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## Synthesis of *para*- and *meta*-imino- or -amino-methyl pyridyl appended *p*-*tert*-butyl-calix[4]arene or *p*-*tert*-butyl-thiacalix[4]arene in 1,3-Alternate conformation

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The multistep synthesis of eight new ligands based on either calix[4]arene or thiacalix[4]arene backbone blocked in 1,3-Alternate conformation was achieved. Both types of backbones were functionalized with pyridyl coordinating units using either imino or amino junctions. The introduction of the pyridyl units was achieved using either the position 3 (*meta*) or 4 (*para*) of the aromatic moiety. Four out of the eight ligands have been structurally investigated in the solid state by X-ray diffraction methods on single crystals.

Dedicated to Prof. Bernard MEUNIER at the occasion of his 70<sup>th</sup> birthday.

### Introduction

Calix[4]arene (CA, **1**, Figure 1)<sup>1</sup> and its analogue thiacalix[4]arene (TCA, **2**, Figure 1)<sup>2</sup>, for which the four methylene groups connecting the phenolic moieties are replaced by S atoms, are interesting backbones interest for the design of receptors and/or ligands. Dealing with thiacalix[4]arene, the thioether junction may be oxidized leading to sulfinyl (SO)<sup>3</sup> or sulfonyl (SO<sub>2</sub>)<sup>4</sup> groups. Not only these two scaffolds may be readily modified at both upper and lower rims, but in addition, these two tetraphenolic macrocycles adopt, for steric reasons, different limit conformations called cone, partial cone, 1,2-Alternate and 1,3-Alternate. Thus, the combination of these two features opens the way to the design of a large variety of abiotic compounds.

Among the four possible conformations mentioned above, the 1,3-Alternate conformation, displaying a S<sub>4</sub> symmetry, is of interest since it allows to position, in an alternate fashion, up to four interaction sites above and below the macrocyclic backbone. In particular, introduction of coordinating units leads to the formation of new discrete complexes<sup>5</sup> or extended coordination networks.<sup>6</sup>

Both CA and TCA backbones have been decorated, both at the upper and/or the lower rims, with monodentate N donor ligands such as cyano<sup>7</sup> or pyrazolyl<sup>8</sup> units. Examples of

thiacalix[4]arene derivatives in different conformations (cone, partial cone, and 1,3-Alternate) bearing four pyridyl units at the lower rim using ester junctions between the macrocyclic moiety and pyridyl group have been described.<sup>9</sup> Examples of tetrasubstituted calix[4]arene derivatives in cone conformation bearing coordinating sites at the upper and lower rims and their propensity to bind transition metals in solution have been reported.<sup>10</sup> The formation of coordination networks resulting from combinations of metal actions such as Hg<sup>2+</sup>, Cd<sup>2+</sup>, Fe<sup>2+</sup>, Co<sup>2+</sup> and Ag<sup>+</sup> with thiacalix[4]arene derivatives blocked in 1,3-Alternate conformation and bearing pyridyl units at the lower rim has been described.<sup>11</sup> Thiacalix[4]arene derivatives in different conformations bearing two pyridyl moieties at their lower rim have been prepared and their binding ability in solution towards silver cation have been described.<sup>12</sup>

Here, we report on the design and detailed synthesis of eight new ligands based on either calix[4]arene or thiacalix[4]arene backbones in 1,3-Alternate conformation bearing at their upper rim imino- or amino-methyl-pyridyl coordinating units (compounds **3–10**, figure 1). The *para*- and *meta*-imino- or -amino-methyl pyridyl derivatives have been used for the formation of new complexes or coordination polymers.<sup>13</sup>

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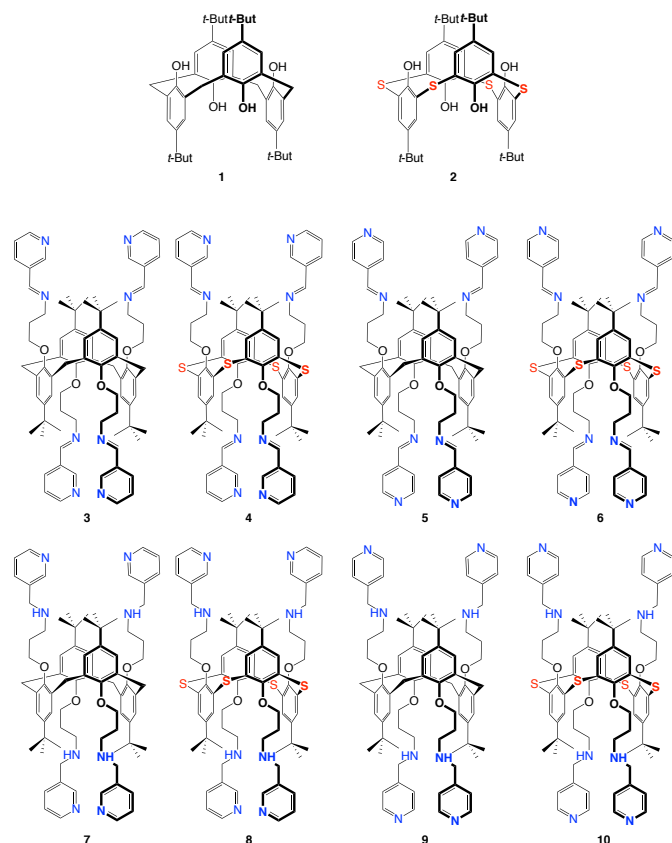


Figure 1: Calix[4]arene (CA, **1**) and thiacalix[4]arene (TCA, **2**) in *1,3*-Alternate conformation, used as platform for the design of ligands bearing four imino or amino-*meta* and *para*-pyridyl units **3-10**.

