{Ln(EGMS)}_n]/[\mathrm{Ln}][\mathrm{EGMS}]^n \qquad (3)$$

Table III. Stability Constants of the Lanthanide(III) Complexes of EGMS and EGDS in Water (I = 1 M (NaClO$_4$); 25 °C)

	EGMS[a]		EGDS[b]
Ln^{III}	log β_{101}	log β_{102}	log β_{101}
La	3.94	6.79	7.10
Pr	4.44	7.42	6.07
Nd	4.48	7.39	6.51
Sm	4.63	7.74	6.16
Eu	4.47	7.49	6.96
Gd	4.40	7.55	6.67
Tb	4.29	7.45	6.45
Dy	4.20	7.34	6.09
Ho	4.22	7.23	6.81
Er	4.24	7.18	5.94
Tm			5.94
Yb	4.41	7.31	5.96

[a] pK_{a1} = 3.07; pK_{a2} = 4.40. [b] pK_{a1} = 2.48; pK_{a2} = 3.29; pK_{a3} = 4.08; pK_{a4} = 4.77.

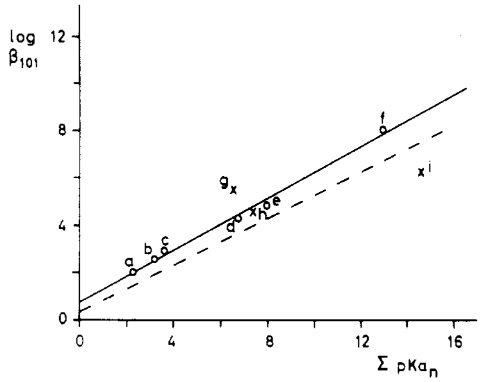

Figure 2. log β_{101} for a series of Sm^{III} complexes of (hydr)oxy carboxylates versus the summed acidity constants ($\sum pK_{an}$) of these ligands, 25 °C (solid line): a = pyruvate, b = glyoxylate, c = glycolate, d = D-tartrate, e = malate, f = citrate, g = oxydiacetate, h = EGMS, i = EGDS. The broken line gives the relationship for non-hydroxylated mono- and dicarboxylates.[29,30]

The values obtained (see Table III) show the usual trend: a regular increase from La through Sm, then a decrease up to Ho, followed by another increase at the end of the series. Several explanations for this phenomenon, in terms of effects related to the decreasing ionic radii from La^{III} to Lu^{III}, have been proposed in the literature.[25-27]

The stability constants of the complexes of a metal ion with a series of related ligands is expected to be linearly correlated with the summed acidity constants of the donor groups involved, when the interaction is strongly ionic and no variations in steric effects occur.[28] Choppin has shown that the magnitudes of β_{101} of the Sm^{III} complexes of a variety of mono- and dicarboxylates and amino polycarboxylates conform with such a linear relationship.[29,30] In Figure 2, we have plotted the β_{101} values of a series of α-(hydr)oxy carboxylates, taken from the literature,[31] as a function of the $\sum pK_a$ of these compounds. The line obtained appears to be somewhat above that for the mono- and dicarboxylates.[29,30] This probably reflects an increase of stability as a result of the formation of a five-membered chelate of the α-(hydr)oxy car-

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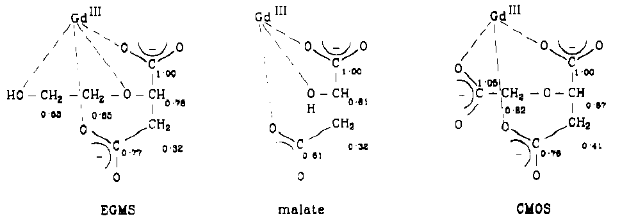


Figure 3. Comparison of the relative Gd^{III}-induced ^{13}C relaxation rate enhancements of EGMS, malate, and CMOS. Schematic representations of the mode of coordination in the predominant Gd^{III} complexes are given.

boxylate function and Sm^{III}. The data for EGMS fall on the line for the α-(hydr)oxy carboxylates, suggesting that all carboxylate functions of EGMS are coordinated to the Ln^{III} ion. If this would not be the case, a much lower stability should be expected. Obviously, conclusions about the involvement of the 6-OH function in the coordination are not possible, on the basis of stability constants.

