Design of Calixarene-Type Ligands for Second Sphere Complexation of Noble Metal Ions

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Macrocyclic ligands were designed according to the principle of ion recognition, synthesized and tested in their capability to extract Au^{III}. Different from other complexants which require ligand exchange prior to complexation, the reported ligands bind the complexes $AuCl_3$ and $AuCl_4^-$. With a sufficiently sized macrocyclic cavity, hydrophobic calix[6]arenes derivatized at the "lower rim' were employed for that purpose. Their ligating functionalities contain pyridino, amide or thioamide groups in order to achieve electron donor-acceptor and electrostatic host-guest interactions. We report the synthesis route and results on extraction, selectivity, kinetics and back-extraction and compare with commercial extractants. Quantitative extraction from hydrochloric acid solutions was achieved as well as over 99% recovery in back-extraction in one step each. Data on the selectivity over base metals, which are representative for the matrix in gold ores are provided. The ligands are powerful extractants for Au^{III} and show fast complexation kinetics.

Introduction

The molecular recognition of metal cations,[1] anions[2,3] and of organic molecules[4] can be achieved with macrocyclic ligands having tailor-made structures. Among the design features are complementary interactions, size compatibility, complementary coordination geometry and balanced complex stability which allows decomplexation. Calixarenes are suited to act as a molecular backbone for subsequent derivatizations to achieve these goals as shown by more than 500 papers on complexation of metal ions.[1,5−10] Solvent extraction is useful to test the molecular recognition mechanism and can be applied for chemical separations, as summarized recently.[11−16]

The complexation and extraction of anions such as oxyanions by calixarenes has been investigated to a smaller extent compared with cations. Complexation was for example achieved by incorporating amino-,[17,18] amido-,[19,20] pyridino-[21] or Schiff base groups,[22] or alternatively metal centers.[23,24]

For the complexation of Au^{III}, S-donor[25−27] or P-donor atoms[28−30] were tethered to either the lower or the upper rim of the calixarene backbone. Some of these ligands quantitatively extract Au^{III} from water. If substituted at the upper rim of a calix[4]arene, the cavity is large enough to accommodate the chloro complex. Data for the extraction of Au^{III} by these ligands at different pH values, especially from very acidic solutions, were not reported.

On the other hand, commercial extractants were investigated with respect to Au^{III}. These contain ketones or alcohols,[31] phosphane oxides,[32] amines[33,34] or thiophosphinic acids.[35,36] Some of them have disadvantages, such as low extraction power from strongly acidic solutions, difficult back-extraction and loss of reagent, low selectivity, slight solubility in water, or degradation during use. One aim of this work was to show whether or not calixarenes can compete with those commercial extractants, and which molecular structures may be suitable for that purpose.

In our previous works, we investigated the complexation abilities of various calix[4]arenes towards noble metal ions.[37] We found that calix[4]arenes bearing both acidic and amido groups at the lower rim extract Au^{III}, Pd^{II} and Pt^{IV} ions from acidic solutions, but in case of Au^{III} not quantitatively ($\log D < 2$ at optimum pH 1). Moreover, in the presence of excess sodium ions, Au^{III} is no longer extracted ($\log D < -1$). These results can be interpreted that the ligand cavity size is too small for the Au^{III} complex anion, but matches the size and coordination sphere of the interfering Na^+. In order to improve the selectivity, we changed to calix[6]arenes[38] and would like to report on the ligands, which are able to selectively extract the chloro

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complexes of metal ions and allow the pH control of extraction and back-extraction.

As the new ligands extract Au^{III} selectively from highly acidic media, there is an environmentally friendly application in hydrometallurgy: ores can be leached with acidic thiourea solution and oxidized[39] as an alternative to cyanide leaching.[40] Sulfidic ores are also subjected to acid-leaching. The extractant in this case must both be very selective and chemically stable. Metals present in gold ores such as the one from Algeria are Fe (4.6%), Al (4.5%), Ca (2.5%), Zn (0.02%), Pb(0.02%), alkali etc. and Au (0.001%). Therefore a high selectivity for gold is required for an extractant to be applied.

Results and Discussion

Ligand Structures

Figure 1 shows the structures of the calix[6]arenes used for this study. Their preparation proceeds smoothly in high yields. Ligand **1** was not applied to extraction because of low solubility in organic solvents. This is probably caused by hydrogen bonding and improves significantly upon thionation (ligand **3**). The solubility can also be improved by changing *tert*-butyl to *tert*-octyl groups (ligand **2**), which render the molecule more hydrophobic. The ^{1}H and ^{13}C NMR spectra of ligands **2** and **3** show sharp signals at room temperature, indicating the predominance of one conformation. From the symmetrical spectral pattern we concluded this to be the cone[41] conformation. It is rare that uncomplexed calix[6]arenes exist in a symmetrical cone shape at room temperature, because of the molecular flexibility. Ligands **4** to **6** and many other calix[6]arenes with smaller functional groups attached to the ethereal oxygens display broadened NMR spectra with temperature-dependent presence of various conformers.