## Results and discussion

### Design of ligands **3-10**

The design of ligands **3-10** (Figure 1) is based on the *p*-*tert*butylcalix[4]arene (**1**) or *p*-*tert*butyltetra-thiacalix[4]arene (**2**) backbones in *1,3*-Alternate conformation. This type of platform, displaying a  $S_4$  symmetry, offers the possibility to introduce up to four interacting sites in an alternate fashion below and above the mean plane of the macrocyclic moiety. Both types of backbones were functionalized at the lower rim with pyridyl coordinating units (**3, 5, 7** and **9** based on **1** and (**4, 6, 8**, and **10** based on **2**). The introduction of the pyridyl units was achieved using either the position 3 (*meta*, ligands **3, 4, 7** and **8**) or 4 (*para*, ligands **5, 6, 9** and **10**) of the aromatic moiety. In all cases, a propyl fragment was used to connect the pyridyl units to the calix backbone using either an iminomethyl (N=CH, compounds **3-6**) or an aminomethyl (N-CH<sub>2</sub>, compounds **7-10**) junctions. Within each family of compounds (imino or amino derivatives), ligands **3** and **5, 4** and **6, 7** and **9** and **8** and **10** are positional isomers.

Compounds **3-10** were prepared by multistep synthesis following a strategy reported for the synthesis of analogues bearing pyridyl units connected using the position 2 (*ortho*).<sup>14</sup> The key intermediates for which the *1,3*-Alternate conformation of the calix moiety is imposed, were phthalimide derivatives **11**<sup>15</sup> and **13**<sup>16</sup> (Figure 2).

The phthalimido derivatives **11**<sup>14</sup> and **13**<sup>16</sup> were prepared in 55 and 68 % yields respectively upon condensation in the presence of Cs<sub>2</sub>CO<sub>3</sub> as base of *N*-(3-bromopropyl)phthalimide with calix[4]arene **1** or thiacalix[4]arene **2**. Compounds **11** and **13** were converted into the corresponding amino derivatives **12** and **14** by treatment with hydrazine.<sup>17,16b</sup>

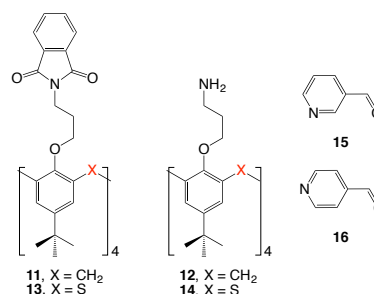


Figure 2: Precursors **11-16** used for the synthesis of ligands **3-10**.

The condensation, at room temperature, of the amino derivatives **12** or **14** with 3-Pyridinecarboxaldehyde **15** or 4-Pyridinecarboxaldehyde **16** in a EtOH/DMF (1/1) mixture, afforded the final ligands **3-6** with yields varying between 64% and 81% (Table 1).

Table 1: Yields for the condensation of the amino derivatives **12** and **14** with 3-Pyridinecarboxaldehyde **15** or 4-Pyridinecarboxaldehyde **16** leading to the formation of iminomethylpyridyl ligands **3-6** and for the formation of aminomethylpyridyl **7-10** obtained upon reduction of the imino groups.

Compound	<b>3</b>	<b>4</b>	<b>5</b>	<b>6</b>
Yield (%)	74	71	64	81
Compound	<b>7</b>	<b>8</b>	<b>9</b>	<b>10</b>
Yield (%)	76	94	93	91

The imino derivatives **3-5** were converted into the amino compounds **7-9** in 76 - 94% yield (Table 1) by reduction using NaBH<sub>4</sub>/MeOH as reducing mixture. The conversion of **6** into **10** was achieved a yield of 91 % yield using LiAlH<sub>4</sub>/THF.

All ligands **3-10** were fully characterized in solution by <sup>1</sup>H- and <sup>13</sup>C-NMR spectroscopy and mass spectrometry. As expected, the <sup>1</sup>H-NMR study revealed that the imino N=CH group signals for **3-6** are downfield shifted (in the 8.04 - 8.11 range) with respect to signals corresponding to the amino HN-CH<sub>2</sub> unit in **7-10** (in the 3.59 - 3.76 range).

### Solid-state description of ligands **4, 5, 6** and **8**

Among the 8 new ligands, four, compounds **4, 5, 6** and **8**, have been characterized in the solid state by X-ray diffraction on single crystals (see Crystallographic table 3). Crystals of compounds **4, 6** and **8** were obtained upon CH<sub>3</sub>CN vapour diffusion into a CHCl<sub>3</sub> solutions of the ligand. Crystals of **5** were obtained upon slow evaporation of solution of CHCl<sub>3</sub> containing **5** (see experimental section).

