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Modification of calix[4]arenes with CMPO-functions at the wide rim. Synthesis, solution behavior, and separation of actinides from lanthanides

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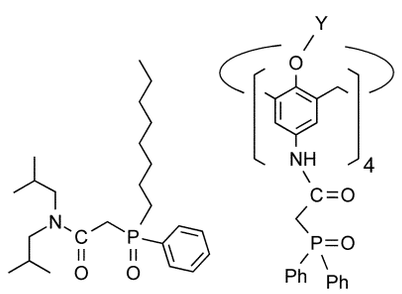
Two calix[4]arene tetraethers (Y = C_5H_{11}, $C_{14}H_{29}$) bearing on their wide rim four –N(Me)–CO–CH_2–P(O)Ph_2 residues were synthesized for the first time. Their ability to extract lanthanides and actinides from an acidic aqueous phase to organic phases (CH_2Cl_2, NPHE) was studied. In comparison to the corresponding –NH-analogs, they are less efficient extractants, the selectivity for the light over the heavy lanthanides is less pronounced, while there is still an interesting selectivity of Am^{3+} over Eu^{3+}. Stability constants for selected lanthanide salts were determined also in homogenous phase (methanol, acetonitrile) but do not account for the different extraction results. The complexation of Gd^{3+} was also followed by relaxivity (NMRD) measurements, which suggest an even stronger aggregation for the *N*-methyl compound while the 1 : 1 complex is reached for a smaller ratio [L]/[Gd^{3+}] compared to the NH analog. The formation of aggregates is also supported by dynamic light scattering measurements. A single crystal X-ray structure of the pentyl ether reveals a C_2-symmetrical pinched cone conformation for the free ligand.

Introduction

Carbamoylmethylphosphine oxides (CMPOs) are well known to extract actinides and lanthanides from a strongly acidic aqueous phase to an organic phase.[1] Among numerous examples studied[2] the *N*,*N*′-diisobutylcarbamoyl(octyl)phenylphosphine oxide **1** has been selected as extractant for an industrial application, the so-called "TRUEX"-process.[3] Since it has been found that three molecules of **1** are involved in the complex formed with the trivalent actinide cations, it was reasonable to attach several CMPO groups to a common scaffold. We chose for this purpose the easily available calix[4]arene skeleton, fixed in the cone conformation. The ligating CMPO functions were bound directly to the wide rim *via* the amide nitrogen (**2**)[4,5] or to the narrow rim using appropriate spacers of two to four carbon atoms (**3**)[6,7] All compounds of types **2** and **3** show a drastically improved extraction efficiency in comparison to **1** which gives lower distribution coefficients *D* even at a 100-fold higher concentration. In addition, the wide rim tetra-CMPO derivatives **2** show a pronounced selectivity within the lanthanide series (*D*(La) is nearly three orders of magnitude higher than *D*(Yb)) and a remarkable extraction selectivity of Am(III) over Eu(III) (*D*(Am)/*D*(Eu) ≈ 10) in strongly acidic medium.[8]

In contrast to the standard CMPO, **1**, and to (nearly) all the variations of its structure studied so far,[2] **2** and **3** are secondary amides. We therefore were interested to study the properties of calix[4]arenes bearing on their wide rim tertiary amide functions of the CMPO-type. One could indeed argue that the extraction efficiency of such compounds could be further increased since the complexation of a cation would not have to compete with intramolecular hydrogen bonds –C(O)–N–H ··· O=P–Ph_2 that form six-membered rings within each CMPO arm in compounds **2** and **3**.[9] We report here the synthesis and the first results obtained with wide rim CMPOs of type **4**.



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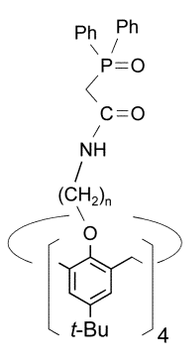

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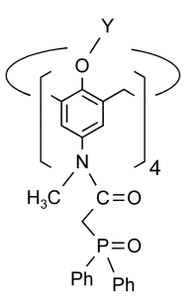

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a: Y=C_5H_{11}
b: Y=$C_{14}H_{29}$

Results and discussion

Synthesis

The preparation of compounds **2** and **3** starts with tetraamines such as **5** which are acylated in the last step of the synthesis by

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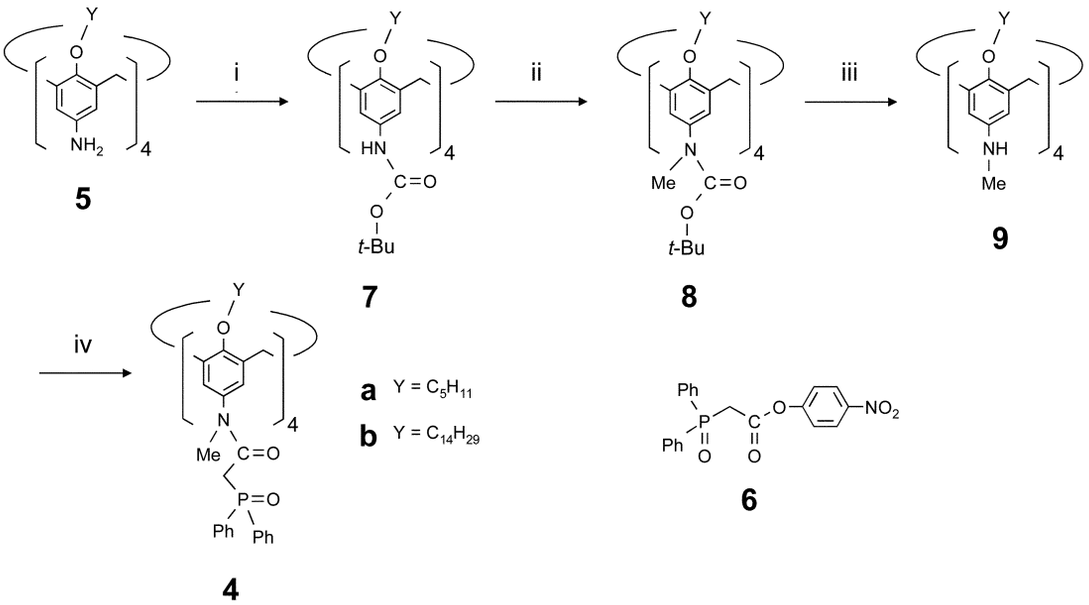
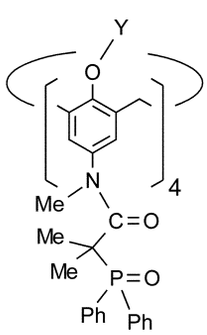


Scheme 1 *Reagents*: i, $(Boc)_2O$; ii, MeI; iii, TFA; iv, **6**.

the active ester **6**. Surprisingly, all attempts to prepare secondary amines from the primary amines **5** *via* acylation and reduction (*e.g.* by $LiAlH_4$) have failed. It is not quite clear if this is somehow due to the calix[4]arene structure. Acetamides derived from **5**, however, could be *N*-alkylated by methyl iodide or decyl bromide under phase transfer conditions,[10] but these tertiary acetamides could not be hydrolysed to the corresponding secondary amines. These observations finally led to the reaction sequence outlined in Scheme 1.