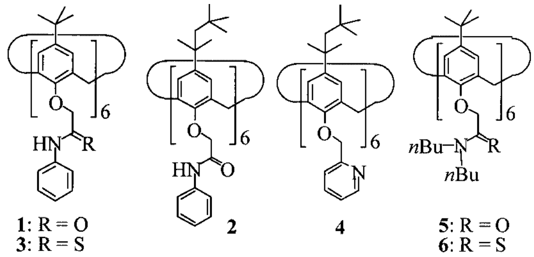


Figure 1. Structures of the investigated calixarenes and numbering

The binding of $AuCl_4^-$ is reflected by changes in the NMR spectra as confirmed for ligand **4**. Compared with the uncomplexed, protonated ligand, the -O-CH_2 and the N-CH_{py} C-signals broaden and shift, the other C_{py} signals shift as well. The C_{Ar} signals of the calixarene backbone shift to a smaller extent. In ^{1}H NMR spectrum, the δ = 3.3 ppm shift of equatorial Ar-CH_2-Ar protons changes to δ = 3.55 ppm upon complexation, partly off-setting the ring current. The axial and the O-CH_2 protons also shift downfield. The H_{py} signals shift as well and two of them broaden, while H_{Ar} and H_{Oct} of the calixarene backbone scarcely change upon complexation. These results indicate that $AuCl_4^-$ interacts with all the py groups inside the molecular cavity. Probably it coordinates not to all of them at the same time, but exchanges rapidly on the NMR timescale.

In the aqueous phase (>0.1 M Cl^-), the complex ion $AuCl_4^-$ exists exclusively (log β_4 = 25 [42]). The ligand cavity (0.3 × 0.8 nm at the ether oxygens,[6] or 0.5 nm as the inner circle) is large enough and retains conformational freedom to match the size of $AuCl_4^-$ (ca. 0.57 nm diameter). In order to render the complex hydrophobic and to avoid tensidic properties, the upper rim of the calixarene bears branched alkyl groups.

Extraction Properties

Figure 2 shows the distribution ratio *D* of Au^{III} on a logarithmic scale as a function of the pH in the aqueous phase after extraction for ligands **3−6**. *D* is defined as $c_{Au,org}$/$c_{Au,aq}$ at equilibrium. In order to characterize and to compare the ligands, their concentration was kept in high excess compared to the concentration of Au^{III}. The pH range was selected to allow protonation of the ligands [approx. pK_a of monomeric functional groups: 5.1 (pyridine), 0.1 (DMF),[43] −0.46 (acetanilide),[44] ≤0 (thioamide)]. pK_a Values of these macrocycles are not known. If more than one N-atom protonates under the experimental conditions (e.g. ligand **4**), this charge is neutralized by Cl^-. The conditional extraction constants take these equilibria into account, because the concentration of Cl^- is nearly constant.

Ligand **3** is characterized by a very high extractability towards Au^{III} (log *D* ≥ 3, which was the upper measurement limit), over the investigated pH range. A variation of *D* could therefore not be observed. Ligands **4−6** display a pH dependency in accordance with their ability to pro-

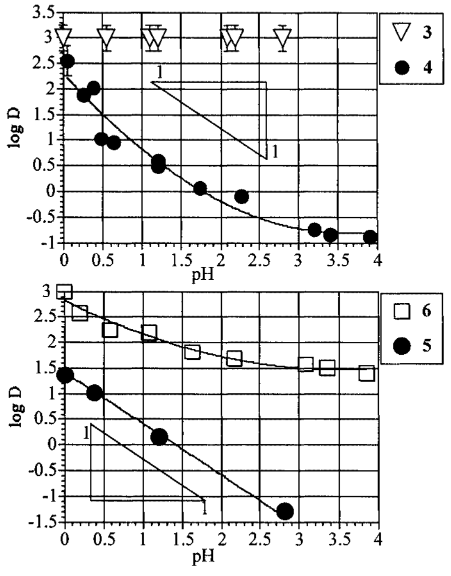


Figure 2. Effect of the pH of the aqueous phase on the extraction of Au^{III} by the ligands **3−6**; aq phase: 14 ppm $AuCl_3$ in HCl/NH_4Cl, pH measured at equilibrium; org. phase: 5 mM ligand in $CHCl_3$

tonate. The protonated ligands form ion-pair complexes with $AuCl_4^-$. In cases of **4** (at higher acidity) and **5** the slope of log D vs. pH corresponds to (−1) as expected for monoprotonation.

The high extraction power of ligands **3** and **6** is interpreted as the result of the thioamide groups. It resembles synergistic extraction systems, in which an ammonium and a sulfur-donor ligand are mixed in the organic phase and achieve better extraction than the individual ligands.[35] The coordination of the unprotonated ligands **3**, **4**, and **6** to $AuCl_4^-$ via N or S, accompanied by dissociation of one Cl^- from the complex ion (ligand exchange) is concluded from the data, which show remaining extraction power even at pH >2. The neutral ligands probably extract $AuCl_3$, similar to the neutral commercial extractants Cyanex® 301, 302 and 471X.

