Synthesis and Application of Iso(thio)cyanate-Functionalized Calix[4]arenes

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Aminocalix[4]arenes **7–12** react with triphosgene and thiophosgene to the corresponding iso(thio)cyanate-functionalized calix[4]arenes **13–20**. Carbamate- (**21–25**) and urea-substituted calix[4]arenes (**26, 27**) can be obtained via isocyanatocalix[4]arenes using a one-pot synthesis starting from the corresponding aminocalix[4]arenes in moderate to good

yields. Isothiocyanate-functionalized calix[4]arenes **16, 18** react selectively with amines to the corresponding thioureas **28–31** in 59–83% yield. Reaction of isothiocyanate-functionalized calix[4]arenes **16, 19, 20** with cavitands **34, 38** gives 2:2 products **42–45** in 35–42% yield.

Introduction

Our strategy for the synthesis of (large) receptor molecules comprises the proper combination of (different) medium-sized building blocks. A prerequisite is that these building blocks should be easily accessible and have relatively rigid structures, and in addition it should be possible to introduce selectively different functional groups. This methodology has been successfully applied for the synthesis of (large) receptor molecules by combination of calix[4]arenes^[1] with β -cyclodextrins^[2], porphyrins^[3], cavitands^[4], or other calix[4]arenes^[5]. Calix[4]arenes and cavitands have been coupled in different combinations. In a 1:1 mode a carcerand is formed that encapsulates amides, sulphoxides, or ketones^[6]. In the 1:2^[7] and 2:1^[8] combination large hydrophobic surfaces are formed which are able to complex neutral molecules such as steroids. Finally, a 2:2 ratio gives a so-called holand having a large, rigid cavity of nanosize dimensions^[9]. In all cases the calix[4]arenes and cavitands were coupled via acetamido spacers. Since in some cases the acetamido bridges were rather flexible, a new strategy for the synthesis of calix[4]arene cavitand coupling products was developed starting from iso(thio)cyanate-functionalized calix[4]arenes.

Reactions between iso(thio)cyanates and alcohols and amines generally proceed smoothly and without the demand for additives, e.g. base or catalyst^[10]. Although the resulting carbamate bond is comparable to the acetamido bridge used previously, since they only differ in the position of the carbonyl function, the resulting (thio)urea bond is more rigid. Furthermore, the iso(thio)cyanate groups can be obtained via selectively functionalized nitrocalix[4]arenes and without interference of other functional groups. Although a wide variety of functional groups has been intro-

duced at the upper rim of calix[4]arenes^[11], iso(thio)cyanate-functionalized calix[4]arenes are not known.

In this paper the chemistry of iso(thio)cyanate-functionalized calix[4]arenes is described. After the synthesis and model reactions of the iso(thio)cyanatocalix[4]arenes, coupling with (aminomethyl)-substituted cavitands will be discussed.

Results and Discussion

Synthesis of Iso(thio)cyanate-Functionalized Calix[4]arenes: In most cases the synthesis starts with the reduction of the known nitrocalix[4]arenes **1–5** using $\text{SnCl}_2 \cdot 2 \text{H}_2\text{O}$ in refluxing EtOH. The use of this reducing agent is preferred over Raney nickel/hydrazine monohydrate because it avoids the use of toxic reagents and, furthermore, gives aminocalix[4]arenes in reproducibly good yields and high purities. Subsequent reaction of aminocalix[4]arenes **8** and **10** with triphosgene^[11] (0.33 equiv. per NH_2 group) in refluxing toluene for two hours afforded isocyanates **13** and **14** which were used without further purification^[12]. The introduction of the isocyanate moieties could clearly be proven by the presence of a characteristic infrared absorption for the $\text{N}\equiv\text{C}$ vibration at ca. 2270 cm^{-1} ^[13].