An unambiguous assignment of the Ln^{III} coordination sites of EGMS could be achieved with the use of Gd^{III}-induced ^{13}C longitudinal relaxation rate enhancement measurements. Among the Ln^{III} cations, Gd^{III} has the longest electronic relaxation time,[32] and therefore it is very suitable for the study of the geometry of bound ligands. Since it can be applied in very low concentrations with respect to the ligand ($\rho < 10^{-4}$), information will be obtained on complexes in which Gd^{III} is coordinated by the maximum number of ligands possible, the Gd^{III}–(EGMS)$_2$ complex in this case. Assuming that the mean residence time of a ligand in its Gd^{III} complex is short with respect to the longitudinal relaxation time (T_1(c)) and that the contribution of intermolecular interactions to the relaxation is negligible, the observed relaxation rate of a nucleus ($1/T_1$(obs)) can be expressed as[33,34]

$$1/T_1(\mathrm{obs}) = n\rho/T_1(\mathrm{c}) + 1/T_1(\mathrm{f}) \qquad (4)$$

where n is the number of ligands bound in the Gd^{III} complex and $1/T_1$(f) is the relaxation rate of that nucleus in the undoped sample. The relaxation rate in the complex is related to the molecular structure via eq 5.[35-37] Here r is the distance between Gd^{III} and the nucleus under consideration, and k is a constant.

$$1/T_1(\mathrm{c}) = k/r^6 \qquad (5)$$

The relaxation rates of the ^{13}C nuclei of EGMS were measured at five different Gd^{III} concentrations ($\rho = 0\text{–}1.3 \times 10^{-4}$). In accordance with eq 4, a linear relationship between the relaxation rates and ρ was found (correlation coefficients > 0.999). From the slopes of the lines the relative relaxation rate enhancements (RRE's) shown in Figure 3 were calculated.

The RRE's of the two carboxylate ^{13}C nuclei of EGMS are of the same magnitude, proving that both are coordinated to Gd^{III}, as was already expected on the basis of the stability constants. The RRE of C(2) is of the same magnitude as well; thus O(2) is also bound to Gd^{III}. Similar RRE values were previously determined for malate[38] and (carboxymethoxy)succinate (CMOS),[39] which both contain, like EGMS, a malate structural unit. It was shown, with the use of several techniques, that this unit in the Gd^{III} complexes of these ligands is also predominantly bound in a tridentate fashion via the two carboxylates and O(2). The RRE's of C(5) and C(6) of EGMS are of the same magnitude as C(1), C(2), and C(4), showing that O(6) is also coordinated to Gd^{III}. It can be calculated with eq 5 and distances estimated from Dreiding models that, if O(6) were not coordinated, the RRE of C(6) would be 0.1. It can be concluded that, in the predominant complex, EGMS coordinates via the two carboxylate groups and O(2) and O(6). Thus, in the 1:2 Ln^{III}–EGMS complex, eight positions on the Ln^{III} cation are occupied by the two EGMS ligands, and as was shown by the Dy^{III}-induced water ^{17}O shifts, the first coordination sphere of the cation is completed with one water ligand. This leads to a coordination number of 9 for Ln^{III}.