In agreement with NMR studies in solution, all four compounds **4, 5, 6** and **8** are, as expected, in *1,3*-Alternate conformation in the crystalline phase (Figure 3). All four

ligands crystallise in the  $P2_1/n$  space groups (monoclinic system). Whereas crystals of compounds **5** and **6** contain  $\text{CHCl}_3$  solvent molecules with no specific interactions with the ligand, for ligands **4** and **8**, solvent molecules could not be refined and squeeze command was applied to solve the structure.<sup>18</sup>

For compounds **4**, **5**, **6** and **8**, the metrics for the macrocyclic part are close to those observed for the parent CA and TCA and will not be detailed here. Relevant bond distances and angles are gathered in table 2. In all four cases, one of the four *tert*-butyl groups I was found to be disordered.

For the imino-derivative **4**, **5** and **6**, the C=N distances are in the 1.169(14)-1.266(8) Å range (see table 2) with the CNC angles ranging from 109.6(10)° to 118.8(9)°. For the amino derivative **8**, the HC-NH distances are in the 1.388(10)-1.488(18) range with CNC angles ranging from 113.0(8)° to 114.6(6)° confirming thus the presence of  $\text{sp}^3$  nitrogen atoms.

Table 2: Relevant angles and distances for compounds **4**, **5**, **6**, and **8**.

	<b>4</b>	<b>5</b>	<b>6</b>	<b>8</b>
$d_{\text{CA}-\text{s}}$ (Å)	1.755(8) - 1.782(8)	-	1.763(4) - 1.780(4)	1.760(4) - 1.774(5)
$d_{\text{CA}-\text{c}}$ (Å)	-	1.513(5) - 1.522(4)	-	-
$d_{\text{O}-\text{CA}}$ (Å)	1.346(13) - 1.453(9)	1.363(9) - 1.422(4)	1.355(5) - 1.436(5) -	1.363(5) - 1.446(12)
C=N	1.169(14)	1.178(5)	1.200(7)	
(imino)	1.240(11)	1.210(5)	1.223(6)	
	1.244(12)	1.253(5)	1.245(7)	
	1.265(13)	1.258(4)	1.266(8)	
C-NH				1.388(10)
(amino)				1.442(9)
				1.459(9)
				1.488(18)
CNC	109.6(10)	113.1(5)	116.5(6)	113.0(8)
(imino or	116.8(9)	116.8(4)	117.0(5)	113.5(9)
amino)	117.6(9)	117.9(5)	118.3(6)	114.1(6)
	118.8(9)	118.0(3)	118.7(5)	114.6(6)

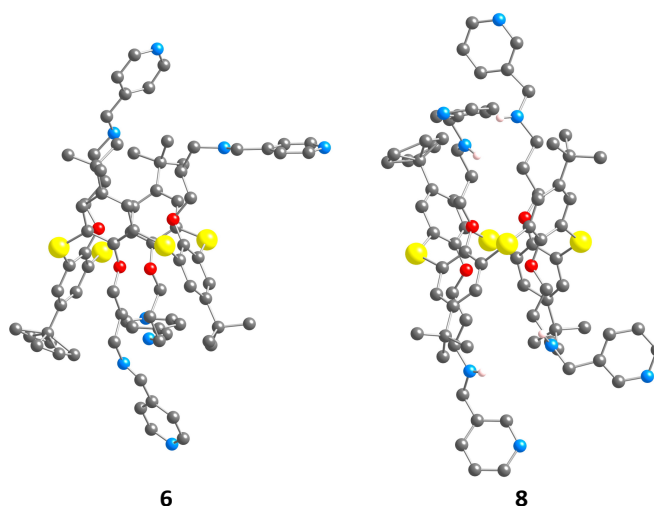
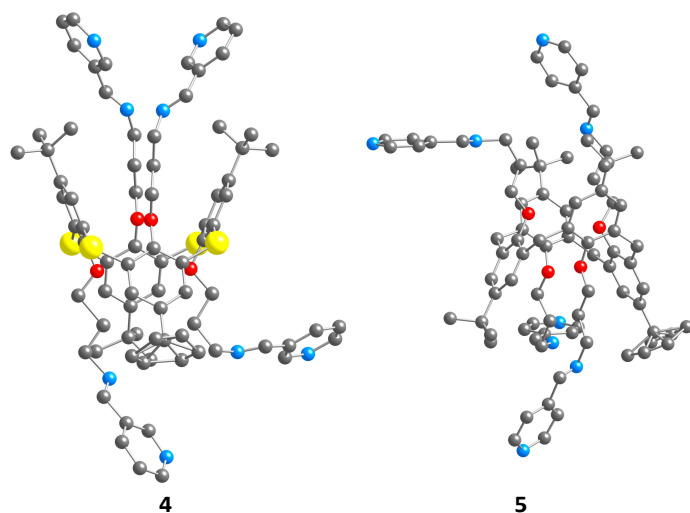


Figure 3: Solid-state structures of **4** (top left), **5** (top right), **6** (bottom left) and **8** (bottom right) showing the 1,3-Alternate conformation of backbones. H atoms, except for compound **8**, and solvent molecules in the case of compound **5** and **6** are not presented for clarity. For bond distances and angles see text.

## Conclusions

Eight new ligands **3-10** based on either calix[4]arene or thiacalix[4]arene backbones blocked in 1,3-Alternate conformation were designed and synthesized using multistep strategies. The two backbones were equipped with four pyridyl derivatives located, in an alternate fashion, above and below the mean plane of the macrocyclic units. Ligands **3-10**, while all based on the same propyl spacer, differ by the nature of the junction (imino or amino groups) and by the position of the junction on the pyridyl units (*meta* or *para*). All ligands have been fully characterized in solution and, for **4**, **5**, **6** and **8**, by X-ray diffraction on single crystals in the solid state.