Diiododinitrocalix[4]arene **5** was used for the synthesis of diphthalimidocalix[4]arene **6** which gave diaminodinitrocalix[4]arene **12** in quantitative yield after deprotection of the phthalimido groups using literature procedures^[14]. Furthermore, reduction of the nitro groups of **5** with $\text{SnCl}_2 \cdot 2 \text{H}_2\text{O}$ afforded aminocalix[4]arene **11** in 70% yield. Isothiocyanates **15–20** were obtained in 52 to > 95% yield from the corresponding amines via reaction with thiophosgene in refluxing toluene. Unlike isocyanates **13** and **14**, isothiocyanates **15–20** are stable and could be isolated by recrystallization of the crude reaction mixture from a $\text{MeOH}/\text{CH}_2\text{Cl}_2$

Nitrocalix[4]arenes

	R ¹	R ²	R ³	R ⁴
1	NO ₂	H	H	H
2	NO ₂	H	NO ₂	H
3	NO ₂	NO ₂	H	H
4	NO ₂	NO ₂	NO ₂	NO ₂
5	NO ₂	I	NO ₂	I
6	NO ₂	Ph	NO ₂	Ph

Aminocalix[4]arenes

	R ¹	R ²	R ³	R ⁴	Yield (%)
7	NH ₂	H	H	H	>95
8	NH ₂	H	NH ₂	H	92
9	NH ₂	NH ₂	H	H	79
10	NH ₂	NH ₂	NH ₂	NH ₂	95
11	NH ₂	I	NH ₂	I	70
12	NH ₂	NO ₂	NH ₂	NO ₂	>95

Iso(thio)cyanatocalix[4]arenes

	R ¹	R ²	R ³	R ⁴	Yield (%)
13	NCO	H	NCO	H	n.i.
14	NCO	NCO	NCO	NCO	n.i.
15	NCS	H	H	H	77
16	NCS	H	NCS	H	56
17	NCS	NCS	H	H	52
18	NCS	NCS	NCS	NCS	>95
19	NCS	I	NCS	I	79
20	NCS	NO ₂	NCS	NO ₂	82

Carbamate-Functionalized Calix[4]arenes

	R ¹ = R ³	R ² = R ⁴
21	NHC(O)OCH ₃	H
22	NHC(O)OCH ₂ Ph	H
23	NHC(O)OCH ₃	NHC(O)OCH ₃
24	NHC(O)OCH ₂ CH ₃	NHC(O)OCH ₂ CH ₃
25	NHC(O)OCH ₂ Ph	NHC(O)OCH ₂ Ph

(Thio)Ureidocalix[4]arenes

	R ¹ = R ³	R ² = R ⁴
26	NHC(O)NHCH ₂ Ph	H
27	NHC(O)NHCH ₂ Ph	NHC(O)NHCH ₂ Ph
28	NHC(S)NHC ₄ H ₉	H
29	NHC(S)NHCH ₂ Ph	H
30	NHC(S)NHC ₄ H ₉	NHC(S)NHC ₄ H ₉
31	NHC(S)NHCH ₂ Ph	NHC(S)NHCH ₂ Ph

mixture^[15]. The isothiocyanates show a characteristic absorption in the infrared spectrum at $\tilde{\nu} = 2110\text{--}2130\text{ cm}^{-1}$ for the N≡C vibration^[13]. The syntheses of **19** and **20** demonstrate the compatibility of the isothiocyanate with other functional groups.

To study the reactivity of the iso(thio)cyanate-functionalized calix[4]arenes model reactions were carried out with common alcohols and amines.

Model Reactions. — **Reactions with Alcohols:** Carbamate-functionalized calix[4]arenes **21–24** were obtained in 54–78% yield, starting from the aminocalix[4]arenes **8** and **10**, via in situ reaction of the corresponding isocyanates **13** and **14** with the appropriate alcohols^[16]. Tetracarbamate **25** could only be isolated in 26% yield, whereas dicarbamate **22** was obtained in 54% yield. In the case of **25** the presence of NEt₃ was required to obtain a pure product. NEt₃ probably acts as a catalyst but may also serve as an acid scavenger avoiding decomposition of the product. Using infrared spectroscopy carbamates **21–25** could easily be identified by characteristic C=O (stretch) absorptions at $\tilde{\nu} = 1710\text{ cm}^{-1}$ ^{[13][17]}. Furthermore, absorptions at ca. 3330 cm^{-1} (NH stretch) and 1530 cm^{-1} (NH bend) indicate that in all compounds the amide moiety adopts a *trans* orientation^{[13][17]}.