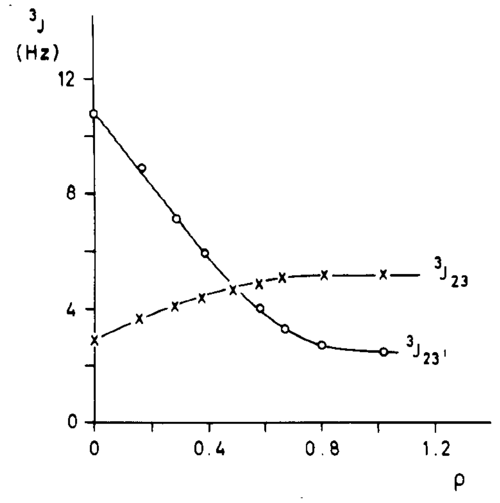
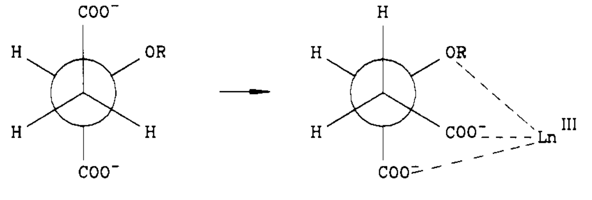


Figure 4. Vicinal coupling constants of EGMS in the presence of La^{III} as a function of ρ at pH 7 and 25 °C.



R= - CH$_2$ - CH$_2$OH

Figure 5. Conformational change of EGMS upon coordination to a Ln^{III} cation.

Table IV. ^1H Chemical Shifts (ppm) and Coupling Constants (Hz) of EGMS and Its La^{III} Complexes in D_2O at pH 7 and 25 °C

	free EGMS	La(EGMS)$^+$	La(EGMS)$_2^-$
δ_2	4.08	4.24	4.12
δ_3	2.56	3.05	2.85
$\delta_{3'}$	2.34	2.92	2.69
$^3J_{2,3}$	2.9	5.4	4.8
$^3J_{2,3'}$	10.9	1.2	4.3
$^2J_{3,3'}$	−15.3	−18.7	−17.5

For the coordination of EGMS, a drastic change of conformation is required, as is witnessed by the changes of the vicinal proton–proton coupling constants upon coordination of EGMS with the diamagnetic La^{III} (Figure 4). The magnitudes of $^3J_{2,3}$ and $^3J_{2,3'}$ at pH 7 show that the free ligand is almost exclusively in a antiperiplanar conformation (see Figure 5). The preference for this conformation is higher than in the case of succinate, where, as has been shown by Gil et al.,[40] its population is about 60%. From the experimental coupling constants at various ρ values (see Figure 4) and the molar fractions of the various species as calculated from the stability constants in Table III, the ^1H chemical shifts and the coupling constants in the 1:1 and in the 1:2 complexes could be evaluated with the use of a multiple regression method (Table IV). Previously, we have shown that coordination of a rigid ligand to a Ln^{III} ion has no observable influence on the vicinal proton–proton coupling constants.[41] Therefore, the dra-

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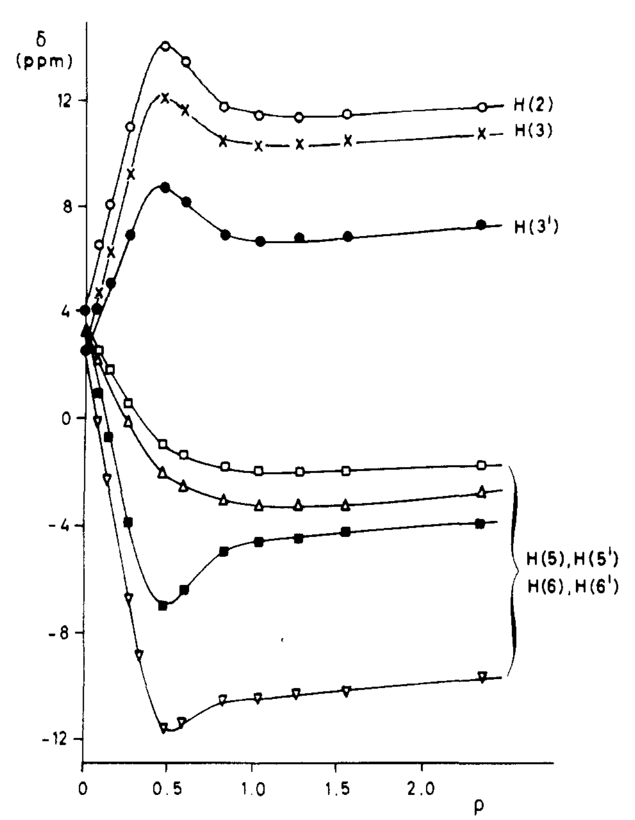