In solution, the coordination propensity of ligands **3-10** towards metal cations such as  $\text{Ni}^{2+}$ ,  $\text{Co}^{2+}$ ,  $\text{Zn}^{2+}$ ,  $\text{Mn}^{2+}$ ,  $\text{Cu}^{2+}$  and  $\text{Ag}^+$  is under investigation. Furthermore, combinations of compounds **3-10** used as tectons with metal cations to generate extended coordination networks in the crystalline phase under self-assembly processes is currently under study.

## Experimental

### Materials and methods

$^1\text{H}$ -NMR and  $^{13}\text{C}$ -NMR spectra were recorded at room temperature on a Bruker (300, 400 or 500 MHz) NMR spectrometer.

Mass spectra (ESI) were obtained on a MicroTOF-Q (BRUKER) equipped with an electrospray source.

Microanalyses were performed by the Service de Microanalyses de la Fédération de Recherche Chimie, Université de Strasbourg, Strasbourg, France.

Melting points were measured in capillary on a Stuart Scientific Melting Point SMP-1 apparatus.

### Single-Crystal Studies

Data were collected at 173(2)K on a Bruker Apex-II-CCD Diffractometer equipped with an Oxford Cryosystem liquid N<sub>2</sub> device, using graphite-monochromated Mo-K $\alpha$  ( $\lambda = 0.71073$  Å) radiation. For all the structures, diffraction data were corrected for absorption. Structures were solved using SHELXS-97 and refined by full matrix least-squares on F<sub>2</sub> using SHELXL-97. The hydrogen atoms were introduced at calculated positions and not refined (riding model).<sup>19</sup> They can be obtained free of charge from the Cambridge Crystallographic Data Centre via [www.ccdc.cam.ac.uk/datarequest/cif](http://www.ccdc.cam.ac.uk/datarequest/cif). CCDC: 1545778-1545781.

### Synthetic procedures

General: All reagents were purchased from commercial sources and used without further purification. *p*-tert-butylcalix[4]arene **1** is commercially available and *p*-tert-butylthiacalix[4]arene **2** was prepared according to the literature procedures.<sup>2</sup> The synthesis of compounds **11-14** has been reported.<sup>14</sup>

All reactions were performed under a N<sub>2</sub> atmosphere.

#### 5,11,17,23-Tetra-tert-butyl-25,26,27,28-tetrakis-(3-pyridylideniminopropoxy)calix[4]arene (3)

3-Pyridinecarboxaldehyde **15** (440  $\mu$ L, 4.55 mmol) and compound **12** (0.5 g, 0.56 mmol) were dissolved in 40 mL of a EtOH/DMF (1/1) mixture and stirred at room temperature during 2 days. 100 mL of CH<sub>3</sub>CN was added to the mixture and the white precipitate thus formed was filtrated and washed several times with petroleum ether (60 mL). Filtrates were combined and placed in the refrigerator over a period of one week leading to further precipitation. Precipitates were combined affording the desired compound **3** in 1,3-Alternate conformation as a white solid (0.52 g, 74 %). mp = 122 °C. <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, 25 °C):  $\delta$ (ppm) = 1.23 (36H, s, *t*-Bu), 1.38 (8H, m, CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>), 3.38 (8H, t, N-CH<sub>2</sub>), 3.48 (8H, t, Ar-O-CH<sub>2</sub>), 3.82 (8H, s, Ar-CH<sub>2</sub>-Ar), 6.96 (8H, s, Ar-*H*), 7.30 (4H, m, Py-*H*), 8.00 (4H, t, Py-*H*), 8.11 (4H, s, Py-CH=N), 8.60 (4H, d, Py-*H*), 8.79 (4H, d, Py-*H*). <sup>13</sup>C-NMR (125 MHz, CDCl<sub>3</sub>, 25 °C):  $\delta$ (ppm) = 30.3, 31.7, 34, 39.1, 58.8, 68.1, 123.6, 125.6, 131.8, 133.0, 134.4, 143.8, 150.0, 151.2, 154.6, 157.2. MS (ESI), *m/z*: 1233.76 {[M]<sup>+</sup>, calculated 1233.67}. Anal. Calcd. for C<sub>80</sub>H<sub>96</sub>N<sub>8</sub>O<sub>4</sub>•H<sub>2</sub>O: C, 76.77%; H, 7.89%; N, 8.95%; Found: C, 76.41 %; H, 7.98%; N, 8.83%. UV-vis (CHCl<sub>3</sub>/MeOH (1/1)):  $\lambda_{\max}$  (nm) /  $\epsilon$  (mol<sup>-1</sup>Lcm<sup>-1</sup>) = 239(62668). IR (cm<sup>-1</sup>):  $\nu_{C=N}$ : 1649.