The capability of the ligands to extract Au^{III} from HCl solutions into the organic phase serves as a measure to estimate their complexation power, although solvent effects during extraction (dehydration, solvation and ion pairing), which were not investigated here, also play a role. Hence, the extraction constant serves as a quantitative measure, assuming comparable solvent effects in the investigated extraction systems.

Complexation Equilibria

By changing the ligand concentration, the extraction mechanism and the stoichiometry can be derived. As concluded from slope 2 in the plot of log D vs. log c in Figure 3, all investigated extractants form complexes with a stoichiometry of 1:2 (metal/ligand) at low concentrations of Au^{III}. This is interpreted as being due to Au^{III} being sandwiched by two calixarene molecules, although size and charge of one calixarene molecule should be sufficient and the Au^{III}-coordination sphere is saturated with one counterion. However, commercial extractants such as thiophosphinic acid (protonated), phosphane oxide and -sulfide extract Au^{III} also as 1:2 complexes as can be concluded from slope analysis.[35]

Taking into account the ligand protonation, we can derive the following, simplified extraction equilibrium [Equation (1)]:

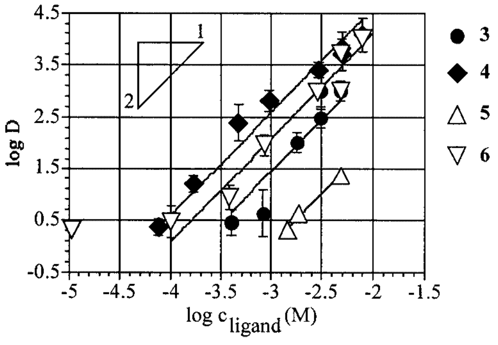


Figure 3. Estimation of the extraction power of the ligands; data are fitted by $\log D = 2\cdot\log(c) + \log(K_{ex})$ with K_{ex} being the extraction constant at pH = 0; aq. phase: 14 ppm $AuCl_3$ in 1 M HCl; org. phase: $CHCl_3$ containing the corresponding ligand

$$AuCl_4^- + 2L_{(org)} + H^+ \rightleftarrows [AuCl_4^-\cdot L\cdot LH^+]_{(org)} \qquad (1)$$

The extraction constants are defined as shown in Equation (2):

$$K_{ex} = \frac{[AuCl_4^- \cdot L \cdot LH^+]_{(org)}}{[AuCl_4^-]\cdot[H^+]\cdot[L_{(org)}]^2} \qquad (2)$$

In order to compare the four ligands with different pH dependencies, we refer K_{ex} as conditional constants to pH = 0 as well as to the other conditions. Table 1 lists the results, obtained by fitting the experimental data in Figure 3 with Equation (3), which is derived from Equation (2). Among the investigated ligands, the amide **5** is characterized by the lowest extraction. This is, however, not a disadvantage, because 96% extracted Au^{III} at pH 0 can be further increased at higher acidity in the aqueous phase.

$$\log D = \log K_{ex} + 2\cdot\log[c_L]_{(org)} \qquad (3)$$

The stoichiometry at high loading of the organic phase was tested by contacting equal volumes of equimolar (20 mM) Au^{III} with ligand **4** at pH 0. The extraction was near quantitative. The extract was dried and subjected to elemental analysis: found C 69.1, H 7.70, N 3.73%. This corresponds to a stoichiometry of 1:1 ($[AuCl_4]^-$:$[ligandH]^+$): calcd. C 68.9, H 7.48, N 3.83%. We conclude that the stoichiometry changes as a function of metal concentration in the organic phase: From diluted solutions, a second ligand molecule can shield the 'bottom' of the 1:1 complex. At high metal concentration there is no excess of ligand available and the 1:1 complex is extracted. Figure 4 schematically depicts that complex.

Table 1. Calculated extraction constants

Ligand	log K_{ex}
3	7.45
4	8.59
5	6.0
6	8.08

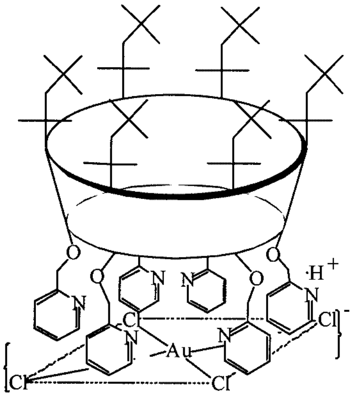


Figure 4 Schematic drawing of the extracted complex between Au^{III} and protonated **4** at high loading

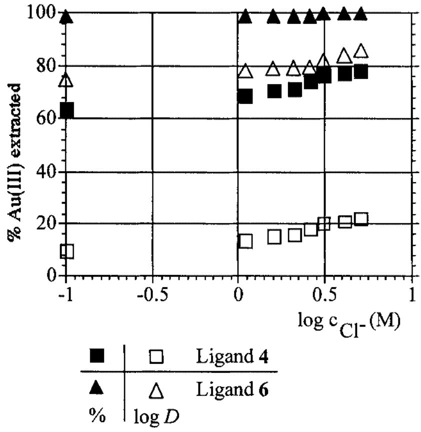


Figure 5. Influence of the chloride concentration on the extraction of Au^{III}; aq. phase: 17 ppm Au^{III} in 0.1 M HCl, up to 5 M NaCl; org. phase: CHCl$_3$ with 5 mM ligand

Variation of the chloride concentration at constant pH of the aqueous phase only causes small changes in the distribution ratio, as tested for ligands **4** and **6** (Figure 5). It is interpreted by the change of activity coefficients (salting-out effect). No change in the extraction mechanism takes place, as concluded from the slope of log D vs. log c_{Cl^-} being $<< +1$.