Tetraamine **5** is completely acylated with Boc anhydride (**7**, 86%)[11] and subsequently *N*-methylated with methyl iodide (**8**, 67%).[12] Cleavage of the Boc-protective groups was easily achieved under the usual conditions (**9**, 87%) and the final acylation by **6** was also possible in high yield (**4**, 86%).[13]

We also attempted the direct *N*-methylation of tetra-CMPOs **2** under the conditions used for the tetra-Boc derivative **7**. However, since *C*-alkylation of the C(O)–CH_2–P(O) groups occurred simultaneously, the exhaustively methylated compound **10** was the only product which could be obtained in pure form, using an excess of methyl iodide.



10 $Y = C_5H_{11}$

While the reductive amination with formaldehyde failed, tetra-azomethines **11** could be obtained by reaction with *p*-methylbenzaldehyde and reduced to the corresponding secondary amines **12**. However, a complete acylation by **6** was not possible. The reaction product obtained was characterized as tri-CMPO derivative **13** (Scheme 2).

Single crystal X-ray structure of 4a

In the solid state, compound **4a** adopts a pinched cone conformation of C_2 symmetry.

Table 1 Distribution coefficients for the extraction of different cations (c(Ln) = 10^{-5} M; c(Am) at trace level) from aqueous HNO_3 to NPHE by calixarenes **4a** and **2a** (c_L = 10^{-3} M)

Ligand/$c(HNO_3)$	La^{3+}	Ce^{3+}	Nd^{3+}	Sm^{3+}	Eu^{3+}	Am^{3+}
4a/3 M HNO_3	2.1	1.8	0.72	0.21	0.14	0.87
4a/4 M HNO_3	6.3	5.6	2.4	0.74	0.41	2.95
2a/3 M HNO_3[a]	145		135	60	45	156

[a] Values taken from ref. 6.

As shown in Fig. 1, two distal aromatic rings of the calixarene are nearly parallel to each other while the two other rings are tilted outwards. The dihedral angles between these rings (5.0° and 114.3° respectively) fall within the range of angles previously reported for similar calix[4]arene structures.[14] The amido methyl groups on the parallel aromatic rings are oriented towards the calixarene cavity while the two other amido methyls are pointing away from this cavity and are nearly collinear with C–O phenolic bonds. This arrangement is chiral but in contrast to a recent structure of a tetra-imide derivative of a calix[4]arene[15] the crystal contains both enantiomers. All bond lengths and bond angles are in the expected range. Two acetonitrile molecules per calixarene fill voids in the crystal. The four calixarene molecules per crystallographic cell are oriented head to foot along the b axis so that all phenolic alkyl chains are close to each other.

Extraction and complexation

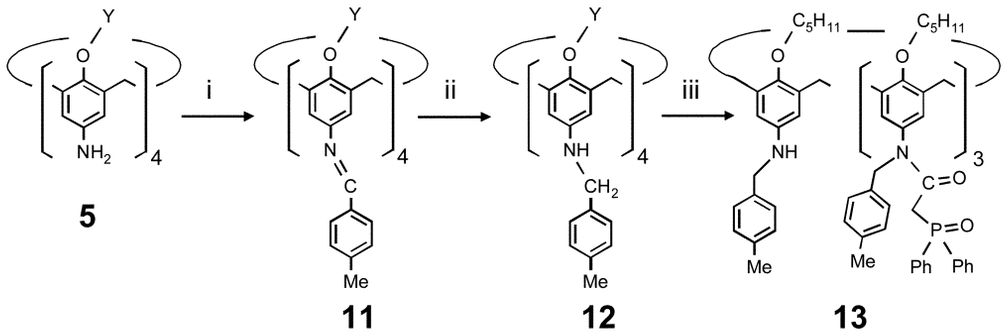
The extraction of selected lanthanides and americium from aqueous nitric acid to *o*-nitrophenyl hexyl ether (NPHE) was studied for **4a**. The distribution coefficients D (determined by γ-spectrometry) are compared in Table 1 with those for the analogous secondary CMPO derivative **2a**. The following general effects may be stated.

a) The secondary CMPO **2a** is a much better extractant for all cations than its *N*-methyl analogue **4a**

b) For both ligands, the distribution coefficient decreases along the lanthanide series.[5,6,8]

c) For both ligands there is a remarkable selectivity for the extraction of Am over Eu which is even better for **4a** ($D_{Am/Eu}$ = 4.8/6.2/7.5 for $c(HNO_3)$ = 2 M/3 M/4 M) than for **2a** ($D_{Am/Eu}$ = 3.5 for $c(HNO_3)$ = 3 M).

This selectivity under strongly acidic conditions makes **4a** interesting as extractant in spite of its lower extraction ability. In addition, **4a** seems to be more resistant towards nitric acid



Scheme 2 *Reagents*: i, *p*-methylbenzaldehyde; ii, H_2, Raney Ni; iii, **6**.