#### 5,11,17,23-Tetra-tert-butyl-25,26,27,28-tetrakis-(3-pyridylideniminopropoxy)thiacalix[4]arene (4)

3-Pyridinecarboxaldehyde **15** (560  $\mu$ L, 5.84 mmol) and compound **14** (0.7 g, 0.73 mmol) were dissolved in 40 mL of a EtOH/DMF (1/1) mixture and stirred at room temperature during 2 days. 100 mL of CH<sub>3</sub>CN was added to the mixture and the white precipitate thus formed was filtrated and washed several times with petroleum ether (100 mL). Washes were combined and placed in the refrigerator over a period of one

week leading to further precipitation which was filtered. Precipitates were combined affording the desired compound **4** in 1,3-Alternate conformation as a white solid (0.65 g, 70.6 %). mp = 188 °C. <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, 25 °C):  $\delta$ (ppm) = 1.21 (36H, s, *t*-Bu), 1.39 (8H, m, CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>), 3.39 (8H, t, N-CH<sub>2</sub>), 3.97 (8H, t, Ar-O-CH<sub>2</sub>), 7.29 (4H, m, Py-*H*), 7.31 (8H, s, Ar-*H*), 8.01 (4H, m, Py-*H*), 8.12 (4H, s, Py-CH=N), 8.60 (4H, d, Py-*H*), 8.79 (4H, d, Py-*H*). <sup>13</sup>C-NMR (75 MHz, CDCl<sub>3</sub>, 25 °C):  $\delta$ (ppm) = 30.0, 31.3, 34.3, 58.8, 66.6, 123.6, 127.5, 128, 131.8, 134.4, 145.7, 150.0, 151.3, 156.8, 157.4. MS (ESI), *m/z*: 1305.59 {[M]<sup>+</sup>, calculated 1305.82}. Anal. Calcd. for C<sub>76</sub>H<sub>88</sub>N<sub>8</sub>O<sub>4</sub>S<sub>4</sub>•C<sub>2</sub>H<sub>5</sub>OH•H<sub>2</sub>O: C, 68.39%; H, 7.06%; N, 8.18%; Found: C, 68.47 %; H, 6.68%; N, 8.20%. UV-vis (CHCl<sub>3</sub>/MeOH (1/1)):  $\lambda_{\max}$  (nm) /  $\epsilon$  (mol<sup>-1</sup>Lcm<sup>-1</sup>) = 239(58044). IR (cm<sup>-1</sup>):  $\nu_{C=N}$ : 1648.

#### 5,11,17,23-Tetra-tert-butyl-25,26,27,28-tetrakis-(4-pyridylideniminopropoxy)calix[4]arene (5)

4-Pyridinecarboxaldehyde **16** (440  $\mu$ L, 4.55 mmol) and compound **12** (0.5 g, 0.56 mmol) were dissolved in 40 mL of a EtOH/DMF (1/1) mixture and stirred at room temperature during 2 days. 100 mL of CH<sub>3</sub>CN was added to the mixture and the white precipitate thus formed was filtrated and washed several times with petroleum ether (60 mL). Filtrates were combined and placed in the refrigerator over a period of one week leading to further precipitation. Precipitates were combined affording the desired compound **5** in 1,3-Alternate conformation as a white solid (0.45 g, 64 %). mp = 166 °C. <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, 25 °C):  $\delta$ (ppm) = 1.23 (36H, s, *t*-Bu), 1.36 (8H, m, CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>), 3.38 (8H, t, N-CH<sub>2</sub>), 3.47 (8H, t, Ar-O-CH<sub>2</sub>), 3.82 (8H, s, Ar-CH<sub>2</sub>-Ar), 6.96 (8H, s, Ar-*H*), 7.50 (8H, d, Py-*H*), 8.04 (4H, s, Py-CH=N), 8.65 (8H, d, Py-*H*). <sup>13</sup>C-NMR (75 MHz, CDCl<sub>3</sub>, 25 °C):  $\delta$ (ppm) = 30.1, 31.7, 34, 39.2, 58.8, 68.0, 121.8, 125.5, 133.0, 143.0, 143.9, 150.4, 154.6, 158.2. MS (ESI), *m/z*: 1234.76 {[M+H]<sup>+</sup>, calculated 1234.67}. Anal. Calcd. for C<sub>80</sub>H<sub>96</sub>N<sub>8</sub>O<sub>4</sub>•H<sub>2</sub>O: C, 76.77%; H, 7.89%; N, 8.95%; Found: C, 76.41%; H, 7.98%; N, 8.83%. UV-vis (CHCl<sub>3</sub>/MeOH (1/1)):  $\lambda_{\max}$  (nm) /  $\epsilon$  (mol<sup>-1</sup>Lcm<sup>-1</sup>) = 238(38180). IR (cm<sup>-1</sup>):  $\nu_{C=N}$ : 1649.

#### 5,11,17,23-Tetra-tert-butyl-25,26,27,28-tetrakis-(4-pyridylideniminopropoxy)thiacalix[4]arene (6)

4-Pyridinecarboxaldehyde (560  $\mu$ L, 5.84 mmol) **16** and compound **14** (0.7 g, 0.73 mmol) were dissolved in 40 mL of a EtOH/DMF (1/1) mixture and stirred at room temperature during 2 days. 100 mL of CH<sub>3</sub>CN was added to the mixture and the white precipitate thus formed was filtrated and washed several times with petroleum ether (100 mL). Filtrates were combined and placed in the refrigerator over a period of one week leading to further precipitation. Precipitates were combined affording the desired compound **6** in 1,3-Alternate conformation as a white solid (0.78 g, 81 %). mp = 244 °C. <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, 25 °C):  $\delta$ (ppm) = 1.21 (36H, s, *t*-Bu), 1.38 (8H, m, CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>), 3.39 (8H, t, N-CH<sub>2</sub>), 3.97 (8H, t, Ar-O-CH<sub>2</sub>), 7.31 (8H, s, Ar-*H*), 7.50 (8H, d, Py-*H*), 8.06 (4H, s, Py-CH=N), 8.64 (8H, d, Py-*H*). <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>, 25 °C):  $\delta$ (ppm) = 29.8, 31.3, 34.3, 58.7, 66.5, 121.8, 127.4, 128.0, 143.0, 145.7, 150.4, 156.7, 158.4. MS (ESI), *m/z*: 1306.59