The FAB mass spectrum of tetracarbamate **23**, in contrast to that of dicarbamate **21**, shows a small signal corresponding to a dimer. The dimer formation is most likely due to intermolecular interactions between the amide moieties of the carbamate group. Previously it has been shown that a bis(acetamido)calix[4]arene dimerizes in CDCl₃ solu-

tion with a K_{dim} of 3.8 M^{-1} ^[18]. This indicates that the intermolecular interactions are weak.

Reactions with Amines: Reaction of iso(thio)cyanatocalix[4]arenes **13**, **14**, **16**, and **18** with amines afforded (thio)urea-functionalized calix[4]arenes **26–31** in 53–83% yield without extensive purification^{[19][20]}.

The infrared spectra of urea derivatives **26** and **27** show characteristic absorptions at $\tilde{\nu} = 1660\text{ cm}^{-1}$ (C=O stretch). Furthermore, absorptions at $\tilde{\nu} = 3300\text{--}3380\text{ cm}^{-1}$ (NH stretch) and $1520\text{--}1550\text{ cm}^{-1}$ (NH bend) indicate that in all products the (thio)amide group adopts the *trans* conformation^{[13][17]}.

Whereas the solubility of tetraureidocalix[4]arene **27** in CDCl₃ is too low to obtain a good ¹H-NMR spectrum, the spectra of tetrakis(thioureido)calix[4]arenes **30** and **31** show extreme line broadening in CDCl₃. This is indicative for the formation of intra- and intermolecular hydrogen bonds. Previously, it has been demonstrated that in upper-rim (thio)urea-functionalized calix[4]arenes intramolecular hydrogen bonding hampers the complexation of anions^[21]. Furthermore, non-covalently bonded assemblies may be formed. The FAB mass spectra of both the di- and tetraureidocalix[4]arenes **26** and **27** reveal the presence of small signals corresponding to the dimers. Thioureidocalix[4]arenes **29** and **31**, which possess a stronger hydrogen bond donating ability but a weaker hydrogen bond accepting ability compared to the ureidocalix[4]arenes^[22], both showed the formation of dimers^[23]. Furthermore, tetrakis(thioureido)calix[4]arene **31** also exhibited the formation of a trimer in the FAB mass spectrum. This might indicate that the hydro-

gen-bonded assembly is not well defined. This was also suggested by the line broadening observed in the ^1H -NMR spectrum. Recently, the formation of well-defined dimers of tetraurea-functionalized calix[4]arenes was reported by Rebek et al.^[24] and Böhmer et al.^[25] Decisive evidence for the presence of the dimers was found by ^1H -NMR spectroscopy. In apolar solvents two different signals are present for the ArH atoms of the calix[4]arene^[26].

The results indicate that dimer formation observed by Rebek et al. and Böhmer et al. might also occur with other calix[4]arenes bearing an amide fragment, viz. carbamate- and (thio)urea-functionalized calix[4]arenes, at the upper rim. It should be noted, however, that the FAB mass-spectrometry experiments only reveal the presence of dimers, but do not give any information concerning the geometry or stability.

Coupling Between Isothiocyanate-Functionalized Calix[4]arenes and Aminomethyl Cavitanes: Although in the model reactions good results were obtained for the isocyanato-calix[4]arenes (vide supra), the use of isothiocyanates for the coupling with cavitanes is preferred since they can be purified and do not have to be used in situ. Recently, we developed reproducible procedures^[27] for the synthesis of (selectively) functionalized cavitanes **32**–**36** which gives the opportunity to study the coupling with isothiocyanate-substituted calix[4]arenes.

Reaction of **36** with sodium acetate followed by deprotection of the phthalimido and acetate groups using hydrazine monohydrate gave 1,3-bis(aminomethyl)-2,4-bis(hydroxymethyl)cavitand (**38**). This compound shows characteristic signals in the ^1H -NMR spectrum for the CH_2OH and CH_2NH_2 atoms at $\delta \approx 4.5$ and $\delta \approx 3.5$, respectively.