Back-Extraction

Ligands **4** and **5** have a pronounced pH dependency in their extraction ability (Figure 1). The organic phase, loaded with gold during extraction can therefore be regenerated by contacting with an aqueous phase of higher pH. The metal is back-extracted and, by using a small aqueous volume, enriched for a second time. The sulfur-containing ligands release their complexed metal only partly when the pH is increased. It is possible to completely recover all the metal by repeated mixing with water. More effective for the purpose of back-extraction is a competing, water-soluble ligand (e.g. thiourea, tu). Table 2 lists the results and shows that the ligands may be applicable not only for separation but also for analytical purposes, because both extraction and back-extraction are quantitative. The ligands were stable during four weeks of continuous extraction/back-extraction as concluded from the NMR spectra.

Table 2. Recovery of Au^{III} (in %) from the complexed ligands

Ligand	Buffer (pH, 5.5)	10 mM tu in H$_2$O	10 mM tu in 1 M HCl
3	5%	64.8%	> 99%
4	86%	89%	> 99%
5	80%	85%	> 99%
6	3.8%	0.1%	> 97%

Selectivity

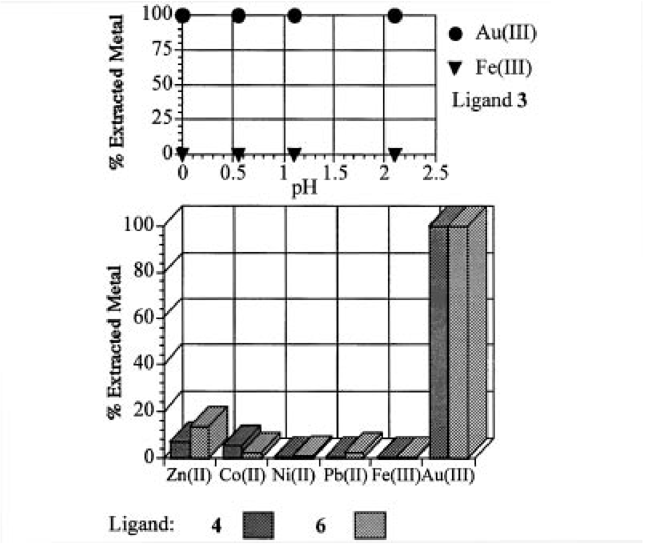


Figure 6 Selectivity of the ligands in competitive extraction; aq. phase:14 ppm Au^{III} and 2 mM Fe^{III} (upper part) or 0.1 mM of each M^{n+} (M = Zn^{2+}, Ni^{2+}, Pb^{2+}, Fe^{3+}, lower part) in 1 M HCl; org. phase: CHCl$_3$ containing 5 mM Ligand

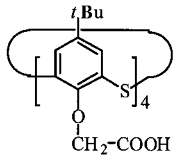
Taking into account the composition from acidic ore leaching, it is important to achieve a high selectivity for Au over the other metal ions, especially Fe(III). Figure 6 depicts results obtained in competitive extraction tests with ligands **3**, **4** and **6**. Under a 30-fold excess of Fe^{III}, ligand **3** still extracts Au^{III} quantitatively, while Fe^{III} is not extracted over the whole pH range. The separation factor S$_f$, defined as D_{Au}/D_{Fe} is $> 10^5$. Among the investigated metal ions only Zn^{II}, which has some thiophilic character, is extracted up to 7 and 13% by ligands **4** and **6** respectively. Alkali, alkaline earth and Al^{III} ions were not extracted from 1 M HCl. The overall high selectivity is discussed in terms of the ligand design: (i) the preferred binding of anions over metal cations due to electrostatic interactions, (ii) the suitable cavity, (iii) the preference for class "B" metal ions due to the presence of S and/or aromatic π-systems, and (iv) the macrocyclic effect. On the other hand, various monodentate ligands (except quaternary amines) extract Au^{I} without selectivity over Fe^{III}: a dithiophosphinic acid (91%:99%), a thiophosphinic acid (93%:99%), a phosphinic acid (93%:99%), DEHPA (76%:99%), an 8-hydroxyquinoline (87%:70%), and a bisphosphonic acid (90%:99%) at pH 2.[36]

Kinetics

Because the ligands are completely water-insoluble, the extraction consists of complexation at the interface followed by transport into the bulk organic phase. The extraction equilibria are reached very fast as expected for ion pairing in the absence of any interfacial resistance to mass transfer: Ligands **3**−**6** extract > 98% Au within 1 min and > 99% within 5 min. The short contact times required are advantageous for analytical as well as scaled up separation purposes.