{[M+H]<sup>+</sup>, calculated 1306.82}. Anal. Calcd. for C<sub>76</sub>H<sub>88</sub>N<sub>8</sub>O<sub>4</sub>S<sub>4</sub>•C<sub>2</sub>H<sub>5</sub>OH•H<sub>2</sub>O: C, 68.54%; H, 6.86%; N, 8.20%; Found: C, 68.76%; H, 6.71%; N, 8.11%. UV-vis (CHCl<sub>3</sub>/MeOH (1/1)): λ<sub>max</sub> (nm) / ε (mol<sup>-1</sup>Lcm<sup>-1</sup>) = 238(57909). IR (cm<sup>-1</sup>): ν<sub>C=N</sub>: 1647.

**5,11,17,23-Tetra-tert-butyl-25,26,27,28-tetrakis -[(3-pyridinylmethylamino)propoxy]calix[4]arene (7)**

NaBH<sub>4</sub> (0.31g, 8.1 mmol) and compound **3** (0.5 g, 0.4 mmol) were dissolved in 30 mL of MeOH and refluxed during 2 days. 50 mL of water was added carefully and the product was extracted three times with CHCl<sub>3</sub> (3x50 mL). The organic phase was evaporated to dryness affording the desired compound **7** in 1,3-Alternate conformation as a white solid (0.38 g, 76 %). mp = 138 °C. <sup>1</sup>H-NMR (500 MHz, CDCl<sub>3</sub>, 25 °C): δ(ppm) = 1.23 (8H, m, CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>), 1.23 (36H, s, *t*-Bu), 2.24 (8H, t, CH<sub>2</sub>-N), 3.36 (8H, t, Ar-O-CH<sub>2</sub>), 3.63 (8H, s, Ar-CH<sub>2</sub>-Ar), 3.74 (8H, s, NH-CH<sub>2</sub>-Py), 6.92 (8H, s, Ar-H), 7.18 (4H, t, Py-H), 7.56 (4H, d, Py-H), 8.44 (4H, d, Py-H), 8.47 (4H, d, Py-H). <sup>13</sup>C-NMR (125 MHz, CDCl<sub>3</sub>, 25 °C): δ(ppm) = 30.1, 31.7, 33.9, 39.0, 46.4, 51.4, 68.5, 123.3, 125.7, 133.0, 135.6, 135.9, 143.6, 148.4, 149.6, 154.5. MS (ESI), *m/z*: 1241.82 {[M]<sup>+</sup>, calculated 1241.73}. Anal. Calcd. for C<sub>80</sub>H<sub>104</sub>N<sub>8</sub>O<sub>4</sub>•H<sub>2</sub>O: C, 76.27%; H, 8.48%; N, 8.89%; Found: C, 76.53%; H, 8.42%; N, 8.52%. UV-vis (CHCl<sub>3</sub>/MeOH (1/1)): λ<sub>max</sub> (nm) / ε (mol<sup>-1</sup>Lcm<sup>-1</sup>) = 237(51820). IR (cm<sup>-1</sup>): ν<sub>NH</sub>: 3293.

**5,11,17,23-Tetra-tert-butyl-25,26,27,28-tetrakis -[(3-pyridinylmethylamino)propoxy]thiacalix[4]arene (8)**

NaBH<sub>4</sub> (0.18g, 4.66 mmol) and compound **4** (0.3 g, 0.23 mmol) were dissolved in 30 mL of MeOH and refluxed during 2 days. 50 mL of water was added carefully and the product was extracted three times with CHCl<sub>3</sub> (3x50 mL). The organic phase was evaporated to dryness affording the desired compound **8** in 1,3-Alternate conformation as a white solid (0.28 g, 94 %). mp = 192 °C. <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, 25 °C): δ(ppm) = 1.15 (8H, m, CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>), 1.22 (36H, s, *t*-Bu), 2.37 (8H, t, CH<sub>2</sub>-N), 3.59 (8H, s, NH-CH<sub>2</sub>-Py), 3.86 (8H, t, NH-CH<sub>2</sub>-Py), 7.18 (4H, m, Py-H), 7.27 (8H, s, Ar-H), 7.53 (4H, t, Py-H), 8.43 (4H, d, Py-H), 8.45 (4H, d, Py-H). <sup>13</sup>C-NMR (125 MHz, CDCl<sub>3</sub>, 25 °C): δ(ppm) = 29.4, 31.3, 34.3, 46.2, 51.3, 66.6, 123.3, 127.4, 127.9, 135.6, 135.9, 145.6, 148.4, 149.6, 156.7. MS (ESI), *m/z*: 1313.65 {[M]<sup>+</sup>, calculated 1313.89}. Anal. Calcd. for C<sub>76</sub>H<sub>96</sub>N<sub>8</sub>O<sub>4</sub>S<sub>4</sub>•H<sub>2</sub>O: C, 68.53%; H, 7.42%; N, 8.41%; Found: C, 68.25%; H, 7.32%; N, 8.18%. UV-vis (CHCl<sub>3</sub>/MeOH (1/1)): λ<sub>max</sub> (nm) / ε (mol<sup>-1</sup>Lcm<sup>-1</sup>) = 265(49900). IR (cm<sup>-1</sup>): ν<sub>NH</sub>: 3300.