	R ¹	R ²	R ³	R ⁴
32	NH ₂	H	H	H
33	NH ₂	NH ₂	H	H
34	NH ₂	H	NH ₂	H
35	NH ₂	NH ₂	NH ₂	NH ₂
36	Pht	Br	Pht	Br
37	Pht	OAc	Pht	OAc
38	NH ₂	OH	NH ₂	OH

Mono(isothiocyanato)calix[4]arene: In order to investigate the reactivity of isothiocyanate-functionalized calix[4]arenes toward (aminomethyl)cavitanes, mono(isothiocyanato)calix[4]arene **15** was allowed to react with mono- and

tetrakis(aminomethyl)cavitanes **32** and **35** in refluxing CHCl_3 . Both reactions gave the expected products, i.e. 1:1 and 4:1 coupled products **39** and **40** in 53 and 87% yield, respectively.

The FAB mass spectra of compounds **39** and **40** both show molecular ion peaks that correspond to the 1:1 and 4:1 coupled product, respectively. Furthermore, characteristic signals for the ArHNH and CH_2NH atoms were found in the ^1H -NMR spectra at $\delta \approx 6.4$ and $\delta \approx 4.6$, respectively. The compounds show no line broadening in the ^1H -NMR spectra indicating that both systems are flexible on the NMR chemical shift timescale. These reactions show that it is possible to couple isothiocyanate-functionalized calix[4]arenes and aminomethyl-functionalized cavitanes.

39 **40**

Bis(isothiocyanato)calix[4]arenes: The results from the coupling reactions with mono(isothiocyanato)calix[4]arene **15**, led us to investigate the coupling between disubstituted calix[4]arenes and cavitands.

Although ^1H -NMR and FAB mass spectrometry indicated that some reaction had occurred no pure coupled products could be obtained from reactions between 1,2-bis(isothiocyanato)calix[4]arene **17** and 1,2-bis(aminomethyl)- and tetrakis(aminomethyl)cavitands **33** and **35**. This may indicate that the distance between the isothiocyanate groups of calix[4]arene **17** is too small to allow reaction with both aminomethyl groups of cavitands **33** and **35**. Therefore, we

explored the coupling reaction between 1,3-bis(isothiocyanato)calix[4]arenes **16**, **19**, and **20** and 1,3-bis(aminomethyl)-cavitands **34** and **38**.

Reaction between 1,3-bis(isothiocyanato)calix[4]arene **16** and 1,3-bis(aminomethyl)cavitands **34** under high-dilution conditions in refluxing CHCl_3 resulted in 2:2 coupled product **42** in 37% yield^[28]. Surprisingly, 1:1 coupled product **41** could not be detected^[29]. Inspection of CPK molecular models indicate that 1:1 coupled product **41** can only be formed if the NH atoms point into the cavity. The results might indicate that this orientation is not favored. Furthermore, the distance between the two aminomethyl groups

41 ($R = \text{H, I, NO}_2$)

	42	43	44	45
R^1	H	I	NO_2	H
R^2	H	H	H	OH

might be too large for an intramolecular reaction, i.e. after the first coupling, to occur. The 2:2 coupled compound **42** is comparable to the *holand* reported by Reinhoudt et al.^[30] but in that case the product is obtained by a multistep synthesis with a low overall yield. The main difference, however, is the number of connections between each calix[4]- and cavitand unit; in the *holand* the calix[4]- and cavitand moieties are connected via two bridges, whereas in **42–45** only one bridge is present. Although this may be a disadvantage regarding the flexibility of the thiourea-coupled products, the compounds described here still allow introduction of additional binding sites. This is nicely demonstrated by the reaction of **34** with diiodo- and dinitrobis(isothiocyanato)calix[4]arenes **19** and **20** which gave 2:2 coupled products **43** and **44** in 42 and 35% yield, respectively. Furthermore, the selectivity of the isothiocyanatocalix[4]arenes towards amines is demonstrated by the synthesis of **45** which contains four “free” hydroxymethyl groups. Compounds **42–45** all showed a molecular ion peak in the FAB mass spectrum corresponding to 2:2, and not 1:1, coupled products.