Comparison with Cation Exchangers

We tested thiacalix[4]arene **7** [45] and the analogue **8** (CH$_2$ instead of S)[37], which are known to extract metal ions by cation exchange. The distribution ratio D_{Au} changed scarcely from 0.18 to 0.28 (**7**) when the pH was varied from 2 to 0 while that for **8** was even lower. It indicates that these ligands can hardly compete with Cl^- due to the high pK_a of the acid groups and that the S-bridges in **7** are inaccessible to binding due to steric reasons.



Ligand 7

Figure 7

Conclusion

High distribution ratios of Au^{III} are observed when ligands based on the calix[6]arene contain sulfur and/or nitrogen atoms, resulting in quantitative extraction from strongly acidic solution. Ligands containing only nitrogen as donor atoms extract Au^{III} quantitatively when they are protonated. Thioamide derivatives extract Au^{III} over a wider pH range. The loaded metal is quantitatively back-extracted by pH change or by competing ligands. The ligands have high selectivity which allows potential application in separation chemistry. Further works will be devoted to the extraction of other noble metals by these ligands and to the determination of their protonation constants.

Experimental Section

Complexation Experiments: Metal extraction was carried out batchwise with equal volumes at 298 K. The agitation speed was 54 rpm in an overhead shaker. Metal contents before and after extraction were analyzed by means of AAS (Shimadzu AA 6500) after dilution with 1 M HCl. Solutions were prepared by handling $AuCl_3$ under N_2 in a glove bag and dissolving in HCl. For the pH dependent extraction, the pH was adjusted by adding 1 M NH_3 or 8 M HCl to 0.1 M HCl solutions and mixing them with Au-stock solution. $CHCl_3$ saturated with water served as organic solvent for which reference data are available. The extractants are however, also soluble in less-polar solvents. Equilibrium pH values were measured with a combination glass electrode (Schott N42) after extraction and phase separation. The concentration of uncomplexed ligand ($c_{corrected}$) in Figures showing concentration-dependencies was calculated by taking into account the complexation. Selectivities were determined in competitive extraction. Quantitative stripping was done with 10 mM thiourea solution in 1 M HCl and a 100% mass balance was obtained. Using water or thiourea in water complete stripping was achieved for ligands **4** and **5** after three repetitions. The chemical stability was tested by repeated extraction and stripping cycles, in the course of which no decomposition of the ligands was observed. Metal complex NMR spectra (ligand **4**) were measured after contact with excess amounts of Au^{III} at pH 0 and compared with those of the protonated ligand. These concentrated organic Au^{III} complexes did not decompose. In the case of calix[4]arenes, complexed Au^{III} slowly oxidized thiocarbamoyl groups.[25]

NMR spectra were recorded at room temperature on a Bruker AC-250 instrument at 250 (^{1}H) or 63 MHz (^{13}C), chemical shifts are referenced to TMS and correspond to the neutral (non-protonated) ligands. H_{Ar}/C_{Ar} indicates the calixarene backbone rather than substituents if not stated otherwise. Mass spectra were measured in the EI mode (200 °C, 80 eV, 8 keV, MAT 711 instrument). Analytical TLC was carried out on dry Merck Silicagel $60F_{254}$, the R_f-values somewhat depend on the concentration. Melting points were determined on a Gallenkamp apparatus under air and are uncorrected. They were reconfirmed by DSC, measured with a Netzsch DSC 200 type calorimeter under N_2 atmosphere at 10 K/min. IR spectra were recorded on a Nicolet 5 SCX instrument with a DTGS detector. All solvents were dried and freshly distilled, chemicals were of synthesis grade. NaH (80% in oil) was washed with hexane prior to use. The air-sensitive reactions were carried out under N_2 atmosphere using transfer techniques. Yields are given for purified products. Parent calix[6]arenes were synthesized according to the literature.[46,47] Their purity was greater than 96%.