**5,11,17,23-Tetra-tert-butyl-25,26,27,28-tetrakis -[(4-pyridinylmethylamino)propoxy]calix[4]arene (9)**

NaBH<sub>4</sub> (0.31g, 8.1 mmol) and compound **7** (0.5 g, 0.4 mmol) were dissolved in 40 mL of MeOH and refluxed during 2 days. 50 mL of water was added carefully and the product was extracted three times with CHCl<sub>3</sub> (3x50 mL). The organic phase was evaporated to dryness and the white precipitate is dried under vacuum at 70°C during 24hrs. The desired compound, **9**, in 1,3-Alternate conformation, is obtained as a white solid (0.47 g, 93 %). mp = 142 °C. <sup>1</sup>H-NMR (500 MHz, CDCl<sub>3</sub>, 25 °C): δ(ppm) = 1.24 (36H, s, *t*-Bu), 1.24 (8H, m, CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>), 2.40 (8H, t, CH<sub>2</sub>-N), 3.39 (8H, t, Ar-O-CH<sub>2</sub>), 3.65 (8H, s, Ar-CH<sub>2</sub>-Ar),

3.76 (8H, s, NH-CH<sub>2</sub>-Py), 6.93 (8H, s, Ar-H), 7.18 (8H, d, Py-H), 8.48 (8H, d, Py-H). <sup>13</sup>C-NMR (125 MHz, CD<sub>2</sub>Cl<sub>2</sub>, 25 °C): δ(ppm) = 30.1, 31.7, 33.9, 39, 46.5, 52.8, 68.5, 122.8, 125.7, 133.1, 143.7, 149.7, 154.6. MS (ESI), *m/z*: 1241.82 {[M]<sup>+</sup>, calculated 1241.73}. Anal. Calcd. for C<sub>80</sub>H<sub>104</sub>N<sub>8</sub>O<sub>4</sub>: C, 77.38%; H, 8.44%; N, 9.02%; Found: C, 77.26%; H, 8.57%; N, 8.57%. UV-vis (CHCl<sub>3</sub>/MeOH (1/1)): λ<sub>max</sub> (nm) / ε (mol<sup>-1</sup>Lcm<sup>-1</sup>) = 237(24932). IR (cm<sup>-1</sup>): ν<sub>NH</sub>: 3258.

**5,11,17,23-Tetra-tert-butyl-25,26,27,28-tetrakis -[(4-pyridinylmethylamino)propoxy]thiacalix[4]arene (10)**

Compound **6** (0.2 g, 0.15 mmol) was dissolved in 30 mL of THF and stirred at 0°C. To this mixture, LiAlH<sub>4</sub> (0.057g, 1.5 mmol) was slowly added and the mixture was stirred at room temperature overnight. 30 mL of distilled water was added slowly and the mixture was further stirred at room temperature during two hours. The white precipitate thus formed was filtrated and dried under vacuum at 70 °C during 24 h. The desired compound **10**, in 1,3-Alternate conformation, was obtained as a white solid (0.18 g, 91 %). mp = 264 °C. <sup>1</sup>H-NMR (300 MHz, CD<sub>2</sub>Cl<sub>2</sub>, 25 °C): δ(ppm) = 1.16 (8H, m, CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>), 1.26 (36H, s, *t*-Bu), 2.24 (8H, t, CH<sub>2</sub>-N), 3.63 (8H, s, NH-CH<sub>2</sub>-Py), 3.89 (8H, t, Ar-O-CH<sub>2</sub>), 7.19 (8H, d, Py-H), 7.33 (8H, s, Ar-H), 8.45 (8H, d, Py-H). <sup>13</sup>C-NMR (125 MHz, CD<sub>2</sub>Cl<sub>2</sub>, 25 °C): δ(ppm) = 29.5, 31.1, 34.2, 46.2, 52.6, 65.5, 122.8, 127.3, 127.9, 145.7, 149.6, 149.8, 156.7. MS (ESI), *m/z*: 1313.64 {[M]<sup>+</sup>, calculated 1313.89}. Anal. Calcd. for C<sub>76</sub>H<sub>96</sub>N<sub>8</sub>O<sub>4</sub>S<sub>4</sub>•H<sub>2</sub>O: C, 68.53%; H, 7.42%; N, 8.41%; Found: C, 68.61%; H, 7.40%; N, 8.40%. UV-vis (CHCl<sub>3</sub>/MeOH (1/1)): λ<sub>max</sub> (nm) / ε (mol<sup>-1</sup>Lcm<sup>-1</sup>) = 264(35060). IR (cm<sup>-1</sup>): ν<sub>NH</sub>: 3410

**Crystallisation conditions**

Compound **4**: a vial containing the compound **4** (5 mg, 3.82 10<sup>-3</sup> mmol) in CHCl<sub>3</sub> (0.5 mL) was placed in a closed beaker containing acetonitrile. Slow vapour diffusion of acetonitrile into the CHCl<sub>3</sub> solution produced, after several days, colourless crystals suitable for X-ray diffraction (Formula: C<sub>76</sub>H<sub>88</sub>N<sub>8</sub>O<sub>4</sub>S<sub>4</sub>).