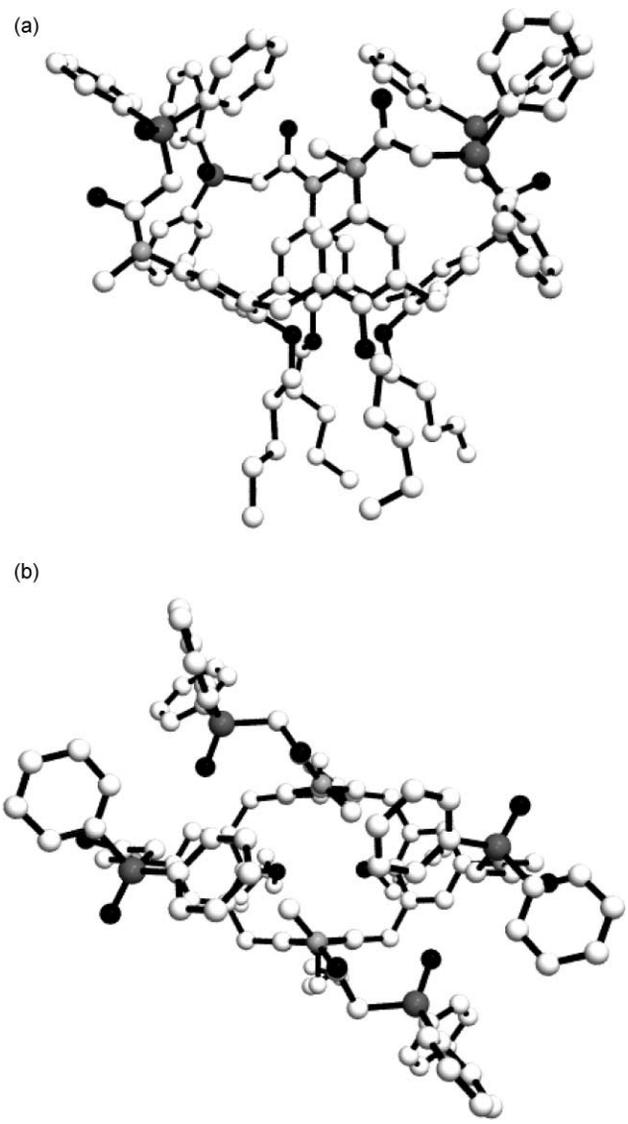


Fig. 1 Molecular conformation of calix[4]arene **4a**, seen from the side (top) and from the wide rim (bottom). Atoms are represented by balls of arbitrary size (C = white; O = black; N = grey, small; P = grey, large).

and irradiation. While for **4a** the distribution coefficient for Eu^{3+} remains practically unchanged for 22 days in contact with 3 M HNO_3, it decreases strongly for calixarenes of type **2** already after 10 days.[16] There is also an interesting selectivity for Am over Cm for compounds **4a** and the more lipophilic **4b**. Under various conditions, $D_{Am/Cm}$ was found in the range 2.5–3.0 when extractions were performed from 3 M HNO_3 aqueous phases.

An independent series of extraction experiments was carried out in the system 1 M HNO_3–dichloromethane using higher concentrations of lanthanides. A colorimetric method was applied to determine the concentration of the metal ions before and after extraction in the aqueous phase. The results are collected in Table 2.

Table 2 Extraction percentages $\%E$ of lanthanide nitrates from 1 M HNO_3 into CH_2Cl_2 by CMPO calix[4]arenes **4a** and **2a** ($c_M = 10^{-4}$ M, volume organic phase/aqueous phase = 1, $T = 20$ °C)

Ligands	La^{3+} $c_L = 10^{-3}$ M	Eu^{3+} $c_L = 10^{-3}$ M	Yb^{3+} $c_L = 10^{-3}$ M	Th^{4+} $c_L = 10^{-4}$ M
4a	8 ± 2	9 ± 2	9 ± 1	9 ± 3
2[a]	98 [b]	58	3	61

[a] Values taken from ref. 6. [b] Value for $c_L = 10^{-4}$ M : $\%E = 23.1$.

A striking difference under these conditions is that the extraction does not change along the lanthanide series. As a consequence, **4a** becomes a better extractant of Yb^{3+} than **2a**, although it is much less effective in other conditions. For both ligands Th^{4+} requires just 1/10 of the ligand concentration to reach $\%E$ values similar to those of Eu^{3+}.

The complexation of La^{3+} and Eu^{3+} by **4a** was also studied in homogeneous solution by UV-spectroscopy. Stability constants ($\log \beta$) for methanol are collected in Table 3 and compared with results previously obtained for **2** (Y = C_3H_7).

Ligand **4a** forms a clean 1 : 1 complex in contrast with **2a** for which a 2 : 1 (M : L) complex was also observed. However, the small differences in the stability constants give no real explanation for the much better extraction by **2a**. Finally, both ligands form stronger complexes in chloride than in nitrate medium ($\Delta \log \beta_{11} \approx 2$). Similar results are found for europium nitrate in acetonitrile: again **4a** forms exclusively a 1 : 1 complex ($\log \beta_{11} = 5.5 \pm 0.2$) while for **2a** the additional formation of a 2 : 1 species ($\log \beta_{11} = 6.1 \pm 0.1$, $\log \beta_{21} = 11.8 \pm 0.2$) was observed. Contrary to what could be expected on the basis of the respective solvating properties of both solvents,[17] the stability constants obtained in acetonitrile are of the same order of magnitude or even slightly lower than those determined in methanol.

NMR studies

Nuclear magnetic resonance already proved useful for obtaining information on the solution structure and the dynamic behavior of lanthanide calixarene complexes.[18–20] On the one hand, the analysis of the relative magnitudes of the paramagnetic shifts of dipolar origin led to information on the conformation of Yb^{3+} complexes. On the other hand, measurements of the dispersion of the nuclear magnetic relaxation (NMRD) allowed determining the stoichiometry and the dynamic behavior of Gd^{3+} complexes. A detailed conformational analysis can best be performed for solutions containing a single monomeric, rigid and symmetrical species. It is then possible to orient reliably the axes of the magnetic susceptibility tensor and to compare experimental paramagnetic shifts with shifts calculated from models obtained by crystallography or molecular modeling. This approach could only be applied semi-quantitatively in the case of **2a**[21] because this ligand forms

Table 3 Stability constants ($\log\beta_{xy} \pm \sigma_{n-1}$) of $La^{3+}$and Eu^{3+} complexes with *p*-CMPO calix[4]arenes **4a** and **2** (Y = C_3H_7) in methanol (I = 0.05 M, Et_4NCl or $NaNO_3$, T = 25 °C)

Ligands	Complexes M : L	NO_3^-		Cl^-	
		La^{3+}	Eu^{3+}	La^{3+}	Eu^{3+}
4a	1 : 1	5.4 ± 0.2	5.3 ± 0.2	7.1 ± 0.1	7.6 ± 0.2
2 (Y = C_3H_7)	1 : 1	6.0 ± 0.2	5.6 ± 0.3 [a]	8.5 ± 0.1	7.2 ± 0.1
	2 : 1	10.6 ± 0.4	11.0 ± 0.3 [a]	13.9 ± 0.3	11.9 ± 0.3

[a] Values for **2a** (Y = C_5H_{11}) : log β_{11} = 6.0 ± 0.3, log β_{21} = 11.1 ± 0.4.

aggregates with lanthanides as shown by NMRD. The induced paramagnetic shifts then originate from a large number of different species in fast exchange and can no longer be related to a single conformer.