Figure 6. ^{1}H chemical shifts of EGMS in the presence of Pr^{III} as a function of ρ at pH 7 and 25 °C.

matic changes in $^3J_{2,3}$ and $^3J_{2,3'}$ are caused by a conformational change of EGMS upon coordination to La^{III}; the magnitudes of these coupling constants show that in the complex the carboxylates groups are in the synclinal configuration, which is actually the conformation that is dictated by a tetradentate coordination of EGMS. It should be noted that the geminal coupling constant $^2J_{3,3'}$ also changes from the free ligand to the complexes. It is known that geminal coupling constants, in contrast to the vicinal ones, are sensitive to coordination of neighboring groups by a Ln^{III} ion.[42] So this is in agreement with coordination of COO(4).[43] The behavior of the vicinal coupling constants $^3J_{2,3}$ and $^3J_{2,3'}$ is very similar to that observed previuosly for CMOS, and this supports the great similarity in coordination of these ligands.

In Figure 6 the ^{1}H shifts of EGMS in the presence of the paramagnetic Pr^{III} cation are shown as a function of ρ. The bend in the curves at $\rho = 0.5$ confirms the existence of 1:1 and 1:2 complexes. These complexes have somewhat different bound shifts. It should be noted that the induced shifts for nuclei in the succinate part and those in the $-OCH_2CH_2OH$ part have opposite signs. If it is assumed that these shifts are of a pseudocontact origin, and that internal reorientations in the complex result in effective axial symmetry, their magnitudes are given by[44-46]

$$\Delta = C(3\cos^2\theta - 1)/r^3 \qquad (6)$$

Here Δ is the bound shift of a nucleus, r is its distance to Pr^{III}, θ is the angle between the vector **r** and the pseudoaxial axis, and C is a constant. The sign of Δ reverses at $\theta = 54.7°$. From previous studies we know that the sign of C is negative for Pr^{III}.[47] Therefore, the nuclei in the succinate part of EGMS are in the equatorial region ($55 < \theta < 125°$), whereas the nuclei of the EG part are in the axial region ($0 < \theta < 55°$, $125 < \theta < 180°$).

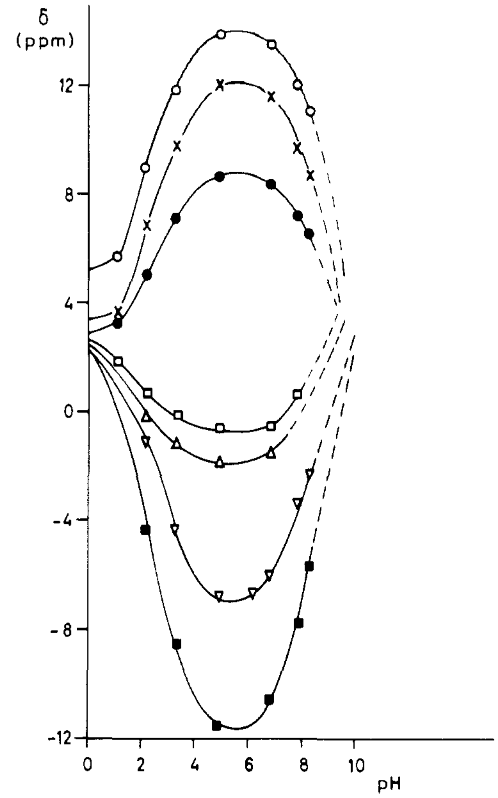

Figure 7. Influence of the pH on the ^{1}H chemical shifts of a 0.2 M solution of EGMS in D_2O, in the presence of Pr^{III} ($\rho = 0.5$) at 25 °C: (○) H(2); (●) H(3); (×) H(3'); (□, △, ▽, and ■) H(5), H(5'), H(6), and H(6').