Ligand 1: The hexakis(carbomethoxy) derivative[48] of *tert*-butylcalix[6]arene (2.5 g, 1.9 mmol) was dried and treated with $(COCl)_2$ (45 equiv.) in CCl_4 under N_2 for 12 h at 75 °C. Volatiles were completely removed in vacuo, the residue dissolved in dry THF and treated with a mixture of pyridine (28 mmol) and aniline (28 mmol) under cooling with an ice bath. After stirring for 24 h at 35 °C the mixture was filtered. The residue was stirred with CH_2Cl_2/H_2O and filtered to give the pure product as a white residue, which is very insoluble in common organic solvents. Yield 87%.5,11,17,23,29,35-Hexakis(*t*ert-butyl)-37,38,39,40,41,42-hexakis(N-phenylcarbamoylmethoxy)calix[6]arene. $C_{114}H_{126}N_6O_{12}$ (M_r = 1772.21): calcd. C 77.26, H 7.17, N 4.74; found C 76.82, H 7.13, N 4.86; m.p. 277−279 °C. ^{1}H NMR [$CDCl_3/CD_3C(O)CD_3/CD_3OD$, 3:1:1]: δ = 1.15 (s, ***t***Bu, 54 H), 3.56 and 4.76 (2 d, Ar-CH_2, each 6 H, J = 16.5 Hz), 4.33 (s, O-CH_2, 12 H), 6.69 (m, pH_{Ar}, 6 H), 6.83 (m, mH_{Ar}, 12 H), 7.10 (s, H_{Ar} of calix, 12 H), 7.31 (m, oH_{Ar}, 12 H), 8.6 (s, NH) ppm, in [D$_8$]THF/[D$_6$]ethanol the spectrum indicates a mixture of conformers frozen on the NMR timescale. IR (KBr): $\tilde{\nu}$ = 1690 cm^{-1} (νCO amide I), 753 and 692 (γCH, 5 neighboring H of aniline), 1531 (Amide II), 3396 (NH); TLC ($CHCl_3$/EtOH, 9:1) R_f = 0.82. Because of the low solubility of 1, we also synthesized the *tert*-octyl analogue and characterized it for reasons of comparison.

Ligand 2: The hexakis(carbomethoxy) derivative of *tert*-octylcalix[6]arene[47] (3.2 g, 1.9 mmol) was treated with $(COCl)_2$ (45 equiv.) in CCl_4 under N_2 for 8 h at 75 °C. Volatiles were completely removed under reduced N_2 pressure, the residue was dissolved in dry THF and treated with a mixture of triethylamine (23 mmol) and aniline (23 mmol) under cooling with an ice bath. The mixture was filtered after stirring for 24 h at 38 °C. The filtrate was evaporated in vacuo, dissolved in CH_2Cl_2, washed 4 times with 1 M HCl, dried and crystallized by addition of EtOH to a CH_2Cl_2 solution. Yield 83%.5,11,17,23,29,35-Hexakis(*tert*-octyl)-37,38,39,40,41,42-hexakis(*N*-phenylcarbamoylmethoxy)calix[6]arene $C_{138}H_{174}N_6O_{12}$ (M_r = 2108.8): calcd. C 78.59, H 8.32, N 3.99; found C 77.88, H 8.24, N 3.76; m.p. 218−220 °C (dec.); DSC: 25.8 J/g at m.p., endothermic phase transition at 167 °C (−18.2 J/g). This is interpreted as the break-up of hydrogen bonds in the solid state (intramolecular H-bonding was concluded from the NMR spectroscopy), and conformational change from the symmetrical to an unsymmetrical, energetically favoured conformation. The ^{1}H and

^{13}C spectra ($CDCl_3$) are characterized by sharp signals, this indicates rigidified and symmetrical conformation (intramolecular H-bonding), while calix[6]arenes with smaller O-substituents usually show broadened peaks in the NMR spectra at room temp. due to conformational flexibility, as do the investigated thioamides. ^1H NMR: δ = 0.72 (s, *t*Oct, 54 H), 1.12 (s, *t*Oct, 36 H), 1.60 (s, *t*Oct, 12 H), 3.57 and 5.03 (2 d, Ar-CH_2, each H, *J* = 16.5 Hz), 4.31 (s, O-CH_2, 2 H), 6.83 (*m*, *p*$H_{aniline}$, 3 H), 7.08 (s, H_{Ar} of calixarene backbone, 2 H), 7.21 (*o*$H_{aniline}$, 2 H), 8.66 (s, NH, 1 H) ppm, ^{13}C NMR: δ = 29.7 (Ar-CH_2), 31.3 (1,1 dimethyl of *t*Oct), 31.8 (3 × CH_3 of *t*Oct), 32.4 (C_3 of *t*Oct), 38.1 (C_1 of *t*Oct), 57.2 (CH_2 of *t*Oct), 72.0 (O-CH_2), 120.8 (*o*C_{Ar} of aniline), 124.3 (*p*C_{Ar} of aniline), 127.4 (C_{Ar}-H of calix), 128.4 (*m*C_{Ar} of aniline), 131.6 (***C***$_{Ar}$-CH_2), 136.8 (C_{Ar}-NH), 146.0 (C_{Ar}-*t*Oct), 151.1 (C_{Ar}-O), 167.3 (CO) ppm. IR (KBr): $\tilde{\nu}$ = 1691 cm^{-1} (νCO amide I), 752 and 691 (γCH, 5 neighboring H's of aniline), 1533 (Amide II), 3391 (NH); TLC (CH_2Cl_2) R_f = 0.30 (tailing), ($CHCl_3$/EtOH, 9:1) R_f = 0.86.

Ligand 3: The precursor **1** (1 g, 0.56 mmol) was dissolved in dry toluene and treated with 2,4-bis(4-methoxyphenyl)-1,3-dithia-2,4-diphosphetane-2,4-disulfide (4 mmol) at 90 °C for 40 h. After cooling, the mixture was filtered and the solvents evaporated. The product precipitated from the residue upon adding MeOH and was recrystallized twice by addition of MeOH to a CH_2Cl_2 solution. Yield 68%. No interfering side products are formed during thionation reactions even in less polar solvents. 5,11,17,23,29,35-Hexakis(*tert*-butyl)-37,38,39,40,41,42-hexakis(*N*-phenylthiocarbamoylmethoxy)calix[6]arene, $C_{114}H_{126}N_6O_6S_6$ (M_r = 1868.6) calcd. C 73.27, H 6.8, N 4.50, S 10.28; found C 72.02, H 6.86, N 4.35, S 9.8; m.p. 240−242 °C (dec.). In the NMR spectra ($CDCl_3$) chemical shifts in *italics* indicate some of the characteristic changes upon thionation. ^1H NMR: δ = 1.12 (s, 54 H, *t*Bu), 3.62 and 4.41 (2 d, *J* = 16.25 Hz, 6 H each, CH_2-Ar), 4.5 (s, -O-CH_2, 12 H), 7.0 (s, 12 H, H_{Ar} of calix backbone), 7.13 (m, 18 H, *m* and *p*H_{Ar}), 7.53 (d, 12 H, *o*H_{Ar}), 9.8 (s, 6 H, NH) ppm. ^{13}C NMR: δ = 29.9 (CH_2-Ar), 31.3 (*t*Bu), 34.2 (quart C), *80.0* (-O-CH_2), 123.0 (*o*C_{Ar} of aniline), 126.6 (*p*C_{Ar} of aniline), 126.9 (C_{Ar}−H of calix), 128.6 (*m*C_{Ar} of aniline), 131.3 (*C*$_{Ar}$-CH_2), 137.3 (C_{Ar}-NH), 146.9 (C_{Ar}-*t*Oct), 151.8 (C_{Ar}-O), *194.4* (CS) ppm, no CO. IR (KBr): $\tilde{\nu}$ = 1394 cm^{-1} (thioamide I), 997 (thioamide IV), disappeared 1690; TLC ($CHCl_3$/EtOH, 9:1) R_f = 0.92.

Ligand 4: *tert*-Octylcalix[6]arene (6 g, 4.6 mmol) was deprotonated with NaH (18 equiv.) in dry THF for 12 h at 60 °C under N_2. A filtered mixture of triethylamine (18 equiv., 11.5 mL) and 2-picolyl chloride hydrochloride (9 equiv., 76.8 g), which had been stirred for 3 h, was added dropwise to the grey suspension under N_2 with ice-cooling. The reaction was completed by warming to 50 °C for 48 h, quenched with EtOH after cooling and the solvents evaporated. The residue was dissolved in CH_2Cl_2/EtOH (9:1), washed with brine and 0.1 M HCl, filtered through a Whatman phase separator and crystallized from hexane. Yield 54%. The *tert*-butylcalix[6]-arene analogue was described earlier.[49] 5,11,17,23,29,35-Hexakis(*tert*-octyl)-37,38,39,40,41,42-hexakis[(2-pyridylmethyl)oxy]-calix[6]arene $C_{126}H_{162}N_6O_6$ (M_r = 1856.62): calcd. C 81.5, H 8.8, N 4.53; found C 81.60, H 8.79, N 3.98; MS (EI), [M^+], 1856 (L); m.p. 243−245 °C. The ^1H NMR spectroscopy ($CDCl_3$): broadened peaks of Ar-CH_2, O-CH_2 and H_{Ar} indicated conformational flexibility, adding CD_3OD (30%) stabilizes a mixture of conformational isomers. ^1H NMR: δ = 0.62 (s, 54H Me of *t*Oct), 1.29 (s, 36 H, dimethyl), 1.77 (s, 12 H, CH_2 of *t*Oct), 3.49 (br., 6 H, Ar-CH_2), 4.0 to 5.0 (br., 18 H, Ar-CH_2 and O-CH_2), 6.79 (s, 6 H, H_{py}), 6.9 to 7.1 (br. s, 24 H, H_{calix} and H_{py}), 8.24 [br. s, 6 H, H_{py}(N-CH)] ppm. ^{13}C NMR: δ = 31.5 (1,1 dimethyl of *t*Oct), 32.1 (3 × CH_3 of *t*Oct), 32.2 (Ar-CH_2), 32.4 (C_3 of *t*Oct), 37.9 (C_1 of *t*Oct), 56.9 (CH_2 of *t*Oct), 75.3 (O-CH_2), 122.0 (*m*C_{py}), 126.5 (C_{Ar}-H of calix), 132.6 (*C*$_{Ar}$-CH_2), 136.6 (*m*C_{py}), 140.2 (*p*C_{py}), 145.3(N-CH_{py}), 147.9 (C_{Ar}-*t*Oct), 151.8 (C_{Ar}-O), 157.9 (CH_2-*C*$_{py}$) ppm. IR (KBr): new (py) 753, 994, 1032, 1147, 1435 cm^{-1}; TLC ($CHCl_3$/EtOH, 9:1) R_f = 0.63 (1 spot); (CH_2Cl_2) R_f = 0 (no starting material).

Ligand 5: The hexakis(carbomethoxy) derivative of *tert*-butylcalix[6]arene[48] (3 g, 2.27 mmol) was dried and treated with $(COCl)_2$ (60 equiv.) in CCl_4 under N_2 for 12 h at 75 °C. Volatiles were completely removed under reduced N_2 pressure, the residue dissolved in dry THF and treated with a mixture of triethylamine (46 mmol) and di-*n*butylamine (46 mmol) under cooling with an ice bath. After stirring for 12 at 30 °C the mixture was filtered, evaporated to dryness, dissolved in CH_2Cl_2 and washed five times with 1 M HCl. The product crystallized from MeOH and was dried in vacuo at 80 °C. Yield 90%. 5,11,17,23,29,35-Hexaakis(*tert*-butyl)-37,38,39,40,41,42-hexakis[(*N*,*N*-di-*n*butylcarbamoylmethoxy)-calix[6]arene, $C_{126}H_{198}N_6O_{12}$ (M_r = 1988.9): calcd. C 76.08, H 10.03, N 4.23; found C 75.74, H 9.72, N 4.06; m.p. 197−199 °C; DSC: 36 J/g. Within the NMR spectra ($CDCl_3$), the presence of two separate, equal H_{Ar} and two -O-CH_2-signals are interpreted in terms of two conformations present, probably due to H-bonding. The structurally similar *N*,*N*-diethylamide derivative also exists as a mixture of conformers at 298 K in $CDCl_3$.[50] In the case of ligand **5**, the more bulky groups may restrict the number of co-existing conformers to two. ^1H NMR: δ = 0.70 (br. s), 0.95 (q), 1.34 (m), 1.62 (br. s), (Σ23 H); 3.34 and 3.63 (m, 4 H), 3.9−5.1 (br. m, O-CH_2 and CH_2-Ar, 4 H), 7.18 and 7.49 (2 s, H_{Ar}, 1H each) ppm. ^{13}C NMR: δ = 13.8 (CH_3 of *n*Bu), 20.0 and 20.2 (*n*Bu), 29.7 (Ar−CH_2-Ar), 31.1 (*t*Bu), 31.5 (*n*Bu), 34.0 (quart C of *t*Bu), 45.5 (N−CH_2), 71.6 (-O-CH_2), C_{Ar}: 124.7, 127.1, 133.2, 146.4, 151.9; 168.0 (CO) ppm. IR (KBr):1646 cm^{-1} (νCO), no 1755 (COOH); TLC ($CHCl_3$/EtOH 9:1) R_f = 0.28 (characteristic short tailing).

Ligand 6: The ligand **5** (0.5 g, 0.25 mmol) was dissolved in dry toluene and treated with 2,4-bis(4-methoxyphenyl)-1,3-dithia-2,4-diphosphetane-2,4-disulfide (2.5 mmol) at 85 °C for 24 h. After cooling, the mixture was filtered and the solvents evaporated. The product was precipitated from hot acetone by adding 3% water, and was crystallized twice from hexane and washed with hot MeOH/H_2O (1:1). Yield 72%. 5,11,17,23,29,35-Hexakis(*tert*-butyl)-37,38,39,40,41,42-hexakis[(*N*,*N*-di-*n*butylthiocarbamoylmethoxy)-calix[6]arene, $C_{126}H_{198}N_6O_6S_6$ (M_r 2085.3): calcd. C 72.57, H 9.57, N 4.03, S 9.21; found C 71.99, H 9.27, N 3.87, S 8.82; m.p. 171−173 °C. In the NMR spectra ($CDCl_3$) chemical shifts in *italics* indicate some of the characteristic changes upon thionation. Similar to ligand **5**, a conformational mixture exists at 298 K. ^1H NMR: δ = 0.80 (d), 0.96 (s), 1.40 (m), 1.80 (br), (Σ138 H), 2.88 (br. d) and 3.43 (d, Ar-CH_2), 3.9 (br. m, N-CH_2), 4.75−5.05 (br., O-CH_2 and Ar-CH_2) (Σ48 H), H_{Ar}: 6.4, 6.53, 7.28, 7.55 (Σ12 H) ppm. ^{13}C NMR: δ = 13.7 (CH_3 of *n*Bu), 20.2 (*n*Bu), 27.8 (Ar−CH_2-Ar), 31.6 (*t*Bu), 32.0 (*n*Bu), 34.1 (quart C of *t*Bu), *53.5* (N-CH_2), *79.2* (-O-CH_2), 123.1 (C_{Ar}), 128.3 (C_{Ar}), 132.3 (C_{Ar}), 145.4 (C_{Ar}), 153.3 (C_{Ar}), *195.2* (CS), IR (KBr): νCO disappeared, new 1505 cm^{-1} (νCS I), 990 (νCS IV), TLC ($CHCl_3$/EtOH, 9:1) R_f = 0.95 (one spot, no partially substituted material), (CH_2Cl_2) R_f = 0.74 (1 spot, no thionation reagent).

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