In relaxivity titrations, one can follow the progressive formation of a Gd^{3+} complex through changes in the solution relaxation time T_1. A complexation process is indeed accompanied by the removal of solvent molecules from the first coordination sphere of the paramagnetic metal ion. The relaxation rate $1/T_1$ thus decreases as the relaxation of the solvent nuclei becomes slower because it takes place in the bulk of the solution rather than close to unpaired electronic spins. The relaxivity titration of Gd^{3+} (perchlorate salt) by ligand **3** (n = 3) in anhydrous acetonitrile is shown in Fig. 2 in which the relaxation rate $1/T_1$ (relaxivity, in s^{-1} per mM of Gd^{3+}) is plotted *vs.* the ligand/metal concentration ratio.

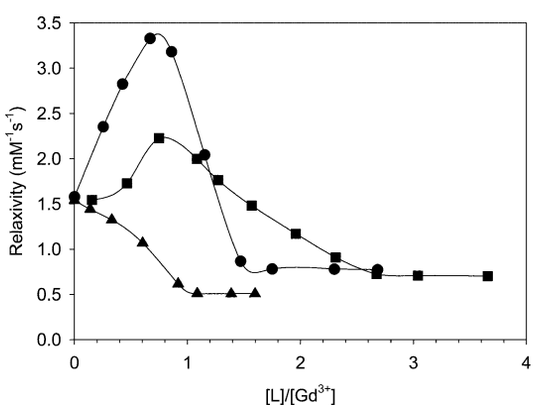


Fig. 2 Relaxivity titration of an anhydrous acetonitrile solution of $Gd(ClO_4)_3$ by ligands **3** (n = 3) (▲), **2a** (■) and **4a** (●). Longitudinal relaxation rates $1/T_1$ (relaxivity in s^{-1} mM^{-1}) *vs.* the [ligand]/[Gd^{3+}] concentration ratio at 25 °C.

A break at low relaxivity for a 1 : 1 concentration ratio followed by a plateau indicates the formation of a stable single complex with **3**. A totally different behavior was observed with calix[4]arene **2a** that features its CMPO substituents on the wide rim.[18] The relaxivity maximum for a ligand/metal concentration ratio of about 0.8 was ascribed to the formation of Gd^{3+}-containing oligomers. Large polymeric structures are tumbling slowly in solution and their relaxivity depends on the electronic longitudinal relaxation time and on the solvent exchange time rather than on the rotational correlation time as the latter is no longer the smallest of these three parameters.[22]

Ligand **4a** appears to form even higher aggregates with Gd^{3+} than **2a** as evidenced by a more pronounced relaxivity maximum. Moreover, a smaller excess of ligand is needed to reach the low relaxivity that characterized fully formed and poorly solvated complexes but as expected, the relaxivities of the two complexes are identical for large ligand/metal ratios. Another difference worth noting between the Gd^{3+} complexes with **2a** and **4a** is the higher aggregation of the later even at low [**4a**]/[Gd^{3+}] ratios. Relatively well-resolved NMR spectra were recorded for the Yb^{3+}**·2a** complex at ligand/metal ratios of 0.5. In this condition, the complex is still partially monomeric while large oligomers of **4a** appear to be formed. In keeping with this observation, the NMR spectra of Yb^{3+}**·4a** feature a large number of poorly resolved resonances that cannot be exploited for a conformational analysis.

Differences in aggregation state between the Gd^{3+}**·2a** and Gd^{3+}**·4a** complexes are also clearly evidenced by the NMRD curves presented in Fig. 3.

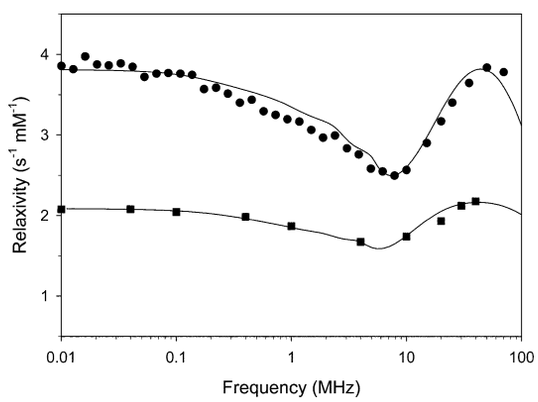


Fig. 3 Nuclear magnetic relaxation dispersion curves of the Gd^{3+}**·2a** (■) and Gd^{3+}.**4a** (●) complexes in anhydrous acetonitrile. Experimental conditions: [$Gd(ClO_4)_3$] = 1 mmol l^{-1}, temperature: 25 °C. The solid lines were computed using computer program developed by Bertini *et al.*.[22]

The relaxivity of the Gd^{3+}**·4a** solution is higher at all frequencies and a pronounced maximum is observed between 20 and 80 MHz as expected for polymeric Gd^{3+}-containing materials. The Solomon–Bloembergen equations account for the shape of the relaxation dispersion curves and a computer program reported by Bertini *et al.*[23] allows one to deduce relaxation parameters from a best fit interpretation of the experimental data. The calculations were performed as reported earlier[18] for Gd^{3+}**·2a** assuming the values of some unknown parameters such as the Gd^{3+} ··· N≡C–CH_3 distance (5.3 Å) and the solvent exchange time (τ_m = 3000 to 5000 ps). The best agreement between the calculated and the experimental relaxivities was obtained for the following parameters: rotational correlation time τ_r = 1360 ps, zero field splitting correlation times τ_{s0} = 460 ps and τ_v = 16 ps, solvation number q_{MeCN} = 2, and splitting of the S manifold of Gd^{3+} D = 0.045 cm^{-1}. Applying the Stokes–Einstein equation[22] leads to a mean radius of the Gd^{3+}**·4a** aggregates a = 1.6 nm. A value of 1.2 nm is computed for the Gd^{3+}**·2a** oligomers from the τ_r = 649 ps value reported earlier. These data must be accepted with some reservation because of the hypotheses that had to be made here on the values of some relaxation parameters and also because of the imperfect fit between the calculated and experimental data. However, the calculated radii of the calix[4]arene oligomers are close to the value found[24] in the solid state (1.5–2 nm) for a complex in which Eu^{3+} ions are coordinated by two ligands **2** (Y = C_3H_7). One can thus assume that metallic dimers or trimers are the major components in solution.