The pK_a of the Ln^{III}-coordinated OH group of EGMS is of importance in relation with the mechanism of the O-alkylation of EG with MAL, in which attack of the ionized OH group to the olefinic bond is supposed to be a crucial step. Therefore, we have investigated the effect of pH on the ^{1}H chemical shifts of EGMS in the presence of Pr^{III} (see Figure 7). The curves obtained have a bell shape, with a plateau at pH 5–6. At lower pH's decomplexation occurs due to protonation of the successive carboxylate groups. The steep decline of the induced shifts at pH >7 can be ascribed to a decomplexation caused by the formation of polynuclear Pr^{III}-hydroxide complexes. At pH >8 the samples became somewhat turbid, and at higher pH values precipitation of the hydroxide occurred. Apparently, the pK_a of the Pr^{III}-coordinated hydroxyl group of EGMS is higher than that of coordinated water. Previously, we have observed that the pK_a of the hydroxyl group of a Ln^{III}-coordinated α-hydroxy carboxylate is somewhat below that of coordinated water.[10,48] Since the order of the pK_a's of hydroxyl groups of the uncoordinated compounds is α-hydroxy carboxylate < H_2O < EG,[49-51] it is reasonable that the order for the coordinated ligands is the same.

Ln^{III}-EGDS in Water. The Ln^{III}-catalyzed O-alkylation of EG with MAL affords the diastereomers of EGDS, the meso compound being slightly more abundant than the racemic mixture. No attempt was made to separate these diastereomers.

The potentiometrically determined log β_{101} values of the Ln^{III}-EGDS complexes are of the same magnitude as the log β_{102} values of the corresponding EGMS complexes. Inclusion of the data for EGDS in the plot of the log β values versus $\sum$pK_a (see Figure 2) shows that the stability constant is lower than should be expected for coordination of EGDS in a hexadentate mode. This may point to a decreased stability due to steric strain or to coordination in a pentadentate fashion.

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Table V. Relative Gd^{III}-Induced Longitudinal ^{13}C Relaxation Rate Enhancements (s^{-1}) in EGDS at pH 7 and 25 °C

nuclei	*meso*-EGDS	*rac*-EGDS	nuclei	*meso*-EGDS	*rac*-EGDS
C(1), C(1′)	1.00[a]	1.00[a]	C(4), C(4′)	0.82	0.76
C(2), C(2′)	0.46	0.59	C(5), C(5′)	0.40	0.55
C(3), C(3′)	0.25	0.54			

[a] The absolute relaxation rate enhancements are 10.7×10^3 and 9.9×10^3 s^{-1} for *meso*-EGDS and *rac*-EGDS, respectively.

The Dy^{III}-induced ^{17}O shifts (see Table II) show that the Dy^{III}–EGDS complex contains two water ligands in the first coordination sphere. So if it is assumed that the coordination number is 8 or 9, then this suggests a hexadentate coordination of EGDS.

The Gd^{III}-induced RRE's are very similar to those observed for EGMS.[52] It can be inferred that EGDS is bound to Gd^{III} analogously to EGMS, thus in a hexadentate fashion with the carboxylates and the ether oxygens as donor sites. The small differences in the RRE's between the two diastereomers can be ascribed to small differences in the conformation of the bound ligands. The largest differences occur in C(3) and C(3′). With the use of eq 5 it can be calculated that the differences observed for these nuclei correspond with only a 13% difference in the Gd^{III}–C distance. These nuclei are part of six-membered chelate rings, and an inspection of molecular models shows that these rings are rather flexible.