Compound **5**: 2.0 mL of acetonitrile was added to a solution of **5** (5 mg, 4.05 10<sup>-3</sup> mmol) in CHCl<sub>3</sub> (2.0 mL). Slow evaporation at room temperature produced, after one day, colourless crystals (Formula: C<sub>80</sub>H<sub>100</sub>N<sub>8</sub>O<sub>4</sub>•CHCl<sub>3</sub>) suitable for X-ray diffraction.

Compound **6**: a vial containing the compound **6** (5 mg, 3.82 10<sup>-3</sup> mmol) in CHCl<sub>3</sub> (0.5 mL) was placed in a closed beaker containing acetonitrile. Slow vapour diffusion of acetonitrile into the CHCl<sub>3</sub> solution produced, after several days, colourless crystals suitable for X-ray diffraction (Formula: C<sub>76</sub>H<sub>88</sub>N<sub>8</sub>O<sub>4</sub>S<sub>4</sub>•CHCl<sub>3</sub>).

Compound **8**: a vial containing the compound **8** (5 mg, 3.80 10<sup>-3</sup> mmol) in CHCl<sub>3</sub> (0.5 mL) was placed in a closed beaker containing acetonitrile. Slow vapour diffusion of acetonitrile into the CHCl<sub>3</sub> solution produced, after several days, colorless crystals suitable for X-ray diffraction (Formula: C<sub>76</sub>H<sub>96</sub>N<sub>8</sub>O<sub>4</sub>S<sub>4</sub>).

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**Table 3:** Crystallographic Parameters for **4**, **5**, **6** and **8** recorded at 173 K.

Formula	<b>4</b>	<b>5</b>	<b>6</b>	<b>8</b>
	C <sub>76</sub> H <sub>88</sub> N <sub>8</sub> O <sub>4</sub> S <sub>4</sub>	C <sub>80</sub> H <sub>96</sub> N <sub>8</sub> O <sub>4</sub> , CHCl <sub>3</sub>	C <sub>76</sub> H <sub>88</sub> N <sub>8</sub> O <sub>4</sub> S <sub>4</sub> , CHCl <sub>3</sub>	C <sub>76</sub> H <sub>96</sub> N <sub>8</sub> O <sub>4</sub> S <sub>4</sub>
Molecular weight	1305.78	1357.05	1425.15	1313.85
Crystal system	Monoclinic	Monoclinic	Monoclinic	Monoclinic
Space group	<i>P</i> 2 <sub>1</sub> / <i>n</i>	<i>P</i> 2 <sub>1</sub> / <i>n</i>	<i>P</i> 2 <sub>1</sub> / <i>n</i>	<i>P</i> 2 <sub>1</sub> / <i>n</i>
<i>a</i> (Å)	14.021(3)	20.9892(10)	20.9999(10)	15.0334(16)
<i>b</i> (Å)	15.136(3)	14.9268(12)	15.0842(6)	13.939(2)
<i>c</i> (Å)	34.374(8)	24.0802(18)	24.1747(13)	36.796(6)
$\alpha$ (deg)	90	90	90	90
$\beta$ (deg)	93.023(3)	98.511(2)	98.065(2)	107.1990(10)
$\gamma$ (deg)	90	90	90	90
<i>V</i> (Å <sup>3</sup> )	7285(3)	7461.3(9)	7582.0(6)	7641.3(18)
<i>Z</i>	4	4	4	4
Colour	colourless	colourless	colourless	colourless
Crystal dim (mm <sup>3</sup> )	0.07 x 0.07 x 0.06	0.07 x 0.07 x 0.06	0.07 x 0.07 x 0.06	0.06 x 0.05 x 0.05
D <sub>calc</sub> (gcm <sup>-3</sup> )	1.191	1.204	1.248	1.142
<i>F</i> (000)	2784	2888	3016	2816
$\mu$ (mm <sup>-1</sup> )	0.184	0.178	0.284	0.175
Wavelength (Å)	0.71073	0.71073	0.71073	0.71073
Number of data meas.	56024	41422	51207	20663
Number of data with <i>I</i> > 2 $\sigma$ ( <i>I</i> )	17081 [R(int) = 0.0821]	17812 [R(int) = 0.0539]	22032 [R(int) = 0.0730]	20663 [R(int) = 0.0850]
<i>R</i>	R1 = 0.1090, wR2 = 0.2164	R1 = 0.0861, wR2 = 0.2098	R1 = 0.0883, wR2 = 0.2363	R1 = 0.1068, wR2 = 0.2769
<i>R</i> <sub>w</sub>	R1 = 0.1536, wR2 = 0.2415	R1 = 0.1552, wR2 = 0.2474	R1 = 0.2124, wR2 = 0.3068	R1 = 0.2218, wR2 = 0.3205
GOF	1.014	1.027	1.025	1.092
Largest peak in final difference (eÅ <sup>-3</sup> )	1.562 and -1.132	1.129 and -0.613	0.975 and -0.845	0.991 and -0.725