Parts of the ^1H -NMR spectra of the 2:2 coupled products **42–44** are presented in Figure 1. The high symmetry of the products is nicely demonstrated. There is a significant difference between the chemical shifts for the CH_2NH atoms of bis(thioureido)calix[4]arenes **28** and **29** and the 2:2 coupled products **42–45**, viz. $\delta \approx 7.1$ and 4.5, respectively. This might indicate that the formation of an intramolecular hydrogen bond is not possible in the coupled products due to steric reasons. Furthermore, it might suggest that the calix[4]arene moieties in coupled products **42–44** do not adopt a pinched cone conformation in which the aromatic moieties that are coupled to the cavitand are parallel oriented. The chemical shift position for the *o*- ArHNO_2 atoms of **44** ($\text{R}^1 = \text{NO}_2$) reveals that these aromatic moieties are most likely also not parallel^[31]. The ^1H -NMR spectrum for **44** ($\text{R}^1 = \text{NO}_2$) shows some differences with respect to the spectra of the other two products; the signals are broadened and the ArCH_2Ar signal at $\delta \approx 3.2$ as well as the signal for the ArHNH atoms at $\delta \approx 6$ are shifted downfield. This suggests that the structural properties of the products are influenced by the substituents on the calix[4]arene moiety. The ^1H -NMR spectra of **42–44** demonstrate that rotation around the $\text{ArC}-\text{NHR}$ bond is fast on the NMR chemical shift timescale since only one signal is found for the ArHNH atoms. Coupled products **42–44** show extreme line broadening of the signals in the ^1H -NMR spectra upon lowering the temperature to -55°C . This indicates that the motions within the coupled products become slow at these temperatures^[32].

Conclusions

In this paper we demonstrated that iso(thio)cyanate-functionalized calix[4]arenes are readily accessible from the corresponding aminocalix[4]arenes via reaction with triphosgene and thiophosgene, respectively. Carbamate- and urea-substituted calix[4]arenes can be obtained via isocyanatocalix[4]arenes using a one-pot synthesis starting from the cor-

Figure 1. Part of the ^1H -NMR spectra (250 MHz, CDCl_3 , room temp.) of 2:2 coupled products **42–44**

responding aminocalix[4]arenes in moderate to good overall yields. Isothiocyanate-functionalized calix[4]arenes react selectively with amines to give thioureas in 59–83% yield. Furthermore, the use of isothiocyanatocalix[4]arenes as molecular building blocks was demonstrated by the reaction with (aminomethyl)cavitands resulting in 2:2 coupled products in 35–42% yield. In conclusion, the results clearly demonstrate that iso(thio)cyanatocalix[4]arenes are useful building blocks for the synthesis of new, potential receptor molecules.

Experimental Section

General: Melting points were determined with a Reichert melting-point apparatus and are uncorrected. – NMR spectra were recorded with a Bruker AC250 (^1H NMR 250 MHz) or a Varian Unity 400 (^1H NMR 400 MHz) spectrometer in CDCl_3 , unless stated otherwise. Residual solvent protons were used as internal standard and chemical shifts are given in ppm relative to tetramethylsilane (TMS). – Fast-atom bombardment (FAB) mass spectra were measured with a Finnigan MAT 90 spectrometer using *m*-nitrobenzyl alcohol (NBA) as a matrix. – Infrared spectra were measured with a BIO-RAD FTS-60 or a Perkin-Elmer 3110 spectrophotometer. – All solvents were purified by standard procedures. Hexanes refers to the fraction with b.p. $60\text{--}80^\circ\text{C}$. All alcohols and amines used for the model reactions were distilled prior to use. All other chemicals were analytically pure and were used without further purification. – All reactions were carried out under argon. The presence of solvent in the analytical samples was confirmed by ^1H -NMR spectroscopy. Flash chromatography was performed on silica gel (SiO_2), E. Merck (0.040–0.063 mm, 230–240 mesh). For drop-

wise additions a perfusor was used. – Nitrocalix[4]arenes **1**,^[33] **2**,^[33] **3**,^[33] **4**,^[34] **5**,^[14] **6**,^[14] and **12**^[14] were prepared according to literature procedures. The synthesis of functionalized cavitands **32–36** was performed as described previously^[27].