Dynamic light scattering studies were performed to complement the NMRD analyses. The NMRD technique is not so

well-known and it was thus interesting to support the contention that relaxivity maxima are indeed due to oligomeric structures in acetonitrile solutions. It should be stressed here that the molecular size deduced from relaxivity measurements is a function of the rotational correlation time at the Gd^{3+} complexation site while light diffusion yields the overall molecular volume. Thus, the two techniques do not necessarily yield the same results. It should also be noted that calix[4]arenes are fairly large molecules but that their size is at the lower limit of the range covered by dynamic light scattering that is about 1 nm. Rigorous tests of the available measurement system were thus a prerequisite. A first test was made with acetonitrile solutions of the simple ligand a tetraester derivative of *p-tert*-butylcalix-[4]arene[25] for which a diameter of 0.7–1 nm is expected. No signal could be recorded for this small monomeric ligand with sample times of 0.7–1 μs even after long accumulation times. The reliability of the measurements was then checked with a calix[4]arene substituted on the wide rim by four urea functions bearing bulky tritylphenyl groups.[26] This macrocycle forms dimers in $CHCl_3$ that are stabilized by hydrogen bonds between the urea functions. The diameter of this dimer is estimated to be close to 2–3 nm on the basis of Dreiding models. As indicated in Fig. 4, the size distribution histogram of the dimer corresponds to a diameter of about 2 nm in agreement with the values deduced from models.

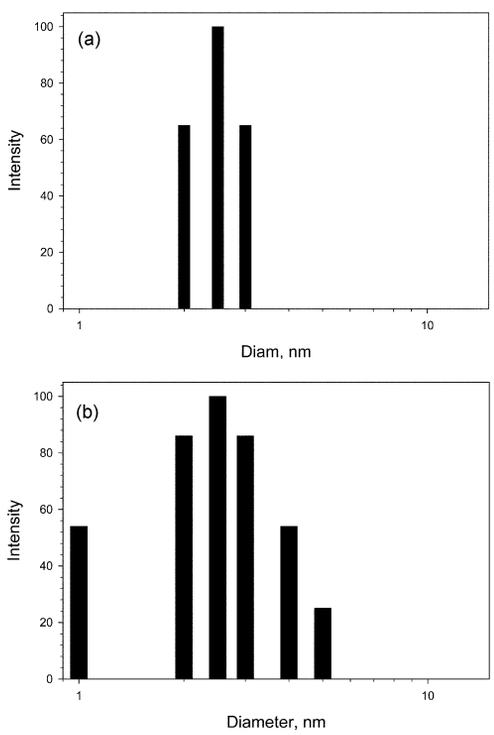


Fig. 4 Size distribution of a dimer of a tritylphenyl-urea substituted calix[4]arene[26] in chloroform (top) and of a solution of Gd^{3+}·**4a** in acetonitrile (bottom, [**4a**] : [Gd^{3+}] = 1.0, [$Gd(ClO_4)_3$] = 1 mmol l^{-1}, temperature: 25 °C).

Fig. 4 also presents the size histogram obtained for a 2 mmol acetonitrile solution of the Gd^{3+}·**4a** complex. Aggregation is clearly indicated by a size range of 1 to 5 nm with a maximum at 2–3 nm. A comparison of this size range with the dimensions of a dimeric calix[4]arene Eu^{3+} complex in the solid state[24] leads to the conclusion that monomeric, dimeric and trimeric forms of Gd^{3+}·**4a** coexist in acetonitrile, the dimer being the major species in agreement with the NMRD analysis. Metal complexes of well defined stoichiometries were found in methanol in presence of Cl^- or NO_3^- anions (see Table 3). As expected, the solution behaviour of ligand **4a** strongly depends on the nature of the solvent and of the counter-ions.

NMRD thus appears as a useful complement to the more classical methods aimed at studying the solution behavior of metal complexes. Another application of NMRD in solvent extraction is illustrated in Fig. 5. Concentrated HNO_3 solutions of wastes are produced by the nuclear industry and are reprocessed by solvent extraction. However, Gd^{3+} perchlorate was used in the above NMRD investigation in order to study aggregation phenomena in absence of any competing anion such as NO_3^-. Tetrabutylammonium nitrate was added to acetonitrile solutions of Gd^{3+}·**4a** with various ligand/metal concentration ratios in order to move closer to practical conditions. The 20 MHz relaxivity sizeably increases upon addition of nitrate ions especially for ligand/metal ratios close to unity when large oligomers are formed in Gd^{3+} perchlorate solutions. It thus seems that nitrate ions are entering the first coordination sphere of the Gd^{3+} ions and that CMPO groups become free to form new intermolecular bonds. A concomitant better solvation is also possible because the nitrate ions with a small O–N–O angle could leave enough room for solvent molecules in the first coordination sphere of Gd^{3+}. Carrying out the same study in the case of ligand **2a** would have been interesting but was limited by the formation of insoluble compounds at NO_3^-/Gd^{3+} concentration ratios above 1.0. Below this ratio, ligands **2a** and **4a** have similar behaviors. It was thus not possible to ascribe differences in extraction efficiency between **2a** and **4a** to a possible role of the nitrate ions. Finally, it should be noted that the addition of up to 10 equivalents of water does not modify the relaxivity of a Gd^{3+}·**4a** acetonitrile solution (ligand/metal ratio = 0.7).

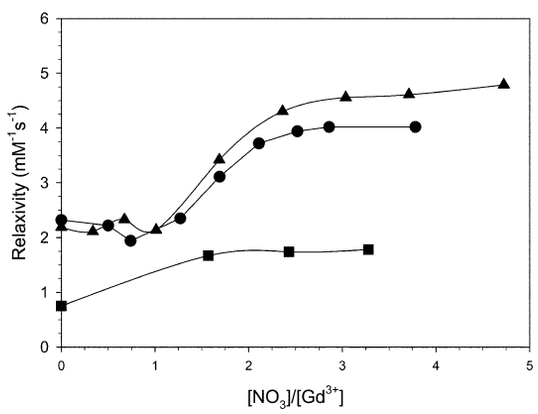


Fig. 5 Influence of the concentration of tetrabutylammonium nitrate on the relaxivity of a solution of $Gd(ClO_4)_3$ and calix[4]arene **4a** in anhydrous acetonitrile. Experimental conditions: [Gd^{3+}] = 1 mmol l^{-1}, temperature: 25 °C, [**4a**]/[Gd^{3+}] concentration ratio: 0.71 (▲), 0.91 (●) and 3.22 (■).

Conclusion

The extraction of metal ions by ligands into an organic phase depends on a number of factors the relative importance of which is not easily assessed. In the present case, simply replacing a secondary amide function by a tertiary one in a calix[4]arene CMPO ligand brings about changes in extraction efficiency and selectivity. Detailed physicochemical studies show differences in the extent of the aggregation of the lanthanide complexes in acetonitrile but little differences in stability in methanol. Aggregation phenomena most probably play a role in the extraction process but are certainly not the only factor to take into account.

Experimental

Reagents and methods

Tetraamino calix[4]arene **5** and *p*-nitrophenyl (diphenylphosphoryl)acetate **6** were prepared according to known procedures.[4,19,27] Melting points were determined with a MEL TEMP 2 capillary melting point apparatus and are uncorrected.

^{1}H NMR spectra were recorded on Bruker 200 and 400 MHz spectrometers. FD mass spectra were recorded with a Finnigan MAT 90 (5kV/10 mA min^{-1}). Anhydrous acetonitrile solutions of lanthanide perchlorate salts were prepared as reported previously.[17] **CAUTION**: lanthanide perchlorates are potentially explosive when brought in contact with organic materials. It is advisable to use only small amounts of metal salt at a time with proper care in a glove box. Details on the measurements of the relaxivity at 20 MHz with a Bruker Minispec 120 (Karlsruhe, Germany) and on measurements of the dispersion of the nuclear magnetic relaxation with a Stelar relaxometer (Mede, Italy) have been given elsewhere.[17–19]

5,11,17,23-Tetra-(*tert*-butyloxycarbonylamino)-25,26,27,28-tetra-pentyloxycalix[4]arene 7a[11]

A solution of $(Boc)_2O$ (2.83 g, 13.0 mmol) in $CHCl_3$ (10 ml) was added to the stirred solution of tetraamine **5a** (2.0 g, 2.60 mmol) in $CHCl_3$ (50 ml). After 1 day at rt the reaction was quenched by the addition of water. The organic layer was collected and dried ($MgSO_4$). The solvent was removed under vacuum to give the crude product. Column chromatography (1 : 1 ethyl acetate–hexane) gave the *N*-Boc protected tetramine **7a** as a white solid. Yield 87%, mp 199–200 °C. ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.83–0.96 (m, 12H, CH_3), 1.25–1.38 (m, 16H, CH_2), 1.48 (s, 36H, *t*-Bu), 1.72–1.91 (m, 8H, CH_2), 3.06 (d, J = 13.2 Hz, 4H, ArCH_2Ar), 3.68 (t, J = 6.4 Hz, 8H, ArOCH_2), 4.34 (d, J = 13.4 Hz, 4H, ArCH_2Ar), 6.15 (s, 4H, NH), 6.59 (s, 8H, ArH), FD-MS m/z = 1165.4 (M$^+$, 100).

5,11,17,23-Tetra-(*tert*-butyloxycarbonylamino)-25,26,27,28-tetrakis-tetradecyloxycalix[4]arene 7b

The reaction was carried out as described for **7a**; oil, yield 86%, ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.84 (t, J = 6.2 Hz, 12H, CH_3), 1.22 (s, 88H, CH_2), 1.45 (s, 36H, *t*-Bu), 1.80 (quin, J = 7.3 Hz, 8H, CH_2), 3.10 (d, J = 12.7 Hz, 4H, ArCH_2Ar), 3.75 (t, J = 7.3 Hz, 8H, ArOCH_2), 4.32 (d, J = 12.7 Hz, 4H, ArCH_2Ar), 6.10 (s, 4H, NH), 6.56 (s, 8H, ArH), FD-MS m/z = 1670.5 (M$^+$, 100).

5,11,17,23-Tetra-(*tert*-butyloxycarbonyl-methylamino)-25,26,27,28-tetra-pentyloxycalix[4]arene 8a

Iodomethane (3 ml) was added dropwise to a refluxing suspension of the Boc-protected amine **7a** (1,0 g, 0.86 mmol), NaOH (0.34 g, 8.6 mmol), K_2CO_3 (0.6 g, 4.3 mmol) and tetra-*n*-butylammonium hydrogensulfate (0.1 g, 0.3 mmol) in toluene (10 ml) and heated under reflux for 12 h. After cooling the solution was filtered, washed with water, dried ($MgSO_4$) and the toluene was finally removed under vacuum. The resulting crude product was recrystallized from chloroform–hexane; yield 80%; mp 90–91 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.91 (t, J = 7.04 Hz, 12H, CH_3), 1.29–1.37 (s, 16H, CH_2), 1.39 (s, 36H, *t*-Bu), 1.82–1.91 (m, 8H, CH_2), 2.88 (s, 12H, NCH_3), 3.07 (d, J = 12.9 Hz, 4H, ArCH_2Ar), 3.82 (t, J = 8.2 Hz, 8H, ArOCH_2), 4.36 (d, J = 13.3 Hz, 4H, ArCH_2Ar), 6.56 (s, 8H, ArH), FD-MS m/z = 1221.6 (M$^+$, 100).

5,11,17,23-Tetra-(*tert*-butyloxycarbonyl-methylamino)-25,26,27,28-tetrakis-tetradecyloxycalix[4]arene 8b

Prepared as described for **8a**; oil, yield 96%. ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.85 (t, J = 6.1 Hz, 12H, CH_3), 1.16–1.35 (m, 88H, CH_2), 1.40 (s, 36H, *t*-Bu), 1.88 (m, 8H, CH_2), 2.90 (s, 12H, N–CH_3), 3.07 (d, J = 12.5 Hz, 4H, ArCH_2Ar), 3.81 (t, J = 7.3 Hz, 8H, ArOCH_2), 4.36 (d, J = 12.6 Hz, 4H, ArCH_2Ar), 6.56 (s, 8H, ArH), FD-MS m/z = 1726.6 (M$^+$, 100).

5,11,17,23-Tetra-methylamino-25,26,27,28-tetra-pentyloxy-calix[4]arene 9a

To a solution of the Boc-protected methylamino calixarene **8a** (2,0 g, 1.63 mmol) in chloroform (20 ml) was added trifluoroacetic acid (20 ml) in one portion and the red solution was stirred at rt for 2 h. The solvent was evaporated under vacuum to give **9a** as a red powder which was used without further purification.

5,11,17,23-Tetra-methylamino-25,26,27,28-tetrakis-tetradecyloxycalix[4]arene 9b

Prepared as described for **9a**. Boc-protected methylamino calixarene **8b** (2.0g, 1.15 mmol), trifluoroacetic acid (20 ml). Yield 95%, mp >300 °C, ^{1}H NMR (200 MHz, DMSO-d_6) δ 0.85 (t, J = 6.1 Hz, 12H, CH_3), 1.16–1.45 (m, 88H, CH_2), 1.85 (m, 8H, CH_2), 2.90 (s, 12H, NCH_3), 3.21 (d, J = 12.2 Hz, 4H, ArCH_2Ar), 3.83 (t, J = 7.3 Hz, 8H, ArOCH_2), 4.41 (d, J = 12.6 Hz, 4H, ArCH_2Ar), 6.81 (s, 8H, ArH), 9.46 (s br, 12H, NH_3^+).

5,11,17,23-Tetra-(diphenylphosphorylacetyl)methylamino-25,26,27,28-tetra-pentyloxycalix[4]arene 4a

Active ester **6** (1.91g, 5 mmol) was added to a stirred solution of methylamino calixarene **9a** (1.3 g, 1 mmol) and triethylamine (1 ml) in chloroform (30 ml). The mixture was stirred at rt for 24 h and the solution was washed repeatedly with 10% aq. NaOH and dried ($MgSO_4$). Evaporation of the solvent afforded a residue which was passed through a short column (silica gel, ethylacetate) and precipitated from chloroform/hexane to give the desired compound **4a** as a pale yellow powder. Yield 80%, mp 91–92 °C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.96 (t, J = 8.1 Hz, 12H, CH_3), 1.31–1.47 (m, 16H, CH_2), 1.82–1.99 (m, 8H, CH_2), 2.65 (s, 12H, NCH_3), 2.95 (d, J = 12.3 Hz, 4H, ArCH_2Ar), 3.28 (d, J = 16.1 Hz, 8H, PCH_2), 3.84 (t, J = 7.3 Hz, 8H, ArOCH_2), 4.30 (d, J = 12.6 Hz, 4H, ArCH_2Ar), 6.30 (s, 8H, ArH), 7.34–7.50 (m, 24H, PPh_2), 7.69–7.80 (m, 16H, PPh_2); ^{13}C NMR (100 MHz, CD_3CN) : δ 14.54 (–O(CH^2)^4–*C*H^3), 23.60 (N*C*H^3), 29.19 (*C*H^2 bridge), 31.02 (d, J_{P-C} = 74.4Hz, P–*C*H^2), 37.55, 37.86, 38.20 (–(*C*H^2)^3–), 76.51(O–*C*H^2), 127.82 (*para*-*C*H), 129.50 and 131.91 (d, J_{P-C} = 11.3Hz and d, J_{P-C} = 8.09Hz, *ortho* and *meta*-*C*H), 132.75 (*C*H calix), 134.68, 135.68, 136.51, 139.18 (quaternary carbons of the calixarene and phenyl groups), 165.90 (*C*=O); FD-MS m/z = 1790.1(M$^+$, 100).

5,11,17,23-Tetra(diphenylphosphorylacetyl)methylamino-25,26,27,28-tetrakis-tetradecyloxycalix[4]arene 4b

Prepared in analogy to **4a** using toluene (50 ml) as solvent; methylamino calixarene **9b** (1.8 g, 1 mmol), active ester **6** (1.91 g, 5 mmol); yellowish powder, yield 78%, mp 80–82 °C. ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.86 (t, J = 6.2 Hz, 12H, CH_3), 1.10–1.49 (m, 88H, CH_2), 1.93 (m, 8H, CH_2), 2.66 (s, 12H, NCH_3), 2.96 (d, J = 12.3 Hz, 4H, ArCH_2Ar), 3.30 (d, J = 16.6 Hz, 8H, PCH_2), 3.85 (t, J = 7.3 Hz, 8H, ArOCH_2), 4.31 (d, J = 12.6 Hz, 4H, ArCH_2Ar), 6.30 (s, 8H, ArH), 7.34–7.57 (m, 24H, PPh_2), 7.66–7.87 (m, 16H, PPh_2), FD-MS m/z = 2295.1 (M$^+$, 100).

5,11,17,23-Tetra(diphenylphosphoryldimethylacetyl)-methylamino-25,26,27,28-tetra-propyloxy-calix[4]arene 10

Prepared as described for **8a**. Iodomethane (5 ml), tetra-CMPO calix[4]arene **2** (Y = C_3H_7) (1.4 g, 0.86 mmol), NaOH (0.34 g, 8.6 mmol), K_2CO_3 (0.6 g, 4.3 mmol), tetra-*n*-butylammonium hydrogensulfate (0.1 g, 0.3 mmol), toluene (10 ml). Recrystallisation from chloroform–hexane gave a crystalline, white powder **10**. Yield 60%, mp 116–118 °C, ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.96 (t, J = 7.5 Hz, 12H, CH_3), 1.13 (s, 12H, CCH_3), 1.21 (s, 12H, CCH_3), 1.76–2.05 (m, 8H, CH_2), 2.73 (b s, 12H, NCH_3), 2.94 (d, J = 14.6 Hz, 4H, ArCH_2Ar), 3.65–3.98 (m, 8H, ArOCH_2), 4.33 (d, J = 13.2 Hz, 4H, ArCH_2Ar), 7.32–7.51 (m, 24H, PPh_2), 7.85–8.05 (m, 16H, PPh_2), FD-MS m/z = 1790.1 (M$^+$, 100).

5,11,17,23-Tetrakis-(*p*-methylbenzylidenimino)-25,26,27,28-tetra-pentyloxycalix[4]arene 11

Tetraamine **5a** (2.0 g, 2.6 mmol) and *p*-methylbenzaldehyde (26 mmol) were heated in dry toluene (30 ml) in the presence of molecular sieves (3–4 Å) for 5 h. The molecular sieves were removed and the solvent evaporated *in vacuo*. The residue was recrystallized from ethanol to give a yellow powder. Yield 75%, mp 167–169 °C, ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.97 (t, J = 6.8 Hz, 12H, CH_3), 1.48–1.38 (m, 16H, CH_2), 1.98 (t, J = 7.0 Hz, 8H, CH_2), 2.32 (s, 12H, ArCH_3), 3.24 (d, J = 12.8 Hz, 4H, ArCH_2Ar), 3.95 (t, J = 7.3 Hz, 8H, ArOCH_2), 4.51 (d, J = 12.5 Hz, 4H, ArCH_2Ar), 6.68 (s, 8H, ArH), 7.02 (d, J = 8.2 Hz, 8H, ArH), 7.53 (d, J = 7.8 Hz, 8H, ArH), 8.07 (s, 4H, ArCHN).

5,11,17,23-Tetrakis-(*p*-methylbenzylamino)-25,26,27,28-tetra-pentyloxycalix[4]arene 12

The tetraimine **11** was dissolved in toluene (200 ml) and hydrogenated under atmospheric pressure in the presence of Raney nickel at 60 °C. The catalyst was filtered off, washed with warm toluene and the solvent evaporated *in vacuo*. The residue was recrystallized from ethanol to give a white powder. Yield 90%, mp 145–146, ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.98 (t, J = 6.5 Hz, 12H, CH_3), 1.49–1.35 (m, 16H, CH_2), 1.91 (t, J = 7.1 Hz, 8H, CH_2), 2.91 (d, J = 12.2 Hz, 4H, ArCH_2Ar), 3.78 (t, J = 7.5 Hz, 8H, ArOCH_2), 4.02 (s, 8H, ArCH_2N), 4.32 (d, J = 12.3 Hz, 4H, ArCH_2Ar), 6.01 (s, 8H, ArH), 7.25–7.05 (m, 20H, ArH and NH), MS-FD m/z = 1181.4 (M^+, 100).

5,11,17-Tri-(diphenylphosphorylacetyl)-*p*-methylbenzyllamino-23-(p-methylbenzylamino)-25,26,27,28-tetra-pentyloxycalix-[4]arene 13

Active ester **6** (6.47 g, 17 mmol) was added to a stirred solution of tetraamine **12** (2 g, 1.7 mmol) and triethylamine (1 ml) in toluene (50 ml). The mixture was refluxed for 48 h and the solution was washed repeatedly with 10% aq. NaOH and dried ($MgSO_4$). Evaporation of the solvent and precipitation from chloroform–hexane gave the tri-CMPO derivative **13** as a yellow powder. Yield 75%, mp 158–159 °C, ^{1}H NMR (400 MHz, DMSO, 110 °C) δ 0.97–0.89 (m, 12H, CH_3), 1.47–1.25 (m, 16H, CH_2), 1.83–1.80 (m, 8H, CH_2), 2.13 (s, 3H, ArCH_3), 2.19 (s, 6H, ArCH_3), 2.24 (s, 3H, ArCH_3), 2.90 (d, J = 12.5 Hz, 2H, ArCH_2Ar), 3.05 (d, J = 12.3 Hz, 2H, ArCH_2Ar), 3.21 (d, J = 14.5 Hz, 2H, PCH_2), 3.33 (d, J = 15.2 Hz, 4H, PCH_2), 3.62 (t, J = 7.1 Hz, 2H, ArOCH_2), 3.69 (t, J = 7.0 Hz, 2H, ArOCH_2), 4.10–3.96 (m, 6H, ArOCH_2 and ArNCH_2), 4.24 (d, J = 12.9 Hz, 2H, ArCH_2Ar), 4.31 (d, J = 12.9 Hz, 2H, ArCH_2Ar), 4.49 (d, J = 14.8 Hz, 2H, ArNCH_2), 4.73 (d, J = 14.7 Hz, 2H, ArNCH_2), 5.62 (s, 2H, ArH), 6.38 (s, 2H, ArH), 6.66 (s, 2H, ArH), 6.78 (d, J = 7.6 Hz, 2H, ArH), 6.83 (d, J = 7.8 Hz, 2H, ArH), 7.00–7.91 (m, 14H, ArH), 7.54–7.41 (m, 18H, PPh_2), 7.66–7.61 (m, 4H, PPh_2), 7.79–7.71 (m, 9H, PPh_2 and NH). FD-MS m/z = 1908.2 (M^+, 100).

X-Ray analysis

Recrystallisation of **4a** from acetonitrile afforded translucent parallelepipedic crystals that were suitable for crystallographic analysis although they tended to crack easily. Crystals were taken out of the solution with a small nylon loop, immediately immersed in Paratone-N® oil and cooled in a flux of nitrogen before collecting the reflection data at 203 K. Table 4 lists the most important parameters of the X-ray analysis. The structure was solved by direct methods, Fourier techniques and full-matrix least-squares calculations with the Bruker SHELXTL(1991) package.[28] In consequence of the weakness of collected intensity data [9203 reflections with $I > 2\sigma(I)$] in comparison with the number of parameters to refine, the non-hydrogen atoms were only refined isotropically. Hydrogen atoms in calculated positions were treated as riding on the attached C atom. Methyl hydrogens of the two acetonitrile molecules could not be located. †

Table 4 Summary of crystal data, [a] data collection and structure solution and refinement of **4a**

Formula	$C_{112}H_{126}N_6O_{12}P_4$
M_w	1872.07
Crystal system	Monoclinic
Space group	$P2(1)/c$
T/K	203(2)
a/Å	27.462(17)
b/Å	20.459(12)
c/Å	18.660(6
α/°	90.00
β/°	102.14(9)
γ/°	90.00
V/Å^3	10249(9)
Z	4
μ (mm^{-1})	0.134
Unique reflns. measured	17988
Unique reflns. [$I \geq 2\sigma(I)$]	9203
Parameters	538
R [$F_2 > 2\sigma(F_2)$]	0.0680
wR	0.1445

[a] Unit cell parameters were obtained by least-squares analysis of the setting angles of 25 carefully centered reflections found in a random search on the reciprocal space.

† CCDC reference number 215208. See http://www.rsc.org/suppdata/ob/b3/b307929e/ for crystallographic data in .cif or other electronic format.

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