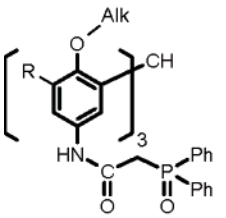
Carbamoylmethylphosphinoxide Derivatives Based on the Triphenylmethane Skeleton. Synthesis and Extraction Properties

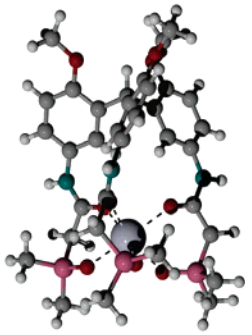
Valentyn Rudzevich,[†,‡] Dieter Schollmeyer,[§] Damien Braekers,[‖] Jean F. Desreux,*[,‖]
Romain Diss,[⊥] Georges Wipff,*[,⊥] and Volker Böhmer*[,†]

*Abteilung Lehramt Chemie, Fachbereich Chemie und Pharmazie and Institut für Organische Chemie,
Johannes Gutenberg-Universität Mainz, Duesbergweg 10-14, D-55099 Mainz, Germany,
Coordination and Radiochemistry, University of Liège, Sart Tilman B16/B6, B-4000 Liège, Belgium, and
Laboratoire MSM, Institut de Chimie, UMR CNRS 7551, Université Louis Pasteur, 4, rue B. Pascal,
67 000 Strasbourg, France*

jf.desreux@ulg.ac.be; wipff@chimie.u-strasbg.fr; vboehmer@mail.uni-mainz.de

Received April 11, 2005





Two different strategies were used to synthesize tri(2-alkoxy-5-nitrophenyl)methanes **6a**,**b**. The X-ray structures of **6a** and its precursor **5** show the molecules in a conformation with a *syn*-orientation of the nitro and alkoxy groups. Hydrogenation and acylation by the appropriate active ester gave the corresponding tri-CMPO derivatives **4a**,**b**. Their ability to complex lanthanide ions was studied by NMR spectroscopy and by nuclear magnetic relaxation dispersion and further characterized by quantum mechanical calculations. Extraction experiments from acidic solution to dichloromethane reveal a reasonable selectivity of Am(III) over Eu(III), but in contrast to similar tetra-CMPOs derivatives of calix[4]arenes the distribution coefficients strongly decrease with increasing concentration of HNO_3.

Introduction

The appropriate treatment and storage of nuclear wastes from technical, military, or medical (or other) sources is one of the permanent and urgent problems of modern/industrial/civilized societies. Consequently, whatever the envisaged strategies are, there is a continuous search for improved ligands/extractants which are able to remove the most harmful elements from the total waste, usually those elements/isotopes with long half-lifes. In the case of actinides this would not only lead to a reduction of the total waste volume to be stored but would also allow for a transmutation into less dangerous elements provided an efficient separation from the lanthanides can be achieved.

Carbamoylmethylphosphine oxides (CMPOs) represent such a general class of compounds,[1] able to extract actinides from highly acidic solutions, and *N*,*N*-diisobutylcarbamoylmethyloctylphenylphosphine oxide is used industrially in the TRUEX process.[2] In a series of studies, we could show that the attachment of four CMPO functions at the wide rim (**1**)[3] or at the narrow rim (**2**)[4] of calix[4]arenes leads to a drastic increase of the extraction efficiency, suggesting a cooperative action of

---

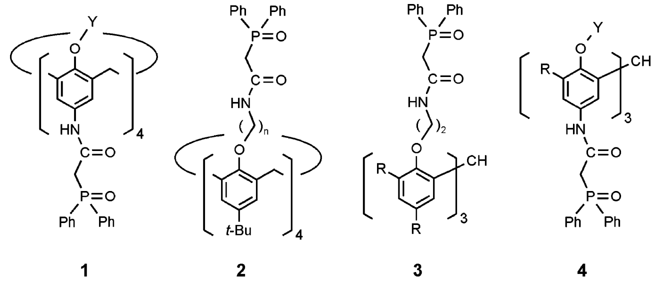
[†] Abteilung Lehramt Chemie, J. G.-Universität Mainz.
[‡] Permanent address: Institute of Organic Chemistry, NAS of Ukraine, Murmanska str. 5, Kyiv-94, 02094, Ukraine.
[§] Institut für Organische Chemie, J. G.-Universität Mainz.
[‖] Coordination and Radiochemistry, University of Liège.
[⊥] Institut de Chimie, Université Louis Pasteur.

(1) (a) Martin, K. A.; Horwitz, E. P.; Ferraro, J. R. *Solvent Extr. Ion Exch*. **1986**, *4*, 1149–1169. (b) Baker, J. D.; Mincher, B. J.; Meikrantz, D. H.; Berreth, J. R. *Solvent Extr. Ion Exch*. **1988**, *6*, 1049–1065.

(2) (a) Horwitz, E. P.; Kalina, D. G.; Diamond, H.; Vandegrift, G. F.; Schultz, W. W. *Solvent Extr. Ion Exch*. **1985**, *3*, 75–109. (b) Chamberlain, D. B.; Leonard, R. A.; Hoh, J. C.; Gay, E. C.; Kalina, D. G.; Vandegrift, G. F. Truex Hot Demonstration: Final Report, Report ANL-89/37, Argonne, IL, April 1990.

10.1021/jo050717a CCC: $30.25

CHART 1



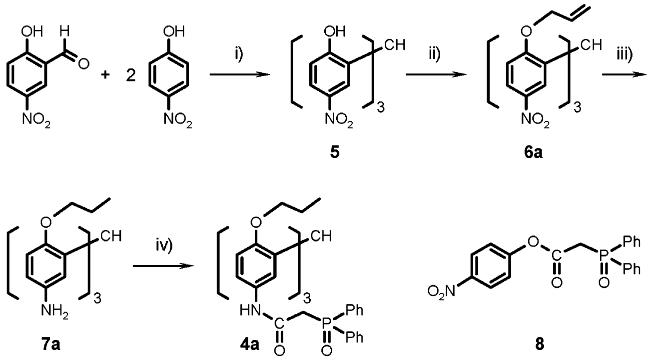
the four CMPO functions (Chart 1). In addition, there is a pronounced selectivity for Am over Eu when extracted from acidic media, as well as within the lanthanide series for the lighter over the heavier elements. Rigidification of the calix[4]arene skeleton surprisingly does not change the selectivity, but increases further the extraction ability.[5]

Early studies from Horwitz et al.[2] indicated that three CMPO molecules are coordinated to the trivalent actinide cation strongly via their P=O and more weakly via their C=O functions in a complex which contains additionally three nitrate anions and three HNO_3 molecules loosely bound to the C=O groups. Consequently, a tripodal arrangement of three CMPO groups should lead to an even better ligand. Thus, trihydroxytriphenylmethane was proposed as a scaffold[6] on which three CMPO groups were bound (**3**) similarly to compounds **2**. Single-crystal X-ray structures of lanthanide complexes showed the expected coordination of **3**.[6] However, although high extraction percentages were found for Th^{4+} the extraction of trivalent cations (lanthanides) was less effective than with **2**. Since subtle differences in the mutual arrangement/orientation of the CMPO groups might have a crucial influence, we decided to study the tri-CMPO derivatives **4**, which are based again on trihydroxytriphenylmethane, but have (in contrast to **3**) the CMPO functions attached to the aromatic moieties as in the wide rim derivatives **1**.

Results and Discussion

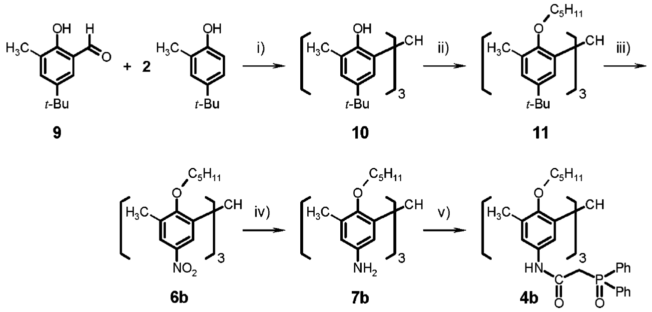
Synthesis. The parent compound **4a**, unsubstituted in the ortho positions relative to the alkoxy groups, was obtained as shown in Scheme 1. Acid-catalyzed condensation of 2-hydroxy-5-nitrobenzaldehyde with an excess of *p*-nitrophenol led to the triphenylmethane **5** in nearly 90% yield. Since *p*-nitrophenol units are less reactive (less nucleophilic) than alkylphenols we chose allyl bromide for the etherification in the presence of K_2CO_3 (92% of **6a**). Subsequent exhaustive hydrogenation gave the propyl ether **7a**[7] in one step which was acylated as usual by the active ester **8**. While the yield of **7a** (40% after column chromatography) leaves room for improvement, 85% of **4a** was obtained in the last step.

SCHEME 1. Synthesis of the Triphenylmethane 4a[a]



[a] Reagents and conditions: (i) H_2SO_4, 155 °C; (ii) All-Br, K_2CO_3, acetone, reflux; (iii) H_2, Raney Ni, THF/EtOH; (iv) **8**, NEt_3 (cat), $CHCl_3$.

SCHEME 2. Synthesis of the Triphenylmethane 4b[a]



[a] Reagents and conditions: (i) H_2SO_4, 105 °C; (ii) C_5H_{11}–Br, K_2CO_3, CH_3CN, reflux; (iii) HNO_3, CH_2Cl_2; (iv) H_2, Raney Ni, THF/EtOH; (v) **8**, NEt_3 (cat), $CHCl_3$.

An alternative reaction sequence, exemplified in Scheme 2, allows (alkyl) substituents ortho to the alkoxy groups. The triphenylmethane **10** was obtained by acid-catalyzed condensation in formal analogy to **5**, however, under much milder conditions. Due to the higher nucleophilicity, a complete *O*-alkylation is possible by simple alkylbromides, e.g., pentyl bromide (K_2CO_3, acetonitrile, reflux, 80% of **11**). The subsequent ipso-nitration (82% of **6b**) and reduction (72% of **7b**) followed procedures described for calixarenes.[8] The final *N*-acylation by **8** furnished **4b** in 86% yield.

All compounds were characterized by ^1H and ^{13}C NMR spectra, which reflect their (dynamic) C_{3v} symmetry, and by FD mass spectra. In addition, the structures of **5** and **6a** (Figure S3, Supporting Information) were confirmed by single-crystal X-ray analysis. Both molecules assume a conformation resembling a three bladed propeller with a *syn*-orientation of the oxygen functions (OH, O-allyl) and nitro groups. Angles between least-squares planes through the aromatic rings are 88.9° for **5**, which lies on a 3-fold axis and 84.8, 82.6, and 82.3° for **6a**. Intramolecular distances for oxygen and nitrogen are O···O 4.10

---

(3) Arnaud-Neu, F.; Böhmer, V.; Dozol, J.-F.; Grüttner, C.; Jakobi, R. A.; Kraft, D.; Mauprivez, O.; Rouquette, H.; Schwing-Weill, M.-J.; Simon, N.; Vogt, W. *J. Chem. Soc., Perkin Trans. 2* **1996**, 1175–1182.

(4) Barboso, S.; Carrera, A. G.; Matthews, S. E.; Arnaud-Neu, F.; Böhmer, V.; Dozol, J.-F.; Rouquette, H.; Schwing-Weill, M.-J. *J. Chem. Soc., Perkin Trans. 2* **1999**, 719–723.

(5) Arduini, A.; Böhmer, V.; Delmau, L.; Desreux, J.-F.; Dozol, J.-F.; Carrera, M. A. G.; Lambert, B.; Musigmann, C.; Pochini, A.; Shivanyuk, A.; Ugozzoli, F. *Chem. Eur. J.* **2000**, *6*, 2135–2144.

(6) Peters, M. W.; Werner, E. J.; Scott, M. *Inorg. Chem.* **2002**, *41*, 1707–1716.

(7) Rudzevich, Y.; Rudzevich, V.; Schollmeyer, D.; Thondorf, I.; Böhmer, V. *Org. Lett.* **2005**, *7*, 613–616.

(8) Jakobi, R. A.; Böhmer, V.; Grüttner, C.; Kraft, D.; Vogt, W. *New J. Chem.* **1996**, *20*, 493–498.

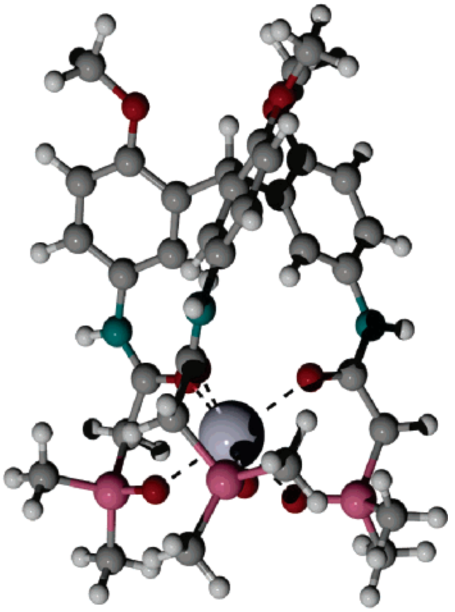


FIGURE 1. Calculated structure of the $Eu^{3+}\cdot$**4** complex.

Å, N···N 6.89 Å for **5** and between O···O 3.61−4.01 Å, N···N 6.60−7.00 Å for **6a**.

Molecular Simulation and Solution Properties. In contrast with their transition-metal analogues, the lanthanide ions have no stereochemical requirements and the conformation of their complexes depends essentially on the ligand properties. No crystal of diffraction quality of the metal trityl-CMPO complexes could be obtained, and it was thus decided to generate structures by quantum mechanics and to study the solution behavior of the complexes by nuclear magnetic resonance techniques. Although a complete encapsulation of the lanthanides by ligand **4a** was expected,[6] the possibility remained that the location of the substituents on the trityl platform was not suitable for complexing these metal ions. Moreover, solid state structures are known in which carbamoylmethylphosphonate units are linked to lanthanide ions either by the two donor groups or only by the P═O function.[6,10,11]

Ab initio QM modeling studies were first undertaken at the HF and DFT levels on the Eu(III) trityl-CMPO, $[Eu\cdot$**4**$]^{3+}$, in which the maximum coordination number (CN) was fixed to six, i.e., less than the common CN of eight or nine. For computing time saving purposes, the $P(Ph)_2$ groups of **4a** were replaced by $P(Me)_2$ moieties. As shown in Figure 1, the metal is coordinated to all the oxygenated binding sites of the ligand and the complex features an approximate 3-fold symmetry. The main Eu−O-optimized distances of the complexes are presented in Table 1.

The DFT results are a priori more accurate as electron correlation effects are somewhat better taken into account. The Eu−O(P) distances are somewhat shorter than the Eu−O(C) ones, indicating a stronger coordination of the more basic phosphine oxide groups as observed by crystallography in the case of a lanthanide CMPO complex.[5] The helical arrangement of ligand **4** around the metal is reflected by gauche O−P−C−C and O−C−C−P torsion angles as reported in Table 1. The $[Eu(H_2O)\cdot$**4**$]^{3+}$ and $[Eu(NO_3)\cdot$**4**$]^{2+}$ complexes with maximum CNs of seven and eight, respectively, were also optimized to assess whether ligand **4** can retain its coordination to Eu^{3+} in the presence of either monodentate (H_2O) or bidentate (nitrate) ligands. The calculations show that the $[Eu\cdot$**4**$]^{3+}$ complex has a high affinity for H_2O and NO_3^- (−17 and −280 kcal/mol, respectively, at the DFT level). The coordination of these groups leads to some weakening and lengthening of the Eu−O bonds (~ 0.05 and 0.1 Å, respectively) but has little influence on the geometry of the ligand. The nitrate ion and the water molecule are located close to the 3-fold axis and the geometry of the trityl unit and of the amide groups remains unchanged. However, the coordination sphere of the Eu^{3+} ion is somewhat flattened (about 0.15 Å) by the NO_3^- and H_2O moieties.

Ligand **4a** is thus firmly coordinated to trivalent lanthanide cations and the arrangement of its substituents is well adapted to forming stable 1:1 inclusion complexes. The encapsulation of paramagnetic lanthanide ions in anhydrous acetonitrile is readily observed by NMR spectroscopy and by nuclear magnetic relaxation dispersion (NMRD). These two techniques were used previously to unravel the properties of various calix[4]-arenes featuring CMPO groups.[12,13] Spectroscopy yields information on the solution structure of a complex because the induced paramagnetic shifts directly depend on simple geometric factors. On the other hand, NMRD allows one to investigate complexation and association processes in solution. Figure 2 presents NMRD titration curves of $Gd(ClO_4)_3$ by a calix[4]arene with four amide groups[12,13] on the narrow rim and by ligands **1**, **4a**, and **4b** in anhydrous acetonitrile. The formation of a complex is accompanied by a decrease in the longitudinal relaxation rate $1/T_1$ of the solvent molecules (relaxivity, in s^{-1} $mmol^{-1}$) when a ligand is added to Gd^{3+} because resonating nuclei are removed from the first coordination sphere of the paramagnetic ions and are thus allowed to relax much more slowly. A linear relaxivity decrease followed by a plateau for a 1:1 metal:ligand concentration ratio is observed for a very stable complex. Figure 2 illustrates the case of a calix[4]arene tetraamide that obviously forms a highly stable 1:1 complex.[12] By contrast, the relaxivity can increase rather than decrease upon addition of a ligand if slowly rotating large polymeric species are formed in solution as already reported for the Gd^{3+} complex with **1**. The relaxivity of Gd^{3+} mixtures with **4a** and **4b** in anhydrous acetonitrile have been measured up to the solubility limit. A plateau is not yet reached in these conditions but the relaxivities are very close to the value obtained for the calix[4]arene tetraamide for which only one acetonitrile molecule is coordinated to the metal

---

(9) Cambridge Crystallographic Data Centre, Cambridge, CB2 1EZ, U.K.

(10) Grüner, B.; Plešek, J.; Báča, J.; Cisařová, I.; Dozol, J. F.; Rouquette, H.; Viñas, C.; Selucký, P.; Rais, J. *New. J. Chem.* **2002**, *26*, 1519−1527.

(11) Caudle, L. J.; Duesler, E. N.; Paine, R. T. *Inorg. Chem.* **1985**, *24*, 4441−4444.

(12) Lambert, B.; Jacques, V.; Shivanyuk, A.; Matthews, S. E.; Tunayr, A.; Baaden, M.; Wipff, G.; Böhmer, V.; Desreux, J. F. *Inorg. Chem.* **2000**, *39*, 2033−2041.

(13) Schmidt, C.; Saadioui, M.; Böhmer, V.; Host, V.; Spirlet, M. R.; Desreux, J. F.; Brisach, F.; Arnaud-Neu, F. Dozol, J.-F. *Org. Biol. Chem.* **2003**, *1*, 4089−4096.

TABLE 1. Main Characteristics of Ln^{3+} Complexes[a] with CMPO Derivatives Obtained from QM Calculations (Top) and Retrieved in the Crystallographic Structural Database[9]

QM optimized structures	CN	method	$Eu-O_P$	$Eu-O_C$	$Eu-O_{wat}$	$Eu-O_{nit}$	φ_1	φ_2
$Eu^{3+}\cdot$**4**	6	HF	2.33	2.40	-	-	30	44
$Eu^{3+}\cdot$**4**	6	DFT	2.32	2.36	-	-	39	39
$Eu(H_2O)^{3+}\cdot$**4**	7	HF	2.38	2.45	2.52	-	45	49
$Eu(H_2O)^{3+}\cdot$**4**	7	DFT	2.39	2.39	2.54	-	50	45
$Eu(NO_3)^{2+}\cdot$**4**	8	HF	2.42	2.51	-	2.49	61	42
$Eu(NO_3)^{2+}\cdot$**4**	8	DFT	2.41	2.47	-	2.46	63	41
X-ray structures[6,10,11]	CN	"REFCODE"	$Ln-O_P$	$Ln-O_C$	$Ln-O_{wat}$	$Ln-O_{nit}$	φ_1	φ_2
$Nd(NO_3)^{2+}\cdot$**3** [6]	8	XILKAE A	2.42	2.39	-	2.54	60	41
$Nd(NO_3)^{2+}(H_2O)\cdot$**1** [6]	9	XILKAE B	2.43	2.47	2.52	2.62	51	44
$La(H_2O)_3^{3+}\cdot$CMPO-dicarbolide$_3$[10]	9	MUMDED	2.49	2.52	2.58	-	39	46
$Nd(NO_3)_3\cdot CMPO_2$[11]	10	DODVAT	2.46	2.49	-	2.60	63	44

[a] Eu−O distances (in Å) and torsional angles (in deg) φ_1 (O−P−C−C) and φ_2 (O−C−C−P) are averaged over the different CMPOs.

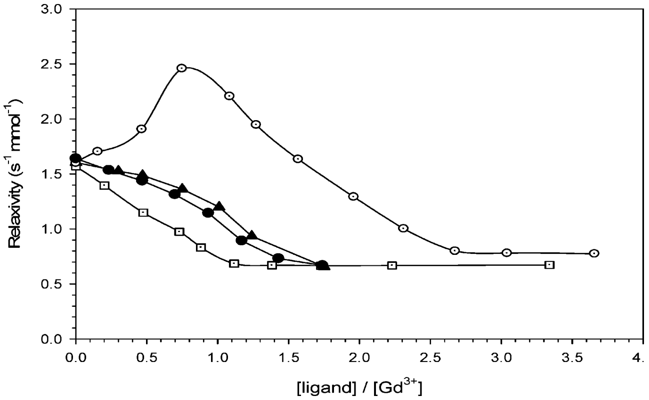


FIGURE 2. Nuclear magnetic relaxation dispersion titration curves. $Gd(ClO_4)_3$ in anhydrous acetonitrile titrated with ⊙: **1**,[12] ▲: **4a**, ●: **4b**, ⊡: 5,11,17,23-Tetra-*tert*-butyl-25,26,27,28-tetrakis(*N*,*N*-diethylaminocarbonyl) methoxycalix[4]arene[12]

ion.[12,14] No quantitative interpretation of the relaxivity titration curves of **4a** and **4b** could be made on the basis of a simple 1:1 equilibrium even if the relaxivity of the complex was included in the fit in addition to the stability constant. A 1:1 complex is most probably formed but other species are certainly present in solution. The same conclusion was reached with calix[4]arene featuring CMPO groups on the wide rim.[12]

Paramagnetic lanthanide complexes of 3-fold symmetry such as those presumably formed by ligands **4a** and **4b** are particularly interesting because their solution structure can be directly deduced from the simplest form of the dipolar equation

$$\delta_i = D\left\langle \frac{3\cos^2\theta_i - 1}{r_i^{\,3}} \right\rangle \tag{1}$$

that links the induced paramagnetic shift δ_i to the polar coordinates θ_i and r_i of nucleus i relative to the C_3 axis and to a magnetic susceptibility factor D which is identical for all nuclei in a complex. However, this equation is only valid if a single rigid species exists in solution.[12] NMRD indicates that this condition is not fulfilled and only qualitative information can then be obtained from spectra that result from rapid dynamic equilibria between different forms. The NMR spectrum of $[Yb\cdot$**4a**$]^{3+}$ as a perchlorate salt in anhydrous acetonitrile at room temperature features relatively narrow peaks that cover about 35 ppm with paramagnetic shifts both toward high and low fields (see the Supporting Information). All resonances become exceedingly broad when the temperature is decreased down to the freezing point of the solvent. A complete assignment of the resonances observed at room temperature is limited by the inability to resolve closely overlapped peaks between 0 and 5 ppm. However, there are a few well-resolved resonances between 7 and 12 ppm and at −4 ppm. Moreover, one resonance at −20 ppm and of relative area one is much more shifted than all other peaks and stands out for special notice. The polar coordinates of each proton have been deduced from the structure reported in Figure 1 for the $Eu^{3+}\cdot$**4a** complex and a linear fit between the paramagnetic shifts and the geometric factors yielded the magnetic susceptibility term D (see the Supporting Information). These calculations showed that the aromatic proton in ortho position relative to the central methine group resonates at −20 ppm while all other protons give rise to peaks between −2 and 12 ppm in keeping with the observed spectrum. It is thus concluded that the monomeric 1:1 $[Yb\cdot$**4a**$]^{3+}$ complex is probably the main solution species but a more detailed analysis appears difficult.

Extraction Data. The reprocessing of nuclear wastes is currently performed by extracting selectively metal ions from concentrated HNO_3 aqueous solutions (1−3 M). (Diisobutylcarbamoyl)methyloctylphenylphosphine oxide (CMPO) is a relatively ineffective extractant and does not allow an easy separation of Am(III) from Eu(III).[15] Much higher distribution coefficients of the trivalent lanthanides and actinides and much better Am(III)/Eu(III) separation factors (about 10) are obtained if four CMPO units are grafted on the wide rim of calix[4]arene, **1**, as shown in Figure 3. Extraction studies were performed in hope that the trityl derivatives **4a** and **4b** would feature the same interesting properties. Figure 3 presents the acid dependency of the extraction coefficients of Am(III) and Eu(III) by **4a** in dichloromethane. Very similar results were obtained in the case of **4b**. In contrast

---

[14] Lambert, B.; Jacques, V.; Desreux, J. F. *Adv. Chem. Ser.* **2000**, *757*, 165−178.

[15] Delmau, L. H.; Simon, N.; Schwing-Weill, M. J.; Arnaud-Neu, F.; Dozol, J. F.; Eymard, S.; Tournois, B.; Böhmer, V.; Grüttner, C.; Musigmann, C.; Tunayar, A. *J. Chem. Soc., Chem Commun.* **1998**, 1627−1628.

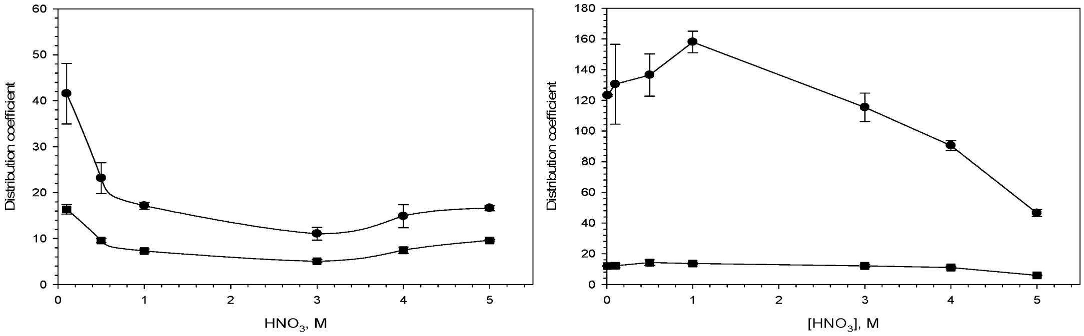


FIGURE 3. Acid dependency of the extraction coefficients of Am^{3+} and Eu^{3+}. Left: extraction by tripodal ligand **4a**; right: extraction by tetrapodal ligand **1** (●: Am^{3+}; ■: Eu^{3+}).

with calix[4]arene **1**, the extraction efficiency of trityl **4a** drastically decreases when nitric acid is added to a 4 M $NaNO_3$ aqueous phase and it slightly increases at high acidities. A selectivity D_{Am}/D_{Eu} of about 2 is observed over the whole range of nitric acid concentrations.

The trivalent *f* elements are extracted as neutral adducts between the trinitrate salts and the ligand.[16] As observed with many CMPO derivatives, the extraction coefficients of **1** increase up to 1 M HNO_3 because the larger concentration of nitrate ions favors the formation of adducts. At higher acidities, the competition between the protons and the metal ions for the complexation sites brings about a decrease in extraction. The position of the extraction maximum depends essentially on the basicity of the phosphine oxide groups.[16]

The extraction of acid by 1 mM solutions of **1** and **4a** in dichloromethane was analyzed by titrating the organic phases after equilibration with equal volumes of 2 M HNO_3/4 M $NaNO_3$ aqueous phases. Under these conditions, the organic phases containing **1** and **4a** were, respectively, 1.41 and 1.11 mM in HNO_3. Furthermore, the addition of $NaNO_3$ to a 0.1 M HNO_3 aqueous phase only brings about a regular increase of the distribution coefficients of Eu(III) and Am(III) (for a 1 mM dichloromethane solution of **4a** from 0.03 and 0.07 to 110 and 190 respectively when the concentration of $NaNO_3$ is increased to 5 M). The same tendency is observed with all CMPO-containing compounds and **4a** is not different in this respect.

The extracted amount of nitric acid reported above corresponds to a protonation of 35−37% of the CMPO functions for both compounds **1** as well as **4a**. The dramatic decrease of the distribution coefficients in the latter case may be understood therefore, assuming that all three ligating CMPO arms are necessary for the complexation of a metal cation in the case of **4a** in addition to nitrate ions. All four CMPO functions of **1** are not necessarily required in the first coordination sphere of the extracted metal ions as shown by the solid-state structure of $La_2(NO_3)_6 \cdot \mathbf{1}_2$[17] and by NMR studies.[12] This would mean that the "better preorganization" intended by the design of **4** is disadvantegous under the envisaged extraction conditions. It is noteworthy in this connection that **4a** readily and reversibly picks up water from the atmosphere whether as a solid or dissolved in an organic solvent.

Conclusions

Since their extraction results are sensitive to acidity, extractants **4a** and **4b** are of little practical interest. However, these ligands illustrate the difficulties encountered when designing a priori ligands featuring scaffolds that seem particularly well suited for extracting metal ions. Ligand **1** with eight donor groups appears ideal for the complexation of lanthanide ions that are well-known to favor large coordination numbers. This ligand is indeed a very effective extracting agent of the *f* elements but its solution behavior is not as simple as anticipated[5,12] and the origin of its selectivity remains uncertain. The trityl-CMPO ligands **4a** and **4b** also appeared as interesting extracting agents before they were synthesized but their sensitivity to acidity turned out to be detrimental. At first glance, extraction processes seem very simple but they are in fact quite complex as they depend on a number of poorly defined parameters. According to small angle neutron diffraction studies, CMPO and extracted lanthanide complexes form large elongated polymers of 17−40 Å in diameter and up to 500 Å long, the size of which decreases if an excess of ligands is added.[18] What happens with grafted CMPOs remains to be investigated.

The assembly of several ligating functions on a common platform and the rigidifying effect of cyclic structures often leads to improved efficiencies as demonstrated many times by calixarene derived ligands. However, because of the complex nature of the extraction process selecting and developing new extractants still remains essentially a trial and error process, as shown by the present results.

Experimental Section

Tris(2-hydroxy-5-nitrophenyl)methane (5). A mixture of 5-nitrosalicylaldehyde (5.20 g, 0.031 mol) and *p*-nitrophenol (26.0 g, 0.187 mol) was stirred with a mechanical stirrer at 110 °C under nitrogen until a homogeneous dark yellow melt was formed. After that, sulfuric acid (4 mL) was added, the temperature was increased to 155 °C, and stirring of the dark brown viscous mass was continued for 2 h. To remove the excess of *p*-nitrophenol the reaction mixture was extracted first with hot water (3 × 150 mL). The remaining dark-brown

---

(16) Horwitz, E. P.; Martin, K. A.; Diamond, H.; Kaplan, L. *Solvent Extr. Ion Exch.* **1986**, *4*, 449−494.

(17) Cherfa, S. Ph.D. Thesis, University of Paris, 1998.

(18) Diamond, H.; Thiyagarajan, P.; Horwitz, E. P. *Solvent Extr. Ion Exch.* **1990**, *8*, 503−513.

powder was dissolved in 5% aqueous sodium hydroxide (300 mL), and an insoluble black solid was filtered off. The yellow brown solution was added dropwise with stirring to 3.5% aqueous hydrochloric acid (700 mL). The precipitate was filtered off and dried at 140 °C on the air to give compound **5** (11.9 g, 89%) as a brown powder. Crystals suitable for X-ray diffraction were obtained by crystallization from acetone: mp 310−320 °C dec; ^{1}H NMR (400 MHz, DMSO-d_6) δ 6.16 (s, 1H), 7.04 (d, 3H, $^3J_{HH}$ = 9 Hz), 7.53 (d, 3H, $^4J_{HH}$ = 3 Hz), 8.12 (d × d, 3H, $^3J_{HH}$ = 9 Hz, $^4J_{HH}$ = 3 Hz); ^{13}C{^{1}H} NMR (100.6 MHz, DMSO-d_6) δ 37.8 (s), 115.5 (s), 124.5 (s), 124.9 (s), 128.7 (s), 139.4 (s), 161.5 (s); MS (FD) *m/z* 427.6 (100) [M$^+$] (calcd 427.33).

Tris(2-allyloxy-5-nitrophenyl)methane (6a). Potassium carbonate (1.94 g, 14.0 mmol) and allyl bromide (2.26 g, 18.7 mmol) were added to a solution of compound **5** (1.0 g, 2.3 mmol) in acetone (10 mL) under nitrogen. The reaction mixture was stirred at 65 °C for 2 days. The precipitate was filtered off. Acetone and the excess allyl bromide were removed under reduced pressure. The residue was dissolved in chloroform and washed with 5% aqueous potassium carbonate and water. The organic layer was separated, dried ($MgSO_4$), and evaporated to yield compound **6a** (1.18 g, 92%) as a brown powder. Crystals suitable for X-ray diffraction were obtained by crystallization from acetone: mp 164−165 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.56 (m, 6H), 5.18 (m, 6H), 5.77 (m, 3H), 6.39 (s, 1H), 6.94 (d, 3H, $^3J_{HH}$ = 9 Hz), 7.73 (d, 3H, $^4J_{HH}$ = 3 Hz), 8.20 (d × d, 3H, $^3J_{HH}$ = 9 Hz, $^4J_{HH}$ = 3 Hz); ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$) δ 39.6 (s), 69.4 (s), 111.6 (s), 117.9 (s), 125.1 (s), 125.3 (s), 130.4 (s), 131.4 (s), 141.4 (s), 160.8 (s); MS (FD) *m/z* 547.9 (100) [M$^+$] (calcd 547.53).

Tris(2-propoxy-5-aminophenyl)methane (7a). Compound **6a** (1.10 g, 2.0 mmol) was dissolved in a mixture of THF (30 mL) and ethanol (25 mL) and hydrogenated for 24 h at room temperature in the presence of the Raney nickel. The catalyst was filtered off and washed with THF, and the combined organic layers were evaporated under reduced pressure. The pure product **7a** (0.35 g, 38%) was isolated by column chromatography (THF/hexane 3:2) as a brown powder: mp = 182−184 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.83 (t, 9H, $^3J_{HH}$ = 7 Hz), 1.57 (m, 6H), 3.11 (br s, 6H), 3.68 (t, 6H, $^3J_{HH}$ = 7 Hz), 6.22 (d, 3H, $^4J_{HH}$ = 2.8 Hz), 6.39 (d × d, 3H, $^3J_{HH}$ = 9 Hz, $^4J_{HH}$ = 2.8 Hz), 6.41 (s, 1H), 6.61 (d, $^3J_{HH}$ = 9 Hz); ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$) δ 10.4 (s), 22.8 (s), 36.9 (s), 70.7 (s), 113.0 (s), 113.6 (s), 117.7 (s), 134.5 (s), 139.2 (s), 150.1 (s); MS (FD) *m/z* 463.8 (100) [M$^+$] (calcd 463.63).

Tris(2-propoxy-5-diphenylphosphorylacetamidophenyl)methane (4a). Triethylamine (0.4 mL) was added to a solution of *p*-nitrophenyl (diphenylphosphoryl)acetate[3] (0.98 g, 2.57 mmol) and amino compound **7a** (0.34 g, 0.73 mmol) in chloroform (10 mL), and the reaction mixture was stirred for 12 h at room temperature. After the addition of chloroform (10 mL), the organic solution was washed with 10% aqueous potassium carbonate and water. After drying ($MgSO_4$), the chloroform was removed under reduced pressure and the residue was precipitated from chloroform by diethyl ether to give compound **4a** (0.74 g, 85%) as a light brown powder. The product obtained as described contains three molecules of water per molecule of **4a** (according to the ^{1}H NMR) which can be removed by drying in a vacuum (0.1 mm/Hg) at 110 °C. ^{1}H NMR investigations in $CDCl_3$ show broad signals due to weak association: mp = 146−150 °C; ^{1}H NMR (400 MHz, THF-d_8) δ 0.75 (t, 9H, $^3J_{HH}$ = 7 Hz), 1.47 (m, 6H), 3.41 (d, 6H, $^2J_{PH}$ = 14 Hz), 3.65 (t, 6H, $^3J_{HH}$ = 6 Hz), 6.43 (s, 1H), 6.50 (br s, 3H), 6.62 (d, 3H, $^3J_{HH}$ = 9 Hz), 7.39 (m, 18H), 7.73 (br d, 3H, $^3J_{HH}$ = 9 Hz), 7.82 (m, 12H), 9.34 (s, 3H); ^{13}C{^{1}H} NMR (100.6 MHz, THF-d_8) δ 10.8 (s), 23.6 (s), 38.0 (s), 41.0 (d, $^1J_{PC}$ = 61.5 Hz), 70.5 (s), 112.1 (s), 119.4 (s), 121.9 (s), 129.1 (d, $^2J_{PC}$ = 12.3 Hz), 132.0 (d, $^3J_{PC}$ = 9.8 Hz), 132.2 (d, $^4J_{PC}$ = 1.9 Hz), 132.9 (s), 133.8 (s), 134.8 (d, $^1J_{PC}$ = 100.9 Hz), 154.0 (s), 163.3 (d, $^2J_{PC}$ = 5 Hz); ^{31}P{^{1}H} NMR (162 MHz, THF-d_8) δ 26.2 (s); MS (FD) *m/z* 1191.1 (73) [M$^+$], 948.6 (100) [{M − $Ph_2P(O)CH_2C(O)$}$^+$] (calcd 1190.27); MS (ESI-TOF) *m/z* calcd for $C_{70}H_{70}N_3NaO_9P_3$ 1212.4217 (M + Na)$^+$, found 1212.4196.

5-*tert*-Butyl-2-hydroxy-3-methylbenzaldehyde (9). A mixture containing 4-*tert*-butyl-2-methylphenol (50 g, 0.304 mol), hexamethylenetetramine (HTM) (85.4 g, 0.609 mol), and acetic acid (150 mL) was stirred at 130 °C for 3 h under nitrogen. After cooling to 70 °C, aqueous sulfuric acid (33%, 150 mL) was added, and stirring was continued at 100 °C for 1 h. The resulting mixture was finally extracted with diethyl ether (5 × 80 mL), and the extract was washed with water (5 × 80 mL) and dried ($MgSO_4$). The solvent was removed under reduced pressure to yield a dark yellow oil still containing acetic acid. The crude product was purified by column chromatography (chloroform) to yield **9** (30.0 g, 51%) as a yellow oil which slowly crystallized: mp = 43−45 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.32 (s, 9H), 2.27 (s, 3H), 7.35 (d, 1H, $^4J_{HH}$ = 2.4 Hz), 7.44 (d, 1H, $^4J_{HH}$ = 2.4 Hz), 9.86 (s, 1H), 11.11 (s, 1H); ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$) δ 15.3 (s), 31.3 (s), 34.0 (s), 119.4 (s), 126.2 (s), 127.3 (s), 135.7 (s), 142.2 (s), 157.9 (s), 196.9 (s); MS (FD) *m/z* 192.4 (100) [M$^+$] (calcd 192.26).

Tris(5-*tert*-butyl-2-hydroxy-3-methylphenyl)methane (10). A mixture of **9** (10.0 g, 0.052 mol) and 4-*tert*-butyl-2-methylphenol (25.6 g, 0.156 mol) was stirred at 105 °C under nitrogen until a homogeneous melt was formed. Sulfuric acid (0.5 mL) was added, and stirring of the dark-red viscous mass was continued for 2 h. The cooled reaction mixture was treated with methanol (160 mL), and the precipitate formed was filtered off and dried on the air to give compound **10** (23.5 g, 90%) as a white powder: mp 335−340 °C dec; ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.10 (s, 27H), 2.13 (s, 9H), 6.62 (s, 1H), 6.73 (d, 3H, $^4J_{HH}$ = 2.4 Hz), 6.87 (d, 3H, $^4J_{HH}$ = 2.4 Hz), 7.83 (s, 3H); ^{13}C{^{1}H} NMR (100.6 MHz, DMSO-d_6) δ 17.0 (s), 31.2 (s), 33.4 (s), 35.9 (s), 123.1 (s), 124.4 (s), 124.5 (s), 130.5 (s), 139.9 (s), 149.9 (s); MS (FD) *m/z* 503.3 (100) [M$^+$] (calcd 502.74).

Tris(5-*tert*-butyl-2-pentoxy-3-methylphenyl)methane (11). Potassium carbonate (11.6 g, 0.084 mol) and 1-bromopentane (16.8 g, 0.111 mol) were added under nitrogen to a solution of compound **10** (7.0 g, 0.014 mol) in acetonitrile (200 mL). The reaction mixture was stirred at 90 °C for 6 days. After the mixture was diluted with chloroform (200 mL), the potassium salts were filtered off and the solvents were removed under reduced pressure. Crystallization of the yellow residue from chloroform/methanol gave compound **11** (7.96 g, 80%) as white crystals: mp 90−92 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.88 (t, 9H, $^3J_{HH}$ = 7 Hz), 1.15 (s, 27H), 1.28 (m, 12H), 1.66 (m, 6H), 2.22 (s, 9H), 3.40 (t, 6H, $^3J_{HH}$ = 7 Hz), 6.63 (s, 1H), 6.84 (d, 3H, $^4J_{HH}$ = 2.4 Hz), 6.95 (d, 3H, $^4J_{HH}$ = 2.4 Hz); ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$) δ 14.1 (s), 16.8 (s), 22.7 (s), 28.2 (s), 29.9 (s), 31.4 (s), 34.1 (s), 37.5 (s), 72.4 (s), 125.4 (s), 125.8 (s), 129.7 (s), 136.7 (s), 144.8 (s), 153.4 (s); MS (FD) *m/z* 713.8 (100) [M$^+$] (calcd 713.15).

Tris(5-nitro-2-pentoxy-3-methylphenyl)methane (6b). Nitric acid (8 mL) was slowly added to a solution of compound **11** (4.2 g, 5.9 mmol) in methylene chloride (100 mL) and acetic acid (12 mL). After being stirred for 2 h, the reaction mixture was washed with water and dried ($MgSO_4$), and the solvents were removed under reduced pressure. Crystallization of the yellow residue from chloroform/methanol gave compound **6b** (3.30 g, 82%) as beige crystals: mp 167−169 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.87 (t, 9H, $^3J_{HH}$ = 6.6 Hz), 1.25 (m, 12H), 1.57 (m, 6H), 2.36 (s, 9H), 3.49 (t, 6H, $^3J_{HH}$ = 6.6 Hz), 6.64 (s, 1H), 7.57 (d, 3H, $^4J_{HH}$ = 2.8 Hz), 8.05 (d, 3H, $^4J_{HH}$ = 2.8 Hz); ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$) δ 14.0 (s), 17.1 (s), 22.5 (s), 27.9 (s), 29.7 (s), 38.7 (s), 73.3 (s), 122.8 (s), 126.4 (s), 133.0 (s), 136.9 (s), 143.4 (s), 161.1 (s); MS (FD) *m/z* 680.7 (100) [M$^+$] (calcd 679.82).

Tris(5-amino-2-pentoxy-3-methylphenyl)methane (7b). Compound **7b** was prepared as described for **7a**. The pure product **7b** (72%) was isolated by column chromatography (ethyl acetate/hexane 1:1) as a brown powder: mp = 207−

210 °C; ^{1}H NMR (400 MHz, CDCl$_3$) δ 0.87 (t, 9H, $^3J_{HH} = 6.6$ Hz), 1.27 (m, 12H), 1.62 (m, 6H), 2.14 (s, 9H), 3.21 (br s, 6H), 3.38 (t, 6H, $^3J_{HH} = 6.6$ Hz), 6.17 (d, 3H, $^4J_{HH} = 2.8$ Hz), 6.31 (d, 3H, $^4J_{HH} = 2.8$ Hz), 6.42 (s, 1H); ^{13}C{^{1}H} NMR (100.6 MHz, CDCl$_3$) δ 14.1 (s), 16.5 (s), 22.7 (s), 28.2 (s), 29.9 (s), 37.6 (s), 72.6 (s), 115.4 (s), 115.7 (s), 131.6 (s), 138.5 (s), 141.1 (s), 148.6 (s); MS (FD) *m/z* 590.4 (100) [M$^+$] (calcd 589.87).

Tris(5-diphenylphosphorylacetamido-2-pentoxy-3-methylphenyl)methane (4b). Compound **4b** was synthesized as described for **4a** and isolated as a light brown powder with 86% yield: mp = 160−164 °C; ^{1}H NMR (400 MHz, CDCl$_3$) δ 0.85 (t, 9H, $^3J_{HH} = 6.6$ Hz), 1.24 (m, 12H), 1.58 (m, 6H), 2.02 (br s, 9H), 3.15−3.35 (br m, 12H), 6.58 (s, 1H), 6.63 (br s, 3H), 7.30−7.45 (m, 18H), 7.68 (m, 12H); ^{13}C{^{1}H} NMR (100.6 MHz, CDCl$_3$) δ 14.0 (s), 16.5 (s), 22.6 (s), 28.1 (s), 29.8 (s), 36.6 (s), 39.9 (d, $^1J_{PC} = 61.4$ Hz), 72.6 (s), 120.2 (s), 122.2 (br s), 128.6 (d, $^2J_{PC} = 12.2$ Hz), 130.9 (d, $^3J_{PC} = 9.5$ Hz), 131.6 (s), 131.8 (d, $^1J_{PC} = 101.9$ Hz), 132.3 (s), 132.8 (s), 137.4 (s), 152.5 (s), 163.0 (br s); ^{31}P{^{1}H} NMR (162 MHz, CDCl$_3$) δ 29.5 (br s); MS (FD) *m/z* 1319.4 (3) [M + 3H$^+$], 1075.5 (100) [M − Ph$_2$P(O)CH$_2$C(O) + H$^+$], 833.0 [M − 2{Ph$_2$P(O)CH$_2$C(O)} + H$^+$] (calcd 1316.52); MS (ESI-TOF) *m/z* calcd for $C_{79}H_{88}N_3NaO_9P_3$ 1338.5626 (M + Na)$^+$, found 1338.5593.

Single-Crystal X-ray Diffraction. All intensity data were collected on a Enraf Nonius CAD4 diffractometer with Cu Kα radiation (graphite monochromator) at −80 °C (**5**) or at room temperature (**6a**). The structures were solved using SIR92[19] and refined with SHELX97.[20] All non-hydrogen atoms were refined anisotropically with C−H hydrogen atoms generated at idealized positions and refined as riding atoms with individual isotropic displacement parameters. The refinement converged at $R_1 = 0.071$ for **5** and $R_1 = 0.055$ for **6a**. The position of the second disordered solvent molecule in crystals of **5** could not be clarified.

Extraction Studies. Aqueous solutions containing the $^{152-154}$Eu and ^{241}Am nuclides in tracer amounts were equilibrated at 25 °C with equal volumes of dichloromethane solutions of ligands **1**, **4a**, and **4b**. After phase separation, the activities of the aqueous and organic solutions were determined with a Canberra Genie 2000 γ spectroscopy system. All extraction experiments were performed in triplicate.

Nuclear Magnetic Resonance Studies. The NMR spectra were recorded under the conditions reported elsewhere.[12] Relaxivities $1/T_1$ were measured between 0.01 and 80 MHz with a relaxometer equipped with a 2 T permanent magnet. Anhydrous Yb(ClO$_4$)$_3$ was prepared as reported previously.[12] CAUTION: lanthanide perchlorates are potentially explosive when brought into contact with organic materials. It is highly advisable to use only small quantities of metal salts with proper care. All materials were handled under argon in a glovebox.

Methods/Quantum Mechanics (QM) Calculations. The metal complexes were optimized without symmetry constraints by quantum mechanical calculations at the Hartree−Fock (HF) and DFT (B3LYP functional) levels of theory, using Gaussian98 software.[21] As *f*-orbitals do not play a major role in the studied metal−ligand bonds,[22] the 46 core and 4*f* electrons of europium were described by quasi-relativistic effective core potentials (ECP) of the Stuttgart group, enhanced by an additional single *f*-function with an exponent of 0.591.[23,24] For the valence orbitals, the affiliated (7s6p5d)/[5s4p3d] basis set was used, enhanced by an additional single *f*-function. For the ligands we used the 6-31G* basis set.

Acknowledgment. Financial support by the European Commission (Contracts No. FIKW-CT-2000-00088 and No. FI6W-CT-2003-508854) and by the Deutsche Forschungsgemeinschaft (SFB 625) are gratefully acknowledged. R.D. and G.W. thank the CNRS IDRIS and CINES for allocation of computing time. J.F.D. and D.B. acknowledge the financial support of the Institut Interuniversitaire des Sciences nucléaires of Belgium.

Supporting Information Available: General experimental procedures; ^{1}H NMR spectrum of Yb(ClO$_4$)$_3$·**4a** in anhydrous acetonitrile; correlation between the calculated and the experimental paramagnetic shifts; crystallographic data for compounds **5** (CCDC 268244) and **6a** (CCDC 268245); Cartesian coordinates optimized by HF and DFT calculations; selected ^{1}H and ^{13}C NMR spectra of newly synthesized compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

JO050717A

---

[19] Altomare, A.; Cascarano, G.; Giacovazzo, C.; Guagliardi. A.; Burla, M. C.; Polidori, G.; Camalli, M. *J. Appl. Crystallogr*. **1994**, *27*, 435−436.

[20] (a) Sheldrick, G. M. SHELXS97. Program for the Crystal Structure Solution. University of Göttingen, Germany, 1997. (b) Sheldrick, G. M. SHELXS97. Program for the Crystal Structure Refinement. University of Göttingen, Germany, 1997.

[21] Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Zakrzewski, V. G.; Montgomery, J. A., Jr.; Stratmann, R. E.; Burant, J. C.; Dapprich, S.; Millam, J. M.; Daniels, A. D.; Kudin, K. N.; Strain, M. C.; Farkas, O.; Tomasi, J.; Barone, V.; Cossi, M.; Cammi, R.; Mennucci, B.; Pomelli, C.; Adamo, C.; Clifford, S.; Ochterski, J.; Petersson, G. A.; Ayala, P. Y.; Cui, Q.; Morokuma, K.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Cioslowski, J.; Ortiz, J. V.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Gonzalez, C.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Andres, J. L. Gonzalez, C.; Head-Gordon, M.; Replogle, E. S.; Pople, J. A. Gaussian 98, Revision A.5 ed.; Gaussian, Inc.: Pittsburgh, PA, 1998.

[22] Maron, L.; Eisenstein, O. *J. Phys. Chem. A* **2000**, *104,* 7140−7143.

[23] Dolg, M.; Stoll, H.; Savin, A.; Preuss, H. *Theor. Chim. Acta* **1989**, *75,* 173−194.

[24] Dolg, M.; Stoll, H.; Savin, A.; Preuss, H. *Theor. Chim. Acta* **1993**, *85,* 441−450.