Conclusions

Multinuclear NMR techniques have been proven to be very valuable for the establishment of the structures of species occurring in the reaction mixture of the lanthanide-catalyzed O-alkylation of EG with MAL. Ln^{III} cations have a preference for the coordination of EG over that of water, which is in agreement with the observation made previously[2] that water does not interfere in the O-alkylation reaction as long as it is not present in a large amount. The Cl^- ion is not in the first coordination sphere of the Ln^{III} cation, whereas MAL is able to compete with EG for coordination. The products of the first and the second O-alkylation steps (EGMS and EGDS, respectively) are strong chelators for the Ln^{III} ions. Therefore, the water addition is not an important side reaction in the second O-alkylation step (EGMS → EGDS), and product inhibition plays a role in the O-alkylation reactions.

Deprotonation of the Ln^{III}-coordinated hydroxyl groups of EG and EGMS could not be observed, in contrast to that of the previously studied glycolate, for which the pK_a was determined to be about 8.[10] Mixed-ligand complexes with deprotonated hydroxyl groups are supposed to be the key intermediates in the O-alkylation of hydroxy compounds with MAL. The observations on EG and EGMS, suggesting a relatively high pK_a of the Ln^{III}-coordinated hydroxyl group of these compounds, are therefore in agreement with the relatively low reaction rates in the O-alkylation reaction of EG with MAL in comparison with the corresponding reaction with glycolate.[10,24]

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(52) The assignments of the peaks in the ^{13}C NMR spectrum were made previously[2] with the use of a chiral shift reagent, except for the peaks of the carboxylate groups, which almost coincided. The relative relaxation rate enhancements of the carboxylate carbons were 1.0 and 0.8, which is very similar to the values observed for the related nuclei in EGMS. On the basis of the comparison of the magnitudes of the relative relaxation rates the signal with a RRE of 1.0 is assigned to C(1) and C(1′).

Contribution from the Nuclear Research Centre Negev, Beer-Sheva, Israel,
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Oxidation of Copper(II) Bis(glycinate) by Methyl Free Radicals in Aqueous Solutions. A Pulse-Radiolysis Study

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The reaction of $^{\bullet}CH_3$ free radicals with $Cu^{II}(NH_2CH_2CO_2^-)_2$ in aqueous solutions was studied. The formation of the unstable intermediate $(NH_2CH_2CO_2^-)_2Cu^{III}–CH_3(aq)$ in this reaction was observed. This intermediate decomposes into $Cu^{III}(NH_2CH_2CO_2^-)_2^+(aq) + CH_4$. The formation of $Cu^{III}(NH_2CH_2CO_2^-)_2^+(aq)$ is not observed, as this complex is short-lived under these conditions and decomposes via ligand oxidation. The $^{\bullet}CH_3$ free radicals react with the transient complex $(NH_2CH_2CO_2^-)_2Cu^{III}–CH_3(aq)$ to form ethane and $Cu^{II}(NH_2CH_2CO_2^-)_2$; the specific rate of this reaction approaches the diffusion-controlled limit. The results thus point out that aliphatic free radicals can oxidize copper(II) complexes to copper(III) complexes. The results suggest that the reactions of aliphatic free radicals with copper complexes might cause the reported radiosensitization by copper compounds.

In a recent study it was reported that *N*-benzylglycine is formed quantitatively when an alkaline aqueous solution containing $Cu^{II}(NH_2CH_2CO_2^-)_2$ and $ClCH_2C_5H_6$ is sonolyzed.[2] No plausible mechanisms for this process were proposed.

In previous studies[3,4] we have shown that aliphatic free radicals, $^{\bullet}R$, react with Cu^{II}(peptidate), where peptidate = tri- or tetraglycinate, to form transient complexes of the type (peptidate)-Cu^{III}–R. As sonochemistry in aqueous solutions stems from the formation of free radicals,[5] it seems reasonable to suggest that

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