Aminocalix[4]arenes 7–11. – *General Procedure:* A suspension of the appropriate nitrocalix[4]arene and $\text{SnCl}_2 \cdot 2 \text{H}_2\text{O}$ (5 equiv. per nitro group) in EtOH (25 ml) was refluxed until no starting material was detected by TLC (about 4–8 h). After cooling to room temp., the mixture was poured onto crushed ice and the pH was adjusted to 9–10 with 1 N KOH. After extraction with CH_2Cl_2 ($3 \times 25 \text{ ml}$), the combined organic layers were washed with brine (25 ml) and dried with MgSO_4 or Na_2SO_4 . Aminocalix[4]arenes **7–11** were obtained after concentrating and drying in vacuo and used without further purification.

5-Amino-25,26,27,28-tetrapropoxycalix[4]arene (7): The reaction was carried out using **1** (0.50 g, 0.78 mmol) and $\text{SnCl}_2 \cdot 2 \text{H}_2\text{O}$ (0.88 g, 3.92 mmol) in EtOH (25 ml), yield 0.45 g (99%), m.p. 195–196°C. – ^1H NMR: $\delta = 6.75\text{--}6.5$ (m, 9 H, ArH), 5.94 (s, 2 H, ArHNH₂), 4.45 and 4.38 (2 d, 4 H, $J = 13.4 \text{ Hz}$, ArCH₂Ar), 3.9–3.8 (m, 6 H, OCH₂), 3.79 (t, 2 H, $J = 7.7 \text{ Hz}$, OCH₂), 3.15 and 3.12 (2 d, 4 H, $J = 13.4 \text{ Hz}$, ArCH₂Ar), 2.75 (br. s, 2 H, NH₂), 2.05–1.8 (m, 8 H, OCH₂CH₂), 1.15–0.95 (m, 12 H, CH₃). – ^{13}C NMR: $\delta = 156.7, 149.8, 140.3, 135.6, 135.2, 128.1, 115.4, 76.7$ and 76.5 (OCH₂), 31.1 (ArCH₂Ar), 23.2, 10.3. – MS-FAB; m/z : 607.8 [M^+], calcd. ($\text{C}_{40}\text{H}_{49}\text{NO}_4$) 607.4.

5,17-Diamino-25,26,27,28-tetrapropoxycalix[4]arene (8): The reaction was carried out using **2** (0.50 g, 0.73 mmol) and $\text{SnCl}_2 \cdot 2 \text{H}_2\text{O}$ (1.69 g, 7.32 mmol) in EtOH (25 ml), yield 0.42 g (92%), m.p. 268–270°C (ref.^[35]; m.p. 243–245°C). The ^1H -NMR spectrum is identical to that in the literature.

5,11-Diamino-25,26,27,28-tetrapropoxycalix[4]arene (9): The reaction was carried out using **3** (1.70 g, 2.48 mmol) and $\text{SnCl}_2 \cdot 2 \text{H}_2\text{O}$ (5.0 g, 21.7 mmol) in EtOH (50 ml), yield 1.21 g (78%), m.p. 219–221°C (hexane). – ^1H NMR: $\delta = 6.75\text{--}6.6$ (m, 6 H, ArH), 6.03 and 5.98 (2 d, 4 H, $J = 2.8 \text{ Hz}$, ArH), 4.50, 4.42, and 4.33 [3 d (1:2:1), 4 H, $J = 13.3 \text{ Hz}$, ArCH₂Ar], 3.9–3.8 (m, 4 H, OCH₂), 3.8–3.75 (m, 4 H, OCH₂), 3.18, 3.05, and 2.95 [3 d (1:2:1), 4 H, $J = 13.3 \text{ Hz}$, ArCH₂Ar], 3.12 (br. s, 4 H, NH₂), 2.0–1.85 (m, 8 H, OCH₂CH₂), 1.05–0.95 (m, 12 H, CH₃). – ^{13}C NMR: $\delta = 156.8, 149.9, 140.3, 135.6, 135.2, 128.1, 128.0, 121.5, 115.4, 76.7$ and 76.6 (OCH₂), 31.1 (ArCH₂Ar), 23.3, 23.2, 10.4. – MS-FAB; m/z : 755.5 [$\text{M} + \text{Cs}^+$], calcd. 755.3. – $\text{C}_{40}\text{H}_{50}\text{N}_2\text{O}_4$ (622.8): calcd. C 77.06, H 8.08, N 4.49; found C 76.84, H 8.29, N 4.42.

5,11,17,23-Tetraamino-25,26,27,28-tetrapropoxycalix[4]arene (10): The reaction was carried out using **4** (0.50 g, 0.65 mmol) and $\text{SnCl}_2 \cdot 2 \text{H}_2\text{O}$ (2.98 g, 12.9 mmol), yield 0.40 g (95%), m.p. 234–236°C. – ^1H NMR: $\delta = 6.05$ (s, 8 H, ArH), 4.31 and 2.91 (AB q, 8 H, $J = 13.5 \text{ Hz}$, ArCH₂Ar), 3.72 (t, 8 H, $J = 7.5 \text{ Hz}$, OCH₂), 3.05 (s, 8 H, NH₂), 1.9–1.8 (m, 8 H, OCH₂CH₂), 0.94 (t, 12 H, $J = 7.5 \text{ Hz}$, CH₃).

5,17-Diamino-11,17-diiodo-25,26,27,28-tetrapropoxycalix[4]arene (11): The reaction was carried out using **5** (1.70 g, 1.82 mmol) and $\text{SnCl}_2 \cdot 2 \text{H}_2\text{O}$ (4.0 g, 13.2 mmol) in EtOH (100 ml), yield 1.11 g (70%), m.p. 299–302°C. – ^1H NMR: $\delta = 7.17$ (s, 4 H, ArHI), 5.81 (s, 4 H, ArHNH₂), 4.30 and 2.98 (AB q, 8 H, $J = 13.4 \text{ Hz}$, ArCH₂Ar), 3.85 (t, 4 H, $J = 7.6 \text{ Hz}$, OCH₂), 3.67 (t, 4 H, $J = 7.1 \text{ Hz}$, OCH₂), 3.13 (br. s, 4 H, NH₂), 1.9–1.8 (m, 8 H, OCH₂CH₂), 1.05–0.85 (m, 12 H, CH₃). – ^{13}C NMR: $\delta = 157.3, 149.3, 140.8, 138.5, 137.0, 134.1, 115.8, 85.4$ (ArCI), 76.9 and 76.6 (OCH₂), 30.8 (ArCH₂Ar), 23.2, 23.0, 10.5, 10.1. – MS-FAB; m/z : 874.7 [M^+], calcd. ($\text{C}_{40}\text{H}_{48}\text{I}_2\text{N}_2\text{O}_4$) 874.7.

Isocyanatocalix[4]arenes 13 and 14. – *General Procedure:* A mixture of **8** or **10** and triphosgene (0.33 equiv. per amino group) was refluxed in dry toluene for two h. The resulting solution of **13** and **14** was directly used for further reactions.

5,17-Bis(isocyanato)-25,26,27,28-tetrapropoxycalix[4]arene (13): The reaction was carried out using **8** (0.84 g, 1.35 mmol) and triphosgene (0.27 g, 0.91 mmol) in toluene (40 ml). – IR (KBr)^[36]: $\tilde{\nu} = 2269 \text{ cm}^{-1}$ (N≡C).

5,11,17,23-Tetrakis(isocyanato)-25,26,27,28-tetrapropoxycalix[4]arene (14): The reaction was carried out using **10** (1.00 g, 1.53 mmol) and triphosgene (0.61 g, 2.05 mmol) in toluene (50 ml). – IR (KBr)^[36]: $\tilde{\nu} = 2268 \text{ cm}^{-1}$ (N≡C).

Isothiocyantocalix[4]arