Tripodal (*N*-alkylated) CMP(O) and malonamide ligands: synthesis, extraction of metal ions, and potentiometric studies

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Received (in Montpellier, France) 13th September 2006, Accepted 13th October 2006
First published as an Advance Article on the web 14th November 2006
DOI: 10.1039/b613254e

Tripodal ligands build on the C-pivot (**9b–e**, **13b–d**, and **17a–d**) and trialkylbenzene platforms (**10a,b**, **11**, **12**, **14a,b**, and **18a,b**) bearing (*N*-alkylated) carbamoylmethylphosphine oxide (CMPO), carbamoylmethylphosphonate (CMP), and malonamide moieties were synthesized. Extraction studies with Am^{3+} and Eu^{3+} show that in general there is a positive influence of the *N*-alkyl substituents in C-pivot CMP(O) ligands on the *D* (distribution) coefficients. The trialkylbenzene CMPO ligands **10a,b**, **11**, and **12** have considerably larger *D* coefficients than the corresponding C-pivot analogues **9a–e**, although hardly having any selectivity, while *N*-alkylation gives rise to smaller *D* coefficients. Although less effective the extraction behavior of the C-pivot CMP analogues **13b–d** shows more or less the same trend as the corresponding CMPO ligands **9b–e** upon substitution of the carboxamide *N*-atom with different alkyl chains. The different malonamide ligands **17a–d** and **18a,b** are bad extractants, while *N*-alkylation makes them even worse. Potentiometric studies of CMP(O) and malonamide ligands in polymeric membranes on Pb^{2+}, Cu^{2+}, Ca^{2+}, Mg^{2+}, Na^{+}, and K^{+} salts revealed that *N*-alkyl substituents increase the stability constants of ion–ionophore complexes compared to unsubstituted ligands. In polymeric membrane electrodes the ligands induce a selectivity pattern that differs significantly from the so-called Hofmeister series, giving the highest selectivity coefficients for UO_2^{2+} among all examined cations (Pb^{2+}, Cu^{2+}, Ca^{2+}, Mg^{2+}, Na^{+}, K^{+}).

Introduction

The interests in nuclear energy fluctuates together with the fossil fuel prices, making the topic very hot nowadays. A particularly important and not sufficiently solved problem is the removal of highly radiotoxic actinides from HLLW (high level liquid waste) formed during the reprocessing of the spent nuclear fuel and to separate the actinides from the more abundant lanthanides.[1] After separation, the actinides can be transformed to less dangerous and easier to handle isotopes by transmutation. The most promising way is extraction of the actinides with highly selective ionophores, however, the design and synthesis of ligands fulfilling industrial requirements for this process, is still a challenge.

The approach to connect different chelating groups to preorganized scaffolds to improve both the extraction efficiency and the selectivity is already explored in the field of actinide/lanthanide separation for quite some time.[2] The main stream of investigations is directed toward ligands bearing four coordinating arms like carbamoylmethylphosphine oxide (CMPO) and carbamoylmethylphosphonate (CMP) substituted calixarenes[3] and resorcinarenes,[4] or calixarene functionalized picolinamides.[5] Despite the evidence that actinides and lanthanides coordinate with bidentate ligands as CMP(O)[6] and malonamides[7] in a 1 : 3 stoichiometry (metal^{3+} : ligand), only a few examples of tripodal ligands[8] based on the triphenoxymethane platform were described by the groups of Scott[8a,b] and Böhmer.[8c] Recently, we reported the synthesis and complexation behavior of CMP(O) functionalized C-pivot tripodal ligands.[9] In these tripodal ligands six donor oxygen atoms are brought together to fill the coordination sphere of the metal resulting in 1 : 1 complexes.

Simple CMPO bidentate ligands[6,10] with short branched *N*-substituents like isobutyl at the amide moiety, lead in general to an improved distribution and minimization of a third phase formation between the aqueous and the organic layer. However, for multicoordinate preorganized ligands mainly *N*-unsubstituted ligands have been investigated, except one *N*-methylated CMPO calix[4]arene[3e] and two CMP(O) *N*-butyl substituted resorcinarenes.[4a]

The 1,3,5-trialkylbenzene platform is attractive for the construction of different types of receptors, because ligating sites at the 2, 4, and 6 positions are preorganized at the same face of the molecule.[11] However, to the best of our knowledge, it has not been used for the preparation of actinide/lanthanide ligands.

In this manuscript we describe the synthesis and complexation with Am^{3+} and Eu^{3+} of C-pivot and trialkylbenzene platform-based tripodal ligands containing (*N*-alkyl

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substituted) CMP(O)[6,10] and malonamide[7,12] ligating groups. Special attention is paid to the influence of the *N*-alkyl substituents on the extraction behavior. The ion–ionophore stability constants of complexes formed by these ligands with selected cations as well as the influence of the structure of these ligands on the response of cation-selective electrodes with polymeric membranes doped with these ligands are presented.

Results and discussion

Synthesis

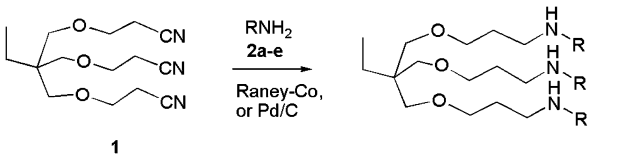
Starting from the known C-pivot nitrile **1**[13] a series of tripodal secondary amines **3b–e** was prepared using a slightly modified reductive alkylation method as described in the literature (Scheme 1).[14] C-Pivot nitrile **1** was reacted with a large excess of the appropriate primary amine at 8 bar of hydrogen in the presence of 10% Pd–C[15] at room temperature to give the tripodal amines **3b–e** in excellent yields.

In addition to correct molecular ion peaks in the HR-FAB mass spectra, their formation followed from their ^{1}H NMR spectra with characteristic triplets at 2.56–2.69 ppm for the –CH_2NHR methylene group. Primary tripodal amine **3a** was synthesized according to the literature procedure.[8d]

Reaction of tris(bromomethyl)benzene **4**[11b] with excess of 3-pentylamine afforded amine **5** in quantitative yield. For ligands with a longer spacer between the platform and the ligating site the tris(aminoethyl)benzenes **7a,b** and **8** were prepared (Scheme 2). Catalytic hydrogenation of tris(cyanomethyl)benzenes **6a**[16a] and **6b**[16b] in the presence of Raney-Co gave the corresponding tripodal amines **7a,b** in almost quantitative yields. The reductive alkylation of **6b** with 3-pentylamine required 100 bar of hydrogen and 70 °C to give tripodal amine **8** in 90% yield. Besides the correct molecular ion signals displayed in the HR-FAB spectra, the ^{1}H NMR spectra of amines **5** and **8** show characteristic multiplets for NCH around 2.45 ppm and that of amines **7a,b** signals for Ph$CH_2CH_2NH_2$ around 2.8 ppm.

Carbamoylmethyl-phosphine oxide (CMPO) and -phosphonate (CMP) functions were introduced *via* reaction with chloroacetyl chloride in the presence of K_2CO_3, followed by an Arbuzov reaction with ethyl diphenyl phosphinite (for CMPO) or triethyl phosphite (for CMP), respectively, of the corresponding acetylated compounds (Schemes 3 and 4).[17]

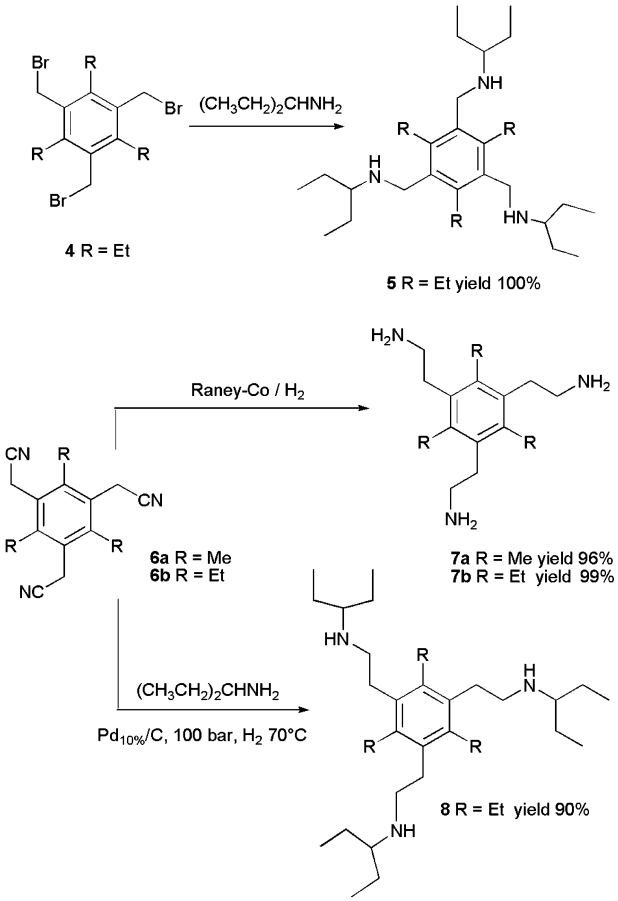
The C-pivot based CMPO derivatives **9b–d** were obtained in excellent yields. However in the case of the more crowded CMPO **9e** the yield was only 13%, probably due to steric hindrance in the reaction of amine **3e** with chloroacetyl



1

3a R = H, Ref. 8d
3b R = $CH_2(CH_2)_2CH_3$ yield 99%
3c R = $CH_2(CH_2)_6CH_3$ yield 97%
3d R = $CH(CH_2CH_3)_2$ yield 94%
3e R = $C(CH_3)_2CH_3$ yield 88%

Scheme 1



4 R = Et

5 R = Et yield 100%

6a R = Me
6b R = Et

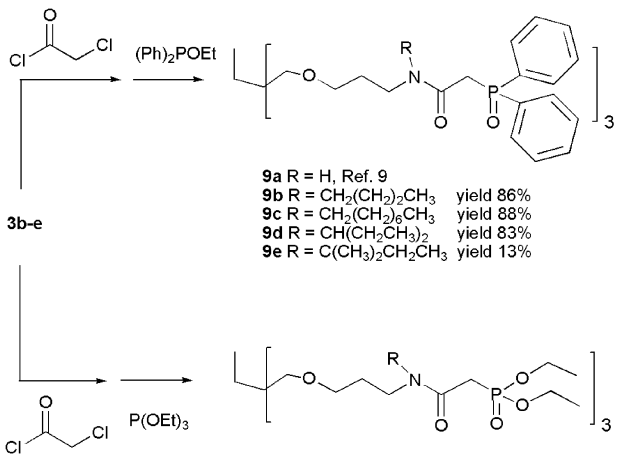
7a R = Me yield 96%
7b R = Et yield 99%

8 R = Et yield 90%

Scheme 2

chloride. The isolated yields of the corresponding CMP derivatives **13b–d** are much lower, mainly due to their higher polarity and as a consequence more difficult chromatographic purification.

The CMPO ligands **9b–e** could be identified based on the characteristic multiplets for the aromatic hydrogens at about

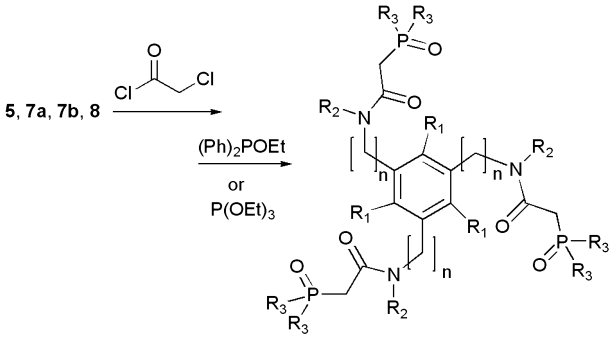


3b-e

9a R = H, Ref. 9
9b R = $CH_2(CH_2)_2CH_3$ yield 86%
9c R = $CH_2(CH_2)_6CH_3$ yield 88%
9d R = $CH(CH_2CH_3)_2$ yield 83%
9e R = $C(CH_3)_2CH_2CH_3$ yield 13%

13a R = H, Ref. 9
13b R = $CH_2(CH_2)_2CH_3$ yield 68%
13c R = $CH_2(CH_2)_6CH_3$ yield 32%
13d R = $CH(CH_2CH_3)_2$ yield 21%

Scheme 3



10a n = 2, R_1 = Me, R_2 = H, R_3 = Ph yield 45%
10b n = 2, R_1 = Et, R_2 = H, R_3 = Ph yield 36%
11 n = 2, R_1 = Et, R_2 = $CH(CH_2CH_2)_2$, R_3 = Ph yield 69%
12 n = 1, R_1 = Et, R_2 = $CH(CH_2CH_2)_2$, R_3 = Ph yield 32%
14a n = 2, R_1 = Me, R_2 = H, R_3 = OEt yield 44%
14b n = 2, R_1 = Et, R_2 = H, R_3 = OEt yield 41%

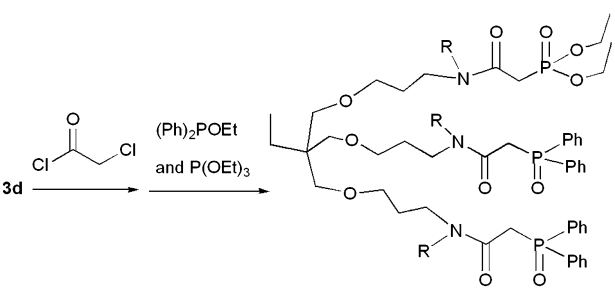
Scheme 4

7.45 (18 H) and 7.85 ppm (12 H) and CMP ligands **13b–d** based on a multiplet for the ethoxy group at around 4.15 ppm (12 H).

In general, the yields of the trialkylbenzene-based CMP(O) ligands **10a,b**, **11**, **12**, and **14a,b** are lower than those of the corresponding C-pivot-based ligands. In the case of the secondary amide containing ligands **10a,b** and **14a,b** ($R^2 = H$) the ^1H NMR spectra exhibit a doublet for the $CH_2P(O)$ methylene bridge (coupling with phosphorus) at ~3.31 and ~2.85 ppm, respectively. This probably indicates the conformational preference for the *trans* form of the secondary amide bonds. Only in the case of CMPO ligand **11** the ^1H NMR spectrum shows a doublet for the $CH_2P(O)$ methylene bridge, indicating the existence of a dominating conformer of this molecule.

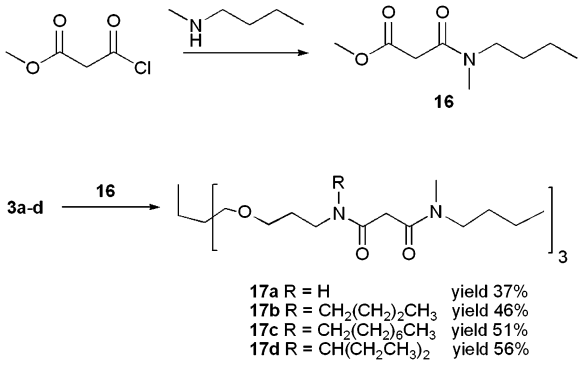
To investigate the influence on the complexation behavior of two different types of ligating sites on the C-pivot platform, tripodal amine **3d** was treated with chloroacetyl chloride followed by reaction with a 1 : 1 mixture of ethyl diphenyl phosphinite and triethyl phosphite. From the reaction mixture ligand **15**, containing two CMPO arms and one CMP, was isolated in 11% yield. The ^1H NMR spectrum displays the characteristic signals for the CMPO and CMP moieties in a 2 : 1 ratio (Scheme 5).

Malonamide methyl ester **16**, obtained by reaction of methyl 3-chloro-3-oxopropionate and *N*-methyl-*N*-butylamine, was directly introduced on the C-pivot amine platforms **3a–d**

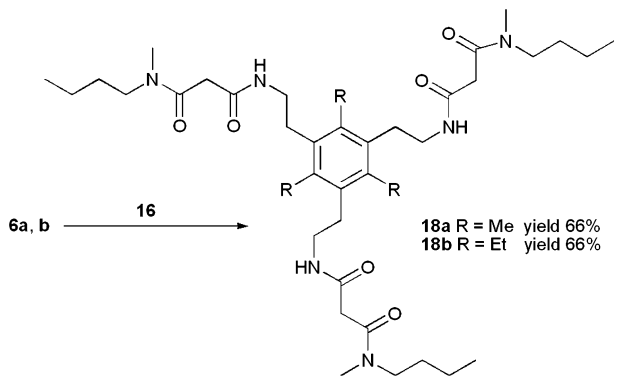


15 R = $CH(CH_2CH_3)_2$ yield 11%

Scheme 5



17a R = H yield 37%
17b R = $CH_2(CH_2)_2CH_3$ yield 46%
17c R = $CH_2(CH_2)_6CH_3$ yield 51%
17d R = $CH(CH_2CH_3)_2$ yield 56%



18a R = Me yield 66%
18b R = Et yield 66%

Scheme 6

resulting in ligands **17a–d**, and on the trialkylphenyl amines **7a,b** giving ligands **18a,b** (Scheme 6).

The ^1H NMR spectra of the malonamide ligands **17a** and **18a,b**, having one secondary and one tertiary amide moiety, show for the NCH_3 group two singlets at about 3 ppm. The more rigid ligands **17b–d** exist as a mixture of conformers giving rise to complicated ^1H NMR spectra. All ligands exhibit the correct molecular ion peak in the HR-FAB mass spectra.

Extraction

In order to study whether CMP(O) ligands **9–15** and malonamides **17** and **18** are good ionophores for actinide/lanthanide separation, spike extraction tests were performed with Am^{3+} and Eu^{3+} as model cations. The extractions were carried out with 1,1,2,2-tetrachloroethane (TCE) and *n*-octanol as the organic phase at two nitric acid concentrations.[18]

From Table 1 and Fig. 1 it is clear that in the case of the C-pivot CMPO ligands **9b–d** there is a positive influence of the *N*-alkyl substituents on the *D* (distribution) coefficients for both cations, solvents, and acidities. With CMPO ligand **9b** in *n*-octanol there is an increase in *D* of 90 times compared with **9a**. Apparently, in **9e** the *N*-substituent is too crowded, since there is hardly any effect on the *D* coefficient. In the cases of **9c,d** it is assumed that the lipophilic alkyl chains enhance the solubility of the complexes and consequently give rise to a better extraction efficiency. For all ligands **9a–e** the separation factors are ~2 in TCE and 2.5 in *n*-octanol, values that are also reported for other CMPO ligands.[3,4]

Table 1 Distribution coefficients for CMPO ligands **9a–e**, **10a,b**, **11**, and **12**

Ligand		Solvent and HNO_3 concentration			
		TCE[b]	*n*-Octanol		
	Concentration/M	1 M	1 M	3 M	
9a[a]	1.4×10^{-2}	Am 0.51	Am 6.9×10^{-3}	2.1×10^{-2}	
		Eu 0.26	Eu 3.6×10^{-3}	1.3×10^{-2}	
9b	4.9×10^{-2}	Am 1.4	Am 0.21	1.7	
		Eu 0.68	Eu 0.09	0.71	
9c	4.4×10^{-2}	Am 1.1	Am 0.14	0.87	
		Eu 0.50	Eu 0.06	0.41	
9d	4.6×10^{-2}	Am 3.2	Am 0.42	3.7	
		Eu 1.5	Eu 0.17	1.5	
9e	3.2×10^{-2}	Am 0.18	Am 2.9×10^{-2}	0.13	
		Eu 8.7×10^{-2}	Eu 2.0×10^{-2}	7.5×10^{-2}	
10a	3.5×10^{-2}	Am 2.0	Am Not soluble		
		Eu 1.2	Eu		
10b	3.1×10^{-2}	Am 1.0	Am 1.28	1.32	
		Eu 0.7	Eu 0.66	0.93	
11	3.0×10^{-2}	Am 0.02	Am 4.8×10^{-3}	0.02	
		Eu 0.01	Eu 6.3×10^{-3}	0.02	
12	3.2×10^{-2}	Am 0.16	Am 0.21	0.05	
		Eu 0.07	Eu 0.11	0.03	

[a] Data from ref. 9. [b] Data for 3 M HNO_3 are presented in Fig. 1.

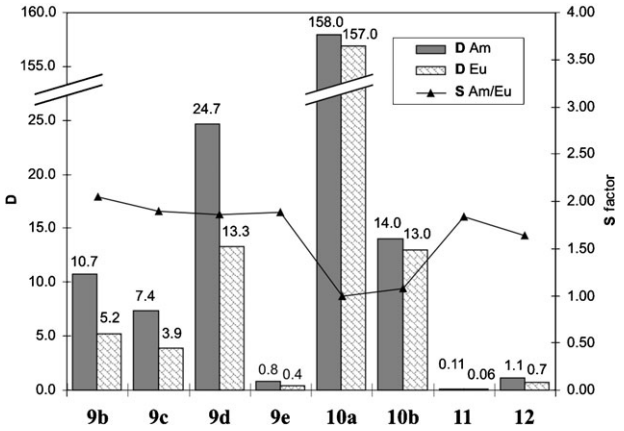


Fig. 1 Distribution and selectivity coefficients of CMPO ligands in 3 M HNO_3–TCE (c_L as in Table 1).

The trialkylbenzene platform-based CMPO ligands **10a,b** have larger *D* coefficients (up to ~200 times higher for **10b** in *n*-octanol) than the corresponding C-pivot analogue **9a**. Apparently, the preorganization on the same face of the molecule is beneficial. Unfortunately, there is hardly any Am^{3+}/Eu^{3+} selectivity. In this series *N*-alkylation with 3-pentyl chains gives rise to much smaller *D* coefficients. This is probably caused by the enlarged stiffness of the chelating groups, which is not compensated by a flexible spacer (here only 1 or 2 C atoms) between the platform and the CMPO group. A similar effect has been observed for calix[4]arene-based CMPO ligands[3e] with the ligating arms directly introduced at the benzene rings of the calix[4]arene.

In general, the CMP ligands are less effective than the corresponding CMPO derivatives (Table 2). The extraction behavior of the C-pivot CMP ligands **13b–d** shows more or less the same trend as the corresponding CMPO ligands **9b–d** upon substitution of the *N*-atom with different alkyl chains. In this series CMP ligands **13b** and **13d** are the most efficient at 3 M HNO_3 in TCE. Attachment of three CMP chelating groups to a trialkylbenzene platform (**14a,b**) in general gave rise to rather low *D* coefficients.

Mixed ligand **15**, containing two CMPO and one CMP moiety does not show improved extraction properties. Its *D* coefficients are even slightly lower than the averaged value of those of the corresponding CMPO ligand **9d** and CMP ligand **13d**.

Tripodal malonamides **17a–d** and **18a,b** show low distribution values similar to those for the simple non-preorganized malonamides.[7,12d] In the case of the C-pivot ligands **17a–d** *N*-alkylation has a negative effect on the extraction behavior, the malonamides **17b–d** hardly extract (Table 3). Possibly six secondary amide groups generate a highly rigid structure and as a result the ligand is not able to fold properly around a metal ion. For the ligands **17a** and **18a,b** the *D* coefficients are higher in *n*-octanol than in TCE. Apparently,

Table 2 Distribution coefficients for CMP ligands **13a–d**, **14a,b**, and mixed ligand **15**

Ligand		Solvent and HNO_3 concentration					
		TCE			*n*-Octanol		
	Concentration/M		1 M	3 M		1 M	3 M
13a[a]	1.5×10^{-2}	Am	Precipitate	Precipitate	Am	$<10^{-3}$	1.0×10^{-2}
		Eu	Precipitate	Precipitate	Eu	$<10^{-3}$	9.9×10^{-3}
13b	7.8×10^{-2}	Am	1.5×10^{-2}	0.3	Am	8.6×10^{-3}	4.0×10^{-2}
		Eu	1.4×10^{-2}	0.2	Eu	5.9×10^{-3}	2.8×10^{-2}
13c	5.1×10^{-2}	Am	7.5×10^{-3}	0.1	Am	4.6×10^{-3}	2.4×10^{-2}
		Eu	4.9×10^{-3}	0.12	Eu	3.3×10^{-3}	1.8×10^{-2}
13d	5.5×10^{-2}	Am	1.8×10^{-2}	0.42	Am	6.3×10^{-3}	3.3×10^{-2}
		Eu	2.0×10^{-2}	0.54	Eu	4.4×10^{-3}	2.5×10^{-2}
14a	4.5×10^{-2}	Am	$<10^{-3}$	2.8×10^{-2}	Am	3.2×10^{-3}	2.0×10^{-2}
		Eu	$<10^{-3}$	5.2×10^{-2}	Eu	4.1×10^{-3}	4.8×10^{-2}
14b	7.2×10^{-2}	Am	4.0×10^{-3}	0.11	Am	1.8×10^{-2}	3.6×10^{-2}
		Eu	3.3×10^{-3}	8.1×10^{-2}	Eu	1.3×10^{-2}	2.5×10^{-2}
15	3.2×10^{-2}	Am	0.67	5.0	Am	0.03	0.26
		Eu	0.39	3.5	Eu	0.02	0.19

[a] Data from ref. 9.

Table 3 Distribution coefficients for malonamide ligands **17a–d** and **18a,b**

Ligand		Solvent and HNO_3 concentration					
		TCE			*n*-Octanol		
	Concentration/M		1 M	3 M		1 M	3 M
17a	9.9×10^{-2}	Am	1.1×10^{-2}	0.18	Am	0.17	0.47
		Eu	8.5×10^{-3}	0.16	Eu	0.13	0.41
17b	6.2×10^{-2}	Am	$<10^{-3}$	5.6×10^{-3}	Am	4.6×10^{-3}	1.6×10^{-2}
		Eu	$<10^{-3}$	5.6×10^{-3}	Eu	3.3×10^{-3}	1.3×10^{-2}
17c	4.6×10^{-2}	Am	$<10^{-3}$	3.1×10^{-3}	Am	3.4×10^{-3}	1.2×10^{-2}
		Eu	$<10^{-3}$	4.2×10^{-3}	Eu	2.2×10^{-3}	1.1×10^{-2}
17d	6.0×10^{-2}	Am	1.3×10^{-3}	8.9×10^{-3}	Am	1.7×10^{-3}	7.6×10^{-3}
		Eu	1.2×10^{-3}	8.9×10^{-3}	Eu	1.1×10^{-3}	6.7×10^{-3}
18a	5.5×10^{-2}	Am	$<10^{-3}$	2.0×10^{-2}	Am	0.12	0.26
		Eu	$<10^{-3}$	5.3×10^{-2}	Eu	9.1×10^{-2}	0.26
18b	4.3×10^{-2}	Am	$<10^{-3}$	9.5×10^{-3}	Am	0.12	0.25
		Eu	$<10^{-3}$	1.8×10^{-2}	Eu	0.11	0.23

intramolecular H-bonding is disfavored in the polar *n*-octanol resulting in a better extraction efficiency.

Using C-pivot CMPO ligands **9b,d** the extraction rate was studied. In both cases the extraction is a fast process with the equilibrium reached in less than 5 min in micro-tubes shaken with a vortex device. For all ligands the distribution coefficients are higher at 3 M than at 1 M nitric acid. This allows the use of diluted HNO_3 to reverse the extraction process and to "strip" the organic phase from the metal ions, and the recovery of the ligand. In the case of ligands **9b,d** stripping of the complexes was performed with 0.1 M HNO_3 in *n*-octanol within 5 min.

Potentiometric measurements

Selected C-pivot tripodal CMPO (**9b–d**), CMP (**13b–d**), and malonamide (**17a–d**) ligands were examined for their complexing ability using the potentiometric so-called "sandwich method" and in polymeric membrane ion-selective electrodes. Stability constants and selectivity coefficients for Na^+, K^+, Mg^{2+}, Ca^{2+}, Cu^{2+}, Pb^{2+} or UO_2^{2+} are summarized in Tables 4 and 5, respectively.

To simplify the discussion and to show the influence of functional groups (donor atoms) on the complexing capability of the examined ligands, three *N*-substituted compounds with an octyl chain were selected (**9c**, **13c**, and **17c**).

From Table 4 it is clear that all the examined ligands form the strongest complexes with the uranyl cation. This behavior can be explained by Pearson's soft–hard acid and base theory. All ligands possess hard oxygen atoms in the ligating centers that assures a strong interaction with the hard UO_2^{2+} cation.

Ligand **9c**, representing the CMPO series, exhibits the highest complexing ability towards all studied cations. Just as for the *D* coefficients for Am^{3+} and Eu^{3+}, the complex formation constants are higher for ligands with phenyl groups (CMPO) than for those possessing ethoxy moieties (CMP). Ligand **17c**, as a representative of the malonamide group, gave the weakest complexes. However, it exhibits a higher preference toward Cu^{2+} ($\log \beta_{ILn} = 17.3$) than CMP ligand **13c** ($\log \beta_{ILn} = 16.3$). It is well known that metal cations interact more strongly with ligands, that, besides P, O, N atoms, also possess aromatic rings. The strong complexation properties of **9c** can be related to the presence of six aromatic rings and possibly some metal–ligand aromatic interactions (MLACπ).[19]

The CMPO (**9c**), CMP (**13c**), and malonamide (**17c**) derivatives were examined as potential ligands in 2-nitrophenyl octyl ether (*o*-NPOE)–PVC membranes in terms of electrode selectivities. The logarithmic values of the selectivity coefficients calculated for Pb^{2+} as the primary cation are presented in Fig. 2. It is well known that selectivity coefficients for neutral carrier-based membranes are mainly related to the stability constants of ion–ionophore complexes in the membrane.[20]

The results reveal that the ionophores **9c**, **13c**, and **17c** induce a selectivity that differs from the so-called Hofmeister

Table 4 Formal complex formation constants[a] $\log \beta_{ILn}$ for ligands **9a–d**, **13a–d**, and **17a–d**

	Ligand											
	CMPO				CMP				Malonamides			
Cation	**9a**[b]	**9b**	**9c**	**9d**	**13a**[b]	**13b**	**13c**	**13d**	**17a**	**17b**	**17c**	**17d**
Na^+	8.4	8.4	8.4	8.5	4.8	5.4	8.1	7.5	3.6	6.5	6.6	6.9
K^+	—	7.4	6.0	6.1	—	4.2	6.0	5.3	2.0	4.9	4.9	4.5
Mg^{2+}	16.4	19.8	19.8	19.0	—	13.3	16.2	16.2	10.6	15.5	15.8	16.6
Ca^{2+}	17	20.5	20.9	21.5	—	14.0	18.3	16.8	8.5	15.8	15.8	16.5
Cu^{2+}	19.1	20.5	20.0	20.1	11.8	13.0	16.3	15.0	11.7	17.2	17.3	16.8
Pb^{2+}	17.4	21.3	20.7	21.5	9.0	14.8	18.1	16.3	10.5	16.7	16.8	16.6
UO_2^{2+}	21.5	23.1	23.1	23.1	12.3	15.9	19.2	17.4	12.5	19.4	19.3	19.5

[a] Standard deviations <0.3 (from at least three replicate measurements). [b] Data from ref. 9.

Table 5 Selectivity coefficients,[a] log $K^{pot}_{Pd,J}$, for electrodes with membranes containing ligands **9a–d**, **13a–d**, and **17a–d**

	Ligand											
	CMPO				CMP				Malonamides			
Cation	**9a**[b]	**9b**	**9c**	**9d**	**13a**[b]	**13b**	**13c**	**13d**	**17a**	**17b**	**17c**	**17d**
Na^+	−4.6	−5.8	−5.7	−6.0	−2.3	−3.5	−3.1	−3.6	−3.0	−3.7	−3.8	−3.0
K^+	—	−6.6	−6.7	−6.4	—	−5.9	−4.1	−5.1	−1.8	−4.1	−3.8	−3.8
Mg^{2+}	—	−2.5	−2.6	−2.3	—	−2.3	−2.2	−2.2	−0.8	−2.3	−2.5	−2.5
Ca^{2+}	—	−1.4	−1.1	−1.0	—	−1.2	−0.9	−0.7	−1.2	−1.4	−1.4	−1.4
Cu^{2+}	−0.9	−2.0	−2.0	−1.3	−1.3	−2.3	−2.7	−2.3	−0.5	−0.5	−0.7	−0.8
Pb^{2+}	0	0	0	0	0	0	0	0	0	0	0	0
UO_2^{2+}	4.1	2.5	2.7	2.2	2.4	1.0	1.0	1.3	1.9	2.8	2.8	2.7

[a] Standard deviations <0.3 (from at least three replicate measurements). [b] Data from ref. 9.

series.[21,22] As expected based on the stability constants (Table 4), the electrodes show an enhanced selectivity towards UO_2^{2+}. In the case of compound **9c** the interaction with the uranyl cation is so strong (log $\beta_{ILn} = 23.1$) that the electrode had an upper detection limit ($c = 10^{-3}$ M). Above this concentration flattening of the calibration curve occurs, which can be explained by coextraction of anions from the aqueous sample solution. However, in the 10^{-5}–10^{-3} M concentration range a linear response with a Nernstian slope can be observed. Since compounds **13c** and **17c** form weaker complexes with UO_2^{2+}, the corresponding electrodes give a linear response in the whole UO_2^{2+} concentration range studied (Fig. 3).

The incorporation of these ligands into a polymeric membrane leads to considerable changes in the selectivity for Pb^{2+} over K^+ and Na^+. It suggests a very weak interaction between the ligands and K^+, Na^+ in comparison to the electrodes containing a membrane with an ion-exchanger (KTFPB). The smallest selectivity changes are observed for Ca^{2+} and Cu^{2+}, which can be attributed to the comparable stability constants of the Pb^{2+}, Ca^{2+}, and Cu^{2+} complexes (Tables 4 and 5).

It should be pointed out that membranes doped with CMPO ligand **9c** exhibit a better differentiation of the selectivity coefficients than those doped with CMP ligand **13c** ($\log K^{pot}_{Pb,UO_2} \approx 3$ and $\log K^{pot}_{Pb,Na} \approx -6$ for **9c**; $\log K^{pot}_{Pb,UO_2} \approx 1$ and $\log K^{pot}_{Pb,Na} \approx -3$ for **13c**). Taking into account the low K^+ and Na^+ selectivity coefficients in the case of the electrode with CMPO **9c** doped membrane, this electrode may be very useful for the determination of UO_2^{2+} in the presence of high levels of alkali metal cations.

Beside the influence of the different types of ligands (CMPO, CMP, malonamide) on the complex stability constants and the selectivity coefficients, the influence of minor structural changes within the ligand groups was also studied. In all cases ligands substituted with alkyl chains (**9b–d**, **13b–d**, and **17b–c**) form stronger complexes with the examined cations than those having an H atom in the same position (**9a**, **13a**, **17a**, respectively). However, the length and the structure of an alkyl chain only have a slight influence on the strength of the interaction between ligands and metal cations. Whereas CMPO and CMP ligands in general maintain the same behavior within the series of compounds for both extraction and potentiometric studies, the malonamides behave differently. In extraction experiments the *N*-substituted malonamides **17b–d** revealed almost no extraction abilities, while in the potentiometric measurements they formed more stable complexes than **17a**.

Where the selectivity coefficients in the malonamide series are concerned, ionophore **17a** does not discriminate against K^+ so much as the other ions (Fig. 4). In line with the influence

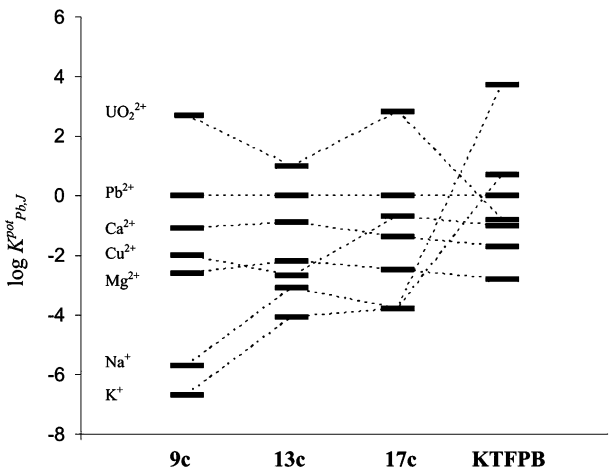


Fig. 2 Selectivity coefficients for electrodes with membranes based on compounds **9c**, **13c**, and **17c** and with only tetrakis[3,4-bis(trifluoromethyl)phenyl]borate (KTFPB).

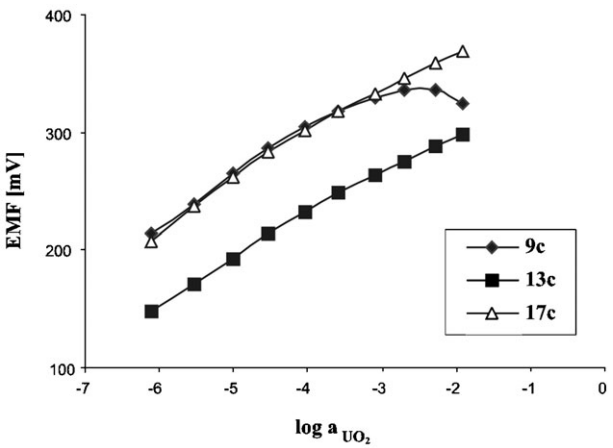


Fig. 3 Calibration curves of electrodes doped with compounds **9c**, **13c**, and **17c** towards UO_2^{2+}.

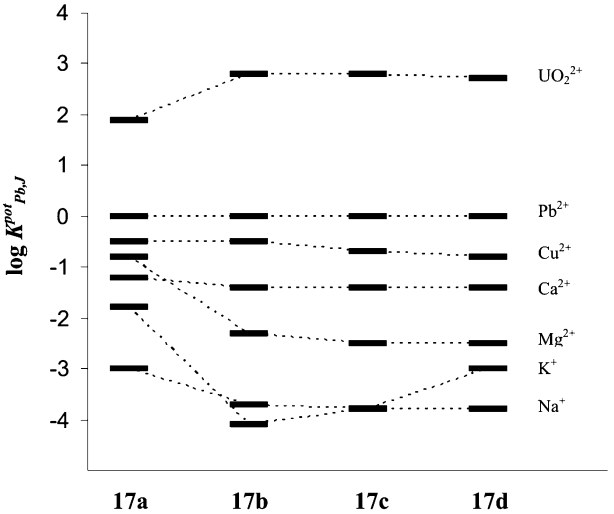


Fig. 4 Selectivity coefficients for electrodes with membranes based on compounds **17a–d**.

of the alkyl chains on the stability constants in the case of the *N*-substituted malonamides **17b–d** the selectivity coefficients only show small differences.

From Table 4 it is clear that in the CMPO ligand series neither length nor shape of the alkyl substituent have any influence on the stability constants. In the CMP ligand series the attachment of a long linear alkyl chain (**13c**) leads to larger stability constants compared to **13b** or **13d**, having a short and branched alkyl chain, respectively. The trend is opposite to that of the extraction results.

There are hardly differences between the selectivity coefficients of the short (C4 and C5) and long (C8) alkyl-substituted CMPO and CMP ligands (Table 5). Despite the differences in the stability constants between the alkyl-substituted CMP ligands **13b–d**, the selectivity coefficients of electrodes doped with these ligands are almost identical. The reason for this behavior is that the relative differences between the stability constants of the complexes of ligands **13c** with the different metal cations (for instance log $\beta_{ILn} = 16.3$ for Cu^{2+} and log $\beta_{ILn} = 19.2$ for UO_2^{2+}, $\Delta \log \beta_{ILn} = 2.9$) are very similar to the differences in the stability constants of the corresponding complexes of ligand **13b** (log $\beta_{ILn} = 13.0$ for Cu^{2+} and log $\beta_{ILn} = 15.9$ for UO_2^{2+}) or **13d** (log $\beta_{ILn} = 14.9$ for Cu^{2+} and log $\beta_{ILn} = 17.4$ for UO_2^{2+}) with the same cations.

Conclusions

Series of tripodal ligands based on the C-pivot and trialkylbenzene platforms bearing (*N*-substituted) CMP(O) and malonamide moieties were prepared. In general, the C-pivot CMP(O) ligands **9a–e** and **13a–d** show a positive effect of the *N*-alkyl substituent on the *D* coefficients for Am^{3+} and Eu^{3+} extraction. The trialkylbenzene CMPO ligands **10a,b** have considerably larger *D* coefficients than the corresponding C-pivot analogues, probably due to preorganization of the ligating sites on one face of the platform. In this series *N*-alkylation with 3-pentyl chains negatively influences the *D* coefficients probably due to the enlarged stiffness of the ligating sites which is not compensated for by a flexible spacer between the platform and the CMPO moieties. For the malonamides **17a–d** *N*-alkylation has a negative effect on the extraction behavior, possibly because **17b–d** are too rigid to properly fold around a metal cation.

In general, there is good coherence between the extraction data and those of the potentiometric measurements, except in the case of the *N*-substituted malonamides.

Experimental

Synthesis

^1H and ^{13}C NMR spectra were recorded on a Varian Unity INOVA 300 MHz and a Varian Unity 400 WB NMR spectrometer, respectively. Residual solvent protons were used as an internal standard and chemical shifts are given in ppm relative to tetramethylsilane (TMS). Fast atom bombardment (FAB) mass spectra were measured on a Finnigan MAT 90 spectrometer using *m*-nitrobenzyl alcohol (NBA) as a matrix. Elemental analyses were carried out using a 1106 Carlo-Erba Strumentazione element analyser. All solvents were purified by standard procedures. All other chemicals were analytically pure and were used without further purification. Melting points (uncorrected) of all compounds were obtained on a Reichert melting point apparatus.

General procedure for the synthesis of C-pivot amines 3b–e. A mixture of nitrile **1**, the appropriate amine **2b–e** (30–50 mL) in MeOH (10 mL) and 10% Pd–C as a catalyst was sealed in an autoclave and vigorously stirred under hydrogen (8 bar) for 48 h at room temperature. After removal of the catalyst by filtration through a layer of Celite, the solvent was evaporated to give the pure product.

C-Pivot tripodal amine **3b**. Reaction of nitrile **1** (2.24 g, 7.64 mmol), amine **2b** (50 mL, 505 mmol) and 10% Pd–C (1.43 g) as a catalyst gave **3b** as a pale yellow oil (3.57 g, 99%). δ_H(300 MHz; $CDCl_3$) 3.44 (6 H, t, *J* 6.2, $OCH_2CH_2CH_2N$), 3.25 (6 H, s, CCH_2O), 2.69 (6 H, t, *J* 6.7, $OCH_2CH_2CH_2N$), 2.60 (6 H, t, *J* 7.4, $NCH_2CH_2CH_2CH_3$), 1.74 (6 H, quintet, *J* 6.7 $OCH_2CH_2CH_2N$), 1.28–1.62 (17 H, m, $NCH_2CH_2CH_2CH_3$, CCH_2CH_3, NH), 0.91 (9 H, t, *J* 7.2, $NCH_2CH_2CH_2CH_3$), 0.83 (3 H, t, *J* 7.5, CCH_2CH_3); δ_C(75 MHz; $CDCl_3$) 71.7, 70.4, 50.1, 48.0, 43.3, 32.6, 30.4, 23.5, 20.8, 14.2, 7.9; *m*/*z* (FAB) 474.4597 ($[M + H]^+$ $C_{27}H_{60}N_3O_3$ requires 474.4635).

C-Pivot tripodal amine **3c**. Reaction of nitrile **1** (1.76 g, 5.99 mmol), amine **2c** (40 mL, 242 mmol) and 10% Pd–C (1.16 g) as a catalyst gave **3c** as an oil (3.72 g, 97%). δ_H(300 MHz; $CDCl_3$) 3.44 (6 H, t, *J* 6.2, $OCH_2CH_2CH_2N$), 3.25 (6 H, s, CCH_2O), 2.69 (6 H, t, *J* 6.9, $OCH_2CH_2CH_2N$), 2.59 (6 H, t, *J* 7.1, $NCH_2C_6H_{12}CH_3$), 1.74 (6 H, quintet, *J* 6.5, $OCH_2CH_2CH_2N$), 1.20–1.55 (41 H, m, $NCH_2C_6H_{12}CH_3$, CCH_2CH_3, NH), 0.81–0.91 (12 H, m, $NCH_2C_6H_{12}CH_3$, CCH_2CH_3); δ_C(75 MHz; $CDCl_3$) 71.7, 70.4, 50.4, 48.0, 43.3, 32.0, 30.5, 30.3, 29.8, 29.5, 27.7, 23.5, 22.8, 14.2, 7.9; *m*/*z* (FAB) 642.6481 ($[M + H]^+$ $C_{39}H_{84}N_3O_3$ requires 642.6513).

C-Pivot tripodal amine **3d**. Reaction of nitrile **1** (2.11 g, 7.19 mmol), amine **2d** (25 g, 291 mmol) and 10% Pd–C (0.99 g) as a catalyst gave **3d** as an oil (3.59 g, 97%). δ_H(300 MHz; $CDCl_3$) 3.44 (6 H, t, *J* 6.0, $OCH_2CH_2CH_2N$), 3.26 (6 H, s, CCH_2O), 2.66 (6 H, t, *J* 7.0, $OCH_2CH_2CH_2N$), 2.37 (3 H, quintet, *J* 6.3, $NCH(CH_2CH_3)_2$), 1.73 (6 H, quintet, *J* 6.5, $OCH_2CH_2CH_2N$), 1.35–1.48 (14 H, m, CH_2CH_3, $NCH(CH_2CH_3)_2$), 0.88 (18 H, t, *J* 7.5, $NCH(CH_2CH_3)_2$), 0.83 (3 H, t, *J* 7.8, CH_2CH_3); δ_C(75 MHz; $CDCl_3$) 71.8, 70.4, 60.3, 44.8, 43.3, 30.7, 26.1, 23.5, 10.1, 8.0; *m*/*z* (FAB) 516.5127 ($[M + H]^+$ $C_{30}H_{66}N_3O_3$ requires 516.5104).

C-Pivot tripodal amine **3e**. Reaction of nitrile **1** (1.33 g, 4.54 mmol), amine **2e** (30 mL, 256 mmol) and 10% Pd–C (0.82 g) as a catalyst gave **3e** as an oil (2.07 g, 88%). δ_H(300 MHz; $CDCl_3$) 3.42 (6 H, t, *J* 6.0, $OCH_2CH_2CH_2N$), 3.25 (6 H, s, CCH_2O), 2.56 (6 H, t, *J* 6.7, $OCH_2CH_2CH_2N$), 1.68 (6 H, quintet, *J* 6.0, $OCH_2CH_2CH_2N$), 1.39 (8 H, q, *J* 7.4, CH_2CH_3), 1.01 (18 H, s, $N(C(CH_3)_2)$, 0.83 (12 H, t, *J* 7.4, CH_2CH_3); δ_C(75 MHz; $CDCl_3$) 71.8, 70.5, 52.5, 43.3, 39.8, 33.3, 31.3, 26.8, 23.5, 8.5, 8.0; *m*/*z* (FAB) 516.5111 ($[M + H]^+$ $C_{30}H_{67}N_3O_3$ requires 516.5104).

Benzene platform tripodal amine 5. A solution of tribromide **4** (2.12 g, 4.81 mmol) and amine **2d** (10 mL, 86 mmol) in THF (100 mL) was stirred at 50 °C for 16 h. After removal of the solvent and the excess of amine the resulting oil was dissolved in $CHCl_3$ (100 mL) and washed with 1 M NaOH (20 mL) and H_2O (3 × 20 mL). The solvent was evaporated to afford **5** as an oil (2.21 g, 100%). δ_H(300 MHz; $CDCl_3$) 3.68 (6 H, s, $PhCH_2NHC$), 2.83 (6 H, q, *J* 7.4, $PhCH_2CH_3$), 2.48 (3 H, quintet, *J* 5.7, $NHCH(CH_2CH_3)_2$), 1.42–1.56 (12 H, m, $NHCH(CH_2CH_3)_2$), 1.24 (9 H, t, *J* 7.4, $PhCH_2CH_3$), 0.92 (18 H, t, *J* 7.5, $NHCH(CH_2CH_3)_2$); δ_C(75 MHz; $CDCl_3$) 142.4, 134.7, 62.0, 46.0, 26.0, 22.8, 17.4, 10.2; *m*/*z* (FAB) 460.4531 ($[M + H]^+$ $C_{30}H_{58}N_3$ requires 460.4631).

Benzene platform tripodal amine 7a. A mixture of nitrile **6a** (2.75 g, 11.6 mmol) and Raney-Co (1.3 g; suspension in water) in methanol saturated with NH_3 (50 mL) was sealed in an autoclave and left with stirring under hydrogen (8 bar) for 16 h at room temperature. The catalyst was removed by filtration through a layer of Celite, whereupon the solvent was evaporated to yield pure **7a** as an oil (2.78 g, 96%). δ_H(300 MHz; $CDCl_3$) 2.83 (12 H, br, $PhCH_2CH_2NH_2$), 2.32 (9 H, s, CH_3), 1.14 (6 H, br s, NH_2); δ_C(75 MHz; $CDCl_3$) 134.7, 133.2, 42.0, 35.5, 16.4; *m*/*z* (FAB) 250.2282 ($[M + H]^+$ $C_{15}H_{28}N_3$ requires 250.2283).

Benzene platform tripodal amine 7b. A mixture of nitrile **6b** (1.70 g, 6.1 mmol) and Raney-Co (1.0 g; suspension in water) in methanol saturated with NH_3 (50 mL) was sealed in an autoclave and left with stirring under hydrogen (8 bar) for 16 h at room temperature. The catalyst was removed by filtration through a layer of Celite, whereupon the solvent was evaporated to yield pure **7b** as an oil (1.77 g, 99%). δ_H(300 MHz; $CDCl_3$) 2.82–2.88, 2.72–2.78 (12 H, m, $PhCH_2CH_2NH_2$), 2.65 (6 H, q, *J* 7.5, CH_2CH_3), 1.29 (6 H, br s, NH_2), 1.19 (9 H, t, *J* 7.5, CH_2CH_3); δ_C(75 MHz; $CDCl_3$) 139.7, 133.5, 43.9, 34.2, 22.9, 16.0; *m*/*z* (FAB) 292.2731 ($[M + H]^+$ $C_{18}H_{34}N_3$ requires 292.2753).

Benzene platform tripodal amine 8. A mixture of nitrile **6b** (0.472 g, 1.69 mmol), amine **2d** (19 g, 218 mmol), and 10% Pd–C (0.5 g) as a catalyst in MeOH (10 mL) was sealed in an autoclave and left with stirring under hydrogen (100 bar) for 48 h at 70 °C. The catalyst was removed by filtration through a layer of Celite, whereupon the solvent was evaporated to yield pure **8** as an oil (0.761 g, 90%). δ_H(300 MHz; $CDCl_3$) 2.61–2.82 (18 H, m, NCH_2CH_2Ph, CH_3CH_2Ph), 2.42 (3 H, quintet, *J* 6.0, $NCH(CH_2CH_3)_2$), 1.40–1.50 (12 H, m, $NCH(CH_2CH_3)_2$), 1.22 (9 H, t, *J* 7.5, $PhCH_2CH_3$), 0.90 (18 H, t, *J* 7.4, $NHCH(CH_2CH_3)_2$); δ_C(75 MHz; $CDCl_3$) 139.8, 133.8, 60.5, 48.6, 31.0, 26.2, 22.8, 16.1, 10.1; *m*/*z* (FAB) 502.5125 ($[M + H]^+$ $C_{33}H_{64}N_3$ requires 502.5100).

General procedure for the preparation of CMPO 9b–e, 10a,b, 11, 12 and CMP ligands 13b–d, 14a,b, and mixed ligand 15. To a suspension of the appropriate tripodal amine and dry K_2CO_3 in dry CH_2Cl_2 (100 mL) chloroacetyl chloride was added at 0 °C followed by slow addition (2 h) of a stoichiometric amount of water at that temperature. Subsequently, the mixture was slowly warmed to room temperature and stirred for 16 h. Upon filtration and evaporation of the solvent the resulting yellow oil was dissolved in diphenyl ethyl phosphinite (for CMPO) or triethyl phosphite (for CMP). The solution was quickly warmed to 100 °C and then slowly to 140 °C over a period of 4 h. After cooling of the mixture, the product was precipitated by addition of diisopropyl ether (20 mL). The crude product was purified by column chromatography (SiO_2; CH_2Cl_2–MeOH = 25 : 1 → 11 : 1) to give the pure compounds as oils, except for **10a,b**.

CMPO ligand **9b**. Reaction of tripodal amine **3b** (1.25 g, 2.63 mmol), chloroacetyl chloride (1.9 mL, 23.9 mmol) and K_2CO_3 (3.5 g, 25 mmol) and subsequently diphenyl ethyl phosphinite (2.3 mL, 10.6 mmol) gave ligand **9b** (2.72 g, 86%). δ_H(300 MHz; $CDCl_3$) 7.80–7.88 (12 H, m, Ph), 7.39–7.53 (18 H, m, Ph), 3.07–3.60 (30 H, m, CH_2O, CH_2N, $CH_2P(O)$), 1.64–1.76, 1.42–1.58, 1.08–1.35 (20 H, m, CH_3CH_2C, $CH_3CH_2CH_2CH_2N$, $OCH_2CH_2CH_2N$), 0.65–0.92 (12 H, m, CH_3); δ_C(75 MHz; $CDCl_3$) 165.1, 133.5, 133.4, 132.2, 131.5, 131.4, 128.8, 128.6, 71.6, 68.9, 68.0, 49.4, 46.2, 46.0, 44.2, 43.2, 38.9, 38.6, 38.0, 37.7, 31.3, 29.8, 29.2, 28.1, 23.5, 20.3, 14.1, 8.0; *m*/*z* (FAB) 1200.6077 ($[M + H]^+$ $C_{69}H_{93}N_3O_9P_3$ requires 1200.6125).

CMPO ligand **9c**. Reaction of tripodal amine **3c** (0.88 g, 1.37 mmol), chloroacetyl chloride (0.9 mL, 11.4 mmol) and K_2CO_3 (1.8 g, 13 mmol) and subsequently diphenyl ethyl phosphinite (2.0 mL, 8.7 mmol) gave ligand **9c** (1.66 g, 88%). δ_H(300 MHz; $CDCl_3$) 7.80–7.87 (12 H, m, Ph), 7.38–7.54 (18 H, m, Ph), 3.05–3.59 (30 H, m, CH_2O, CH_2N, $CH_2P(O)$), 1.64–1.74, 1.42–1.56, 1.08–1.32 (44 H, m, CH_3CH_2C, $CH_3C_6H_{12}CH_2N$, $OCH_2CH_2CH_2N$), 0.85 (9 H, t, *J* 6.7, $CH_3C_7H_{14}N$) 0.64–0.78 (3 H, m, CH_3CH_2C); δ_C(75 MHz; $CDCl_3$) 165.0, 133.5, 133.4, 132.2, 131.5, 131.3, 128.8, 128.6, 71.7, 68.9, 68.0, 49.7, 46.4, 46.0, 44.1, 43.2, 38.5, 38.0, 32.0, 31.9, 29.6, 29.4, 29.2, 28.1,

27.7, 27.1, 27.0, 22.8, 22.7, 14.2, 8.0; *m*/*z* (FAB) 1406.7613 ($[M + K]^+$ $C_{81}H_{116}N_3O_9P_3K$ requires 1406.7562).

CMPO ligand **9d**. Reaction of tripodal amine **3d** (0.93 g, 1.80 mmol), chloroacetyl chloride (1.3 mL, 16.2 mmol) and K_2CO_3 (2.8 g, 20 mmol) and subsequently diphenyl ethyl phosphinite (2.5 mL, 11.6 mmol) gave ligand **9d** (1.87 g, 83%). δ_H(300 MHz; $CDCl_3$) 7.76–7.89 (12 H, m, Ph), 7.39–7.47 (18 H, m, Ph), 3.98–4.08, 3.56–3.74, 3.03–3.42 (27 H, m, CH_2O, CH_2NCH, $CH_2P(O)$), 1.72–1.84, 1.18–1.62 (20 H, m, CH_3CH_2C, $NCH(CH_2CH_3)_2$, $OCH_2CH_2CH_2N$), 0.62–0.90 (21 H, m, CH_3); δ_C(75 MHz; $CDCl_3$) 166.2, 166.1, 166.0, 165.9, 133.8, 133.6, 132.4, 132.2, 132.1, 131.5, 131.4, 128.7, 128.6, 71.6, 69.7, 68.7, 62.3, 58.8, 53.6, 43.3, 42.1, 39.6, 38.5, 38.2, 31.4, 29.1, 26.5, 26.0, 23.5, 11.3, 8.0; *m*/*z* (FAB) 1280.6150 ($[M + K]^+$ $C_{72}H_{98}N_3O_9P_3K$ requires 1280.6153).

CMPO ligand **9e**. Reaction of tripodal amine **3e** (0.86 g, 1.67 mmol), chloroacetyl chloride (1.2 mL, 15 mmol) and K_2CO_3 (2.2 g, 16 mmol) and subsequently diphenyl ethyl phosphinite (1.5 mL, 6.9 mmol) gave ligand **9e** (0.27 g, 13%). δ_H(300 MHz; $CDCl_3$) 7.81–7.86 (12 H, m, Ph), 7.40–7.52 (18 H, m, Ph), 3.65 (6 H, d, J_{P-H} 15.3, $CH_2P(O)$), 3.20–3.60 (12 H, m, $OCH_2CH_2CH_2N$), 3.06 (6 H, s, CCH_2O), 2.20–2.32 (6 H, m, $OCH_2CH_2CH_2N$), 1.68–1.71 (8 H, m, CH_2CH_3), 1.26 (18 H, s, CCH_3), 0.65 (12 H, t, *J* 7.4, CH_2CH_3); δ_C(75 MHz; $CDCl_3$) 165.7, 165.6, 133.8, 132.5, 131.9, 131.5, 131.3, 128.7, 128.5, 71.7, 68.6, 61.4, 44.2, 43.2, 41.0, 40.2, 32.5, 32.1, 27.0, 23.2, 8.9, 8.0; *m*/*z* (FAB) 1280.5921 ($[M + K]^+$ $C_{72}H_{98}N_3O_9P_3K$ requires 1280.6153).

CMPO ligand **10a**. Reaction of tripodal amine **7a** (0.67 g, 2.69 mmol), chloroacetyl chloride (2.03 mL, 25.6 mmol) and K_2CO_3 (3.6 g, 26 mmol) and subsequently diphenyl ethyl phosphinite (2 mL, 9.3 mmol) gave ligand **10a** (1.18 g, 45%) (Found: C, 68.29; H, 5.99; N, 3.80. Calc. for $C_{57}H_{60}N_3O_6P_3 \cdot 0.33CH_2Cl_2$: C, 68.58; H, 6.09; N, 4.18%); mp > 221 °C (melting with decomposition); δ_H(300 MHz; $CDCl_3$) 7.71–7.78, 7.42–7.58 (33 H, m, NH, Ph), 3.31 (6 H, d, J_{H-P} 12.3, $C(O)CH_2P(O)$), 3.15–3.23, 2.64–2.70 (12 H, m, $PhCH_2CH_2N$), 2.21 (9 H, s, CH_3); δ_C(75 MHz; $CDCl_3$) 164.91, 164.85, 133.9, 133.6, 132.7, 132.6, 132.5, 131.1, 131.0, 130.9, 129.2, 129.0, 39.4, 39.3, 38.6, 30.9, 16.0.

CMPO ligand **10b**. Reaction of tripodal amine **7b** (0.76 g, 2.62 mmol), chloroacetyl chloride (1.5 mL, 18.3 mmol) and K_2CO_3 (2.6 g, 19 mmol) and subsequently diphenyl ethyl phosphinite (2.3 mL, 10.6 mmol) gave ligand **10b** (0.96 g, 36%) (Found: C, 70.05; H, 6.40; N, 4.23. Calc. for $C_{60}H_{66}N_3O_6P_3 \cdot 0.1CH_2Cl_2$: C, 70.08; H, 6.48; N, 4.08%); mp 143 °C; δ_H(300 MHz; $CDCl_3$) 7.72–7.79, 7.42–7.57 (33 H, m, CH_2NHCO, Ph), 3.32 (6 H, d, J_{H-P} 12.3, $C(O)CH_2P(O)$), 3.15–3.26, 2.52–2.64 (18 H, m, $PhCH_2CH_2N$ CH_2CH_3), 1.02 (9 H, t, *J* 9.2, CH_2CH_3); δ_C(100 MHz; $CDCl_3$) 164.81, 164.77, 140.5, 132.7, 132.6, 132.4, 132.2, 131.1, 131.0, 130.9, 129.2, 129.0, 41.0, 39.4, 38.8, 29.5, 22.5, 15.9.

CMPO ligand **11**. Reaction of tripodal amine **8** (0.72 g, 1.44 mmol), chloroacetyl chloride (1.0 mL, 12.6 mmol) and K_2CO_3 (1.8 g, 13 mmol) and subsequently diphenyl ethyl phosphinite (4.57 mL, 21.1 mmol) gave ligand **11** (1.22 g, 69%). δ_H(300 MHz; $CDCl_3$) 7.84–7.96 (12 H, m, Ph), 7.42–7.54 (18 H, m, Ph), 3.80–3.91 (3 H, m, $NCH(CH_2CH_3)_2$), 3.70 (6 H, d, J_{P-H} 15.6, $CH_2P(O)$), 3.01–3.10 (6 H, m, NCH_2CH_2Ph), 2.81 (6 H, q, *J* 7.8, CH_3CH_2Ph), 2.37–2.46 (6 H, m, NCH_2CH_2Ph), 1.42–1.70 (12 H, m, $NCH(CH_2CH_3)_2$), 0.79–1.00 (27 H, m, CH_3); δ_C(75 MHz; $CDCl_3$) 166.4, 166.3, 141.3, 133.3, 133.2, 132.2, 131.9, 131.6, 131.4, 128.8, 128.6, 62.4, 42.8, 40.1, 39.2, 27.9, 26.6, 22.6, 15.7, 11.3; *m*/*z* (FAB) 1266.6274 ($[M + K]^+$ $C_{75}H_{96}N_3O_6P_3K$ requires 1266.6149).

CMPO ligand **12**. Reaction of tripodal amine **5** (0.62 g, 1.34 mmol), chloroacetyl chloride (0.9 mL, 11.3 mmol) and K_2CO_3 (1.8 g, 13 mmol) and subsequently diphenyl ethyl phosphinite (2 mL, 9.26 mmol) gave ligand **12** (0.51 g, 32%). δ_H(300 MHz; $CDCl_3$) 7.85–7.92 (12 H, m, Ph), 7.44–7.57 (18 H, m, Ph), 4.45–4.67 (6 H, m, $PhCH_2N$), 3.66–3.80 (6 H, m, $C(O)CH_2P(O)$), 2.35–2.73 (9 H, m, $NHCH(CH_2CH_3)_2$, $PhCH_2CH_3$), 1.42–1.62 (12 H, m, $NHCH(CH_2CH_3)_2$), 0.40–1.25 (27 H, m, CH_3); δ_C(75 MHz; $CDCl_3$) 165.8, 146.5, 133.5, 132.3, 132.2, 131.4, 131.3, 131.2, 128.9, 128.8, 128.6, 61.7, 47.8, 40.9, 40.1, 24.0, 22.8, 16.1, 11.6, 11.5; *m*/*z* (FAB) 1224.5672 ($[M + K]^+$ $C_{72}H_{90}N_3O_6P_3K$ requires 1224.5680).

CMP ligand **13b**. Reaction of tripodal amine **3b** (0.91 g, 1.91 mmol), chloroacetyl chloride (1.2 mL, 15.3 mmol) and K_2CO_3 (2.2 g, 16 mmol) and subsequently triethyl phosphite (4.0 mL, 24.1 mmol) gave ligand **13b** (1.31 g, 68%). δ_H(300 MHz; $CDCl_3$), 4.11–4.21 (12 H, m, $POCH_2CH_3$), 3.24–3.48 (24 H, m, CH_2O, CH_2N), 2.97–3.09 (6 H, m, $C(O)CH_2P(O)$), 1.72–1.85, 1.25–1.61 (38 H, m, CH_3CH_2C, $CH_3CH_2CH_2CH_2N$, $OCH_2CH_2CH_2N$, $P(O)CH_2CH_3$), 0.80–0.97 (12 H, m, CH_3CH_2C, $CH_3CH_2CH_2CH_2N$); δ_C(100 MHz; $CDCl_3$) 164.7, 164.6, 164.5, 71.7, 68.9, 67.9, 62.7, 62.6, 49.3, 46.0, 45.8, 44.1, 43.2, 34.2, 34.0, 32.8, 32.7, 31.3, 29.8, 29.3, 28.1, 23.4, 20.3, 20.2, 16.6, 16.5, 14.0, 8.0; *m*/*z* (FAB) 1008.5818 ($[M + H]^+$ $C_{45}H_{93}N_3O_{15}P_3$ requires 1008.5820).

CMP ligand **13c**. Reaction of tripodal amine **3c** (1.40 g, 2.18 mmol), chloroacetyl chloride (1.5 mL, 18.5 mmol) and K_2CO_3 (2.6 g, 19 mmol) and subsequently triethyl phosphite (5.0 mL, 29.2 mmol) gave ligand **13c** (0.82 g, 32%). δ_H(300 MHz; $CDCl_3$) 4.09–4.19 (12 H, m, $POCH_2CH_3$), 3.20–3.47 (24 H, m, CH_2O, CH_2N), 2.95–3.07 (6 H, m, $C(O)CH_2P(O)$), 1.72–1.82, 1.17–1.58 (62 H, m, CH_3CH_2C, $CH_3C_6H_{12}CH_2N$, $OCH_2CH_2CH_2N$, $POCH_2CH_3$) 0.79–0.88 (12 H, m, CH_3CH_2C, $CH_3C_6H_{12}CH_2N$); δ_C(75 MHz; $CDCl_3$) 164.8, 164.6, 164.5, 71.6, 69.0, 68.0, 62.7, 62.6, 62.5, 49.6, 46.3, 45.8, 44.1, 43.3, 34.5, 32.7, 32.5, 32.0, 31.9, 29.6, 29.5, 29.4, 29.3, 28.2, 27.8, 27.2, 27.1, 23.5, 22.8, 16.6, 16.5, 14.2, 8.1; *m*/*z* (FAB) 1214.7168 ($[M + K]^+$ $C_{57}H_{116}N_3O_{15}P_3K$ requires 1214.7256).

CMP ligand **13d**. Reaction of tripodal amine **3d** (0.87 g, 1.68 mmol), chloroacetyl chloride (1.2 mL, 15.1 mmol) and K_2CO_3 (2.2 g, 16 mmol) and subsequently triethyl phosphite (3.0 mL, 29.1 mmol) gave ligand **13d** (0.37 g, 21%). δ_H(300 MHz; $CDCl_3$) 4.09–4.19 (12 H, m, $POCH_2CH_3$), 3.00–3.08, 3.14–3.63 (27 H, m, CH_2O, CH_2PO, CH_2NCH), 1.75–1.88, 1.35–1.59 (20 H, m, CH_3CH_2C, $NCH(CH_2CH_3)_2$, $OCH_2CH_2CH_2N$), 1.30 (16 H, t, *J* 3.5, $POCH_2CH_3$),

0.79–0.91 (21 H, m, CH_3CH_2C, $NCH(CH_2CH_3)_2$); δ_C(75 MHz; $CDCl_3$) 166.0, 165.9, 165.6, 165.5, 71.9, 71.7, 69.8, 68.7, 62.6, 62.5, 62.3, 58.6, 42.4, 41.9, 39.6, 35.0, 34.8, 33.1, 33.0, 31.6, 29.2, 26.5, 26.1, 23.5, 16.6, 16.5, 11.3, 8.0; *m*/*z* (FAB) 1088.5792 ($[M + K]^+$ $C_{48}H_{98}N_3O_{15}P_3K$ requires 1088.5848).

CMP ligand **14a**. Reaction of tripodal amine **7a** (0.69 g, 2.78 mmol), chloroacetyl chloride (2.1 mL, 26.4 mmol) and K_2CO_3 (3.8 g, 28 mmol) and subsequently triethyl phosphite (6.0 mL, 34.9 mmol) gave ligand **14a** (0.96 g, 44%). δ_H(400 MHz; $CDCl_3$) 7.03 (3 H, t, *J* 5.8, CH_2NHCO), 4.14 (12 H, m, OCH_2CH_2), 3.28–3.33, 2.86–2.92 (12 H, m, $PhCH_2CH_2N$), 2.85 (6 H, d, J_{H-P} 20.4, $C(O)CH_2P(O)$), 2.35 (9 H, s, $PhCH_3$), 1.33 (18 H, t, *J* 6.8, OCH_2CH_3); δ_C(100 MHz; $CDCl_3$) 164.24, 164.21, 134.0, 133.6, 62.9, 39.4, 35.9, 34.6, 30.9, 16.5, 16.1; *m*/*z* (FAB) 784.3481 ($[M + H]^+$ $C_{33}H_{61}N_3O_{12}P_3$ requires 784.3468).

CMP ligand **14b**. Reaction of tripodal amine **7b** (0.65 g, 2.24 mmol), chloroacetyl chloride (1.25 mL, 15.7 mmol) and K_2CO_3 (2.2 g, 16 mmol) and subsequently triethyl phosphite (6 mL, 35 mmol) gave ligand **14b** (0.76 g, 41%). δ_H(400 MHz; $CDCl_3$) 6.92 (3 H, t, *J* 5.8, CH_2NHCO), 4.08–4.16 (12 H, m, OCH_2CH_2), 3.29–3.31, 2.77–2.81 (6 H, m, $PhCH_2CH_2N$), 2.82 (6 H, d, J_{H-P} 20.4, $C(O)CH_2P(O)$), 2.70 (6 H, q, *J* 7.2, $PhCH_2CH_3$), 1.31 (18 H, t, *J* 7.2, OCH_2CH_3), 1.11 (9 H, t, *J* 7.2, $PhCH_2CH_3$); δ_C(100 MHz; $CDCl_3$) 164.2, 164.13, 140.7, 132.4, 63.0, 62.9, 41.1, 35.9, 34.6, 29.5, 22.7, 16.5, 16.1; *m*/*z* (FAB) 826.3972 ($[M + H]^+$ $C_{36}H_{67}N_3O_{12}P_3$ requires 826.3938).

CMPO/*CMP ligand* **15**. Reaction of tripodal amine **3d** (0.89 g, 1.73 mmol), chloroacetyl chloride (1.25 mL, 15.7 mmol) and K_2CO_3 (2.2 g, 16 mmol) and subsequently a mixture of triethyl phosphite (0.7 mL, 4.1 mmol) and diphenyl ethyl phosphinite (1 mL, 4.63 mmol) gave ligand **15** (0.22 g, 11%). δ_H(300 MHz; $CDCl_3$) 7.80–7.89 (8 H, m, Ph), 7.40–7.49 (12 H, m, Ph), 4.12–4.18 (4 H, m, $POCH_2CH_3$), 3.98–4.08, 3.52–3.78, 3.01–3.42 (27 H, m, CH_2O, CH_2NCH, $CH_2P(O)$), 1.66–1.86, 1.21–1.62 (26 H, m, CH_3CH_2C, $NCH(CH_2CH_3)_2$, $OCH_2CH_2CH_2N$, $P(O)CH_2CH_3$), 0.68–0.92 (21 H, m, CH_3CH_2C, $NCH(CH_2CH_3)_2$); δ_C(75 MHz; $CDCl_3$) 166.2, 166.02, 165.96, 165.6, 165.5, 133.6, 133.4, 132.2, 132.1, 131.5, 131.4, 128.73, 128.71, 128.57, 128.55, 71.7, 69.8, 69.7, 68.8, 62.7, 62.6, 62.4, 58.8, 58.6, 43.3, 42.1, 39.6, 39.2, 38.9, 38.4, 34.9, 33.1, 33.0, 31.6, 31.4, 29.2, 29.1, 26.5, 26.1, 25.9, 16.6, 16.5, 11.2, 8.0; *m*/*z* (FAB) 1216.5982 ($[M + H]^+$ $C_{64}H_{98}N_3O_{11}P_3K$ requires 1216.6051).

***N*-Butyl-*N*-methyl-malonic acid methyl ester 16.** A solution of methyl 3-chloro-3-oxopropionate (25 g, 183 mmol), *N*-methylbutylamine (23 mL, 194 mmol) and triethylamine (28 mL, 202 mmol) in CH_2Cl_2 (250 mL) was stirred at room temperature for 16 h. The solution was filtered through a layer of Celite and subsequently passed through a layer of silica gel with CH_2Cl_2. Solvent evaporation yielded **16** as an oil (19.9 g, 58%). δ_H(300 MHz; $CDCl_3$) 3.75 (3 H, s, $COOCH_3$), 3.44 (2 H, s, $COCH_2CO$), 3.85, 3.25 (2 H, 2 × t, *J* 7.5, $NCH_2C_2H_4CH_3$), 2.98, 2.94 (3 H, 2 × s, NCH_3), 1.49–1.61, 1.25–1.38 (4 H, m, $NCH_2C_2H_4CH_3$), 0.95, 0.93 (3 H, 2 × t, *J* 7.2 $NCH_2C_2H_4CH_3$); δ_C(75 MHz; $CDCl_3$) 168.4, 165.8, 52.6, 50.7, 47.9, 41.7, 41.1, 36.1, 33.7, 30.6, 29.4, 20.2, 14.0; *m*/*z* (FAB) 188.1286 ($[M + H]^+$ $C_9H_{18}NO_3$ requires 188.1287).

General procedure for the synthesis of malonamide ligands 17a–d, 18a,b. A solution of tripodal amine and excess of malonic ester **16** in toluene (100 mL) was refluxed for 16 h using a Soxhlet setup containing 4 Å molecular sieves to absorb the formed MeOH. After evaporation of the solvent and excess of **16**, the resulting residue was separated with column chromatography (SiO_2; CH_2Cl_2–MeOH = 25 : 1 → 11 : 1) to give pure ligands as oils.

Malonamide ligand **17a**. Reaction of amine **3a** (1.33 g, 4.35 mmol) with ester **16** (4.67 g 27.9 mmol) gave ligand **17a** (1.23 g, 37%). δ_H(300 MHz; $CDCl_3$) 7.84 (3 H, br s, NH), 3.26–3.48 (30 H, m, $CH_2OCH_2CH_2CH_2N$, $C(O)CH_2C(O)$, $NCH_2C_2H_4CH_3$), 3.03, 2.94 (each 4.5 H, 2 × s, NCH_3), 1.76 (6 H, quintet, *J* 6.5, $OCH_2CH_2CH_2N$), 1.25–1.63 (14 H, m, $NCH_2C_2H_4CH_3$, CH_3CH_2C), 0.90–0.97 (9 H, m, $NCH_2C_2H_4CH_3$), 0.83 (3 H, t, *J* 7.5, CCH_2CH_3); δ_C(75 MHz; $CDCl_3$) 168.5, 168.4, 166.7, 166.6, 71.7, 69.3, 50.6, 48.0, 43.3, 40.7, 40.2, 37.3, 36.1, 34.0, 30.7, 29.6, 29.4, 23.4, 20.2, 20.1, 14.0, 13.9, 7.9; *m*/*z* (FAB) 771.5488 ($[M + H]^+$ $C_{39}H_{75}N_6O_9$ requires 771.5596).

Malonamide ligand **17b**. Reaction of amine **3b** (0.99 g, 2.08 mmol) with ester **16** (3.65 g 21.2 mmol) gave ligand **17b** (0.90 g, 46%); δ_H(300 MHz; $CDCl_3$) 3.23–3.48 (36 H, m, $CH_2OCH_2CH_2CH_2N$, $C(O)CH_2C(O)$, $NCH_2C_2H_4CH_3$), 3.05, 3.03, 2.93, 2.92 (together 9 H, 4 × s, NCH_3), 1.75–1.86 (6 H, m, $OCH_2CH_2CH_2N$), 1.25–1.61 (26 H, m, $NCH_2C_2H_4CH_3$, CH_3CH_2C), 0.89–0.97 (18 H, m, $NCH_2C_2H_4CH_3$), 0.83 (3 H, t, *J* 7.5, CCH_2CH_3); *m*/*z* (FAB) 939.7297 ($[M + H]^+$ $C_{51}H_{99}N_6O_9$ requires 939.7474).

Malonamide ligand **17c**. Reaction of amine **3c** (1.26 g, 1.95 mmol) with ester **16** (3.50 g 20.32 mmol) gave ligand **17c** (1.11 g, 51%); δ_H(300 MHz; $CDCl_3$) 3.23–3.48 (36 H, m, CH_2O, CH_2N, $C(O)CH_2C(O)$), 3.04 (5 H, s, NCH_3), 2.92–2.93 (4 H, m, NCH_3), 1.75–1.86 (6 H, m, $OCH_2CH_2CH_2N$), 1.47–1.59, 1.20–1.39 (50 H, m, $NCH_2C_2H_4CH_3$, $NCH_2C_6H_{12}CH_3$, CCH_2CH_3), 0.81–0.97 (21 H, m, CH_2CH_3); *m*/*z* (FAB) 1145.8746 ($[M + K]^+$ $C_{63}H_{122}N_6O_9K$ requires 1145.8910).

Malonamide ligand **17d**. Reaction of amine **3d** (1.415 g, 2.74 mmol) with ester **16** (4.83 g 28.06 mmol) gave ligand **17d** (1.50 g, 56%); δ_H(300 MHz; $CDCl_3$) 4.05–4.19, 3.53–3.67, 3.12–3.48 (33 H, m, CH_2O, CH_2N, CHN, $C(O)CH_2C(O)$), 3.00–3.02, 2.88–2.90 (together 9 H, m, NCH_3), 1.75–1.87 (6 H, m, $OCH_2CH_2CH_2N$), 1.22–1.56 (26 H, m, $(CH_3CH_2)_2CHN$, $NCH_2C_2H_4CH_3$, CCH_2CH_3), 0.78–0.93 (30 H, m, CH_2CH_3); *m*/*z* (FAB) 981.7777 ($[M + H]^+$ $C_{54}H_{105}N_6O_9$ requires 981.7943).

Malonamide ligand **18a**. Reaction of amine **7a** (0.77 g, 3.08 mmol) with ester **16** (6.04 g 32.25 mmol) gave ligand **18a** (1.45 g, 66%); δ_H(300 MHz; $CDCl_3$) 7.96–8.08 (3 H, m, NH), 3.30–3.41 (18 H, m, CH_2N, $C(O)CH_2C(O)$), 3.03 (4 H, s, NCH_3), 2.95 (5 H, s, NCH_3), 2.87–2.98 (6 H, m,

PhCH_2CH_2N), 2.36 (9 H, s, PhCH_3), 1.47–1.61, 1.26–1.39 (12 H, m, CONCH$_2$C$_2H_4$CH_3), 0.91–0.98 (9 H, m, CONCH$_2$C$_2$H$_4$CH_3); δ_C(100 MHz; $CDCl_3$) 168.6, 166.6, 166.5, 133.9, 133.8, 50.7, 48.1, 40.1, 39.7, 38.9, 36.1, 34.1, 30.9, 30.8, 29.4, 20.2, 20.1, 16.2, 14.0; *m*/*z* (FAB) 753.4661 ([M + K]$^+$ $C_{39}H_{66}N_6O_6K$ requires 753.4681).

Malonamide ligand **18b**. Reaction of amine **7b** (0.49 g, 1.67 mmol) with ester **16** (1.40 g 7.50 mmol) gave ligand **18b** (0.84 g, 66%); δ_H(300 MHz; $CDCl_3$) 8.19–8.29 (3 H, m, NH), 3.31–3.45 (18 H, m, CH_2N, C(O)CH_2C(O)), 3.06 (4.4 H, s, NCH_3), 2.97 (5.6 H, s, NCH_3), 2.80–2.90 (6 H, m, PhCH_2CH_2N), 2.73 (6 H, q, *J* 6.9, PhCH_2CH_3), 1.47–1.61, 1.24–1.40 (12 H, m, CONCH$_2$C$_2H_4$CH_3), 1.16 (9 H, t, *J* 6.9, PhCH$_2$CH_3), 0.92–0.97 (9 H, m, CONCH$_2$C$_2$H$_4$CH_3); δ_C(100 MHz; $CDCl_3$) 168.8, 166.6, 166.5, 140.7, 132.6, 50.7, 48.2, 40.8, 39.9, 39.6, 36.1, 34.1, 30.8, 29.5, 22.7, 20.2, 20.1, 16.1, 13.99, 13.96; *m*/*z* (FAB) 795.5157 ([M + K]$^+$ $C_{42}H_{72}N_6O_6K$ requires 795.5150).

Potentiometric measurements

Reagents. The membrane components potassium tetrakis[3,4-bis(trifluoromethyl)phenyl]borate (KTFPB), 2-nitrophenyl octyl ether (*o*-NPOE), high molecular weight poly(vinyl chloride) (PVC), tetrahydrofuran (THF) and all salts were purchased form Fluka (Ronkonkoma, NY). Aqueous solutions were obtained by dissolving the appropriate salts in water passed through the milliQ system.

Membrane preparation. The polymeric membranes used for the determination of the stability constants contained ionophore (20 mmol kg^{-1} of membrane) and KTFPB (2 mmol kg^{-1} of membrane) in PVC–*o*-NPOE (1 : 2 by weight) polymeric matrix (total 140 mg). Similar membranes consisting of the same components except for ionophore were also prepared. The membrane components were dissolved in THF (1.5 mL). The solution was placed in a glass ring (22 mm i.d.) mounted over a glass plate and then covered with another glass plate to slow down the solvent evaporation. After 24 h, the resulting membrane was peeled from the glass plate and discs of 7 mm diameter were cut out.

The procedure for the preparation of the polymeric membranes evaluated for the potentiometric ion response was similar to that described above. The total amount of membrane components was 200 mg and the membranes consisted of 1 wt% of ionophore, 10 mol% of KTFPB (relative to the ionophore) and PVC–*o*-NPOE (1 : 2 by weight).

Potentiometric response to cations and selectivity measurements. Membrane discs were mounted in conventional ISE bodies (Type IS 561; Philips, Eindhoven, The Netherlands) for electromotive force (EMF) measurements. All measurements were performed at ambient temperature using a galvanic cell of the following type: Ag|$AgCl_{(s)}$|3 M KCl|1 M CH_3COO-Li|sample|ion-selective membrane|0.01 M NaCl|$AgCl_{(s)}$|Ag. The EMF measurements were carried out using a 16-channel electrode monitor (Lawson laboratories). The performance of the electrodes was examined by measuring the EMF of the examined cations in aqueous solutions over the concentration range 10^{-6}–10^{-1} M. Potentiometric selectivity coefficients ($K^{pot}_{I,J}$) were calculated using the separate solution method (SSM) according to the procedure described in literature.[20] Activity coefficients were calculated according to the Debye–Hückel approximation.[23]

Potentiometric determination of stability constants. The measurement setup was the same as described above. Experiments were carried out according to the procedure described earlier.[24] Two sets of membranes were prepared: membranes with and without ionophore. A series of membrane discs were cut from the parent membranes and these discs were conditioned for at least 2 days in appropriate salt solutions. To determine the stability constants for a given cation and an ionophore, two measurements were carried out: for a membrane without ionophore (so-called blank membrane) and then for a sandwich membrane. The sandwich membrane was prepared just before every measurement by attaching the dry membrane with ionophore to the dry blank membrane. The segmented membrane was than mounted into a Philips electrode body (membrane with ionophore faced the sample solution) and immediately immersed into an appropriate salt solution. The potential was recorded as the mean of the last minute of a 15 min measurement period in the test solution. The potential of the electrodes with sandwich membranes remained free of diffusion-induced drift for 30–70 min depending on the ionophore incorporated within the membrane and the ion measured. The formation constants were determined using ΔEMF, calculated by subtracting the EMF of the electrode with the membrane without ionophore from the EMF measured for the electrode with the sandwich membrane according to the equation presented in ref. 24.

Liquid–liquid extractions of americium and europium

2 mL of chloroform were poured into each flask containing the ligand to be tested. After complete dissolution of the latter (quite fast in general), the chloroform solution was separated into 2 batches to perform the liquid–liquid extraction experiments in TCE and *n*-octanol. Chloroform was dried under a depressurized hood for several days, which allowed the amount of tested ligand to be weighed.

500 μL of either TCE or *n*-octanol were added to dissolve the ligand to be tested and to prepare the organic phases for liquid–liquid extraction experiments. The latter were carried out by contacting 200 μL of the organic samples with 1 and 3 M nitric acid solutions ($V_{aq} = V_{org}$), spiked with ^{152}Eu(III) and ^{241}Am(III) in 2 mL Eppendorf micro-tubes, thermostated at (25 ± 0.5) °C and shaken for at least 30 min with a vortex IKA device (Vibrax VXR). Tubes were centrifuged and 40 μL of each phase were diluted either with 560 μL of TCE or *n*-octanol for the organic samples, or with 560 μL of molar nitric acid for the aqueous samples. 550 μL of each sample were taken for radiometric gamma analyses at 59 keV for Am-241 and 121.8 keV for Eu-152, using a Canberra Eurisys pure Ge detector. The acquisition time was long enough to minimize the experimental error: mass balances ($A_{aq}^{ini} - (A_{aq}^{eq} + A_{org}^{eq})/A_{aq}^{ini}$, A_{aq}^{ini}, A_{aq}^{eq} and A_{org}^{eq} being, respectively, the activity of the radiotracer in the aqueous phase initially and at equilibrium, and its activity in the organic phase at equilibrium) were always smaller than 10%.

The acidity of the initial and final aqueous solutions was determined by potentiometric titration on 100 μL samples, using a METROHM 751 GPD Titrino device and a 0.1 M NaOH solution.

Acknowledgements

We are grateful for the financial support of the EEC (contract FIKW-CCT-2000-00088) and of the Warsaw University of Technology for the financial support of the work related to the potentiometric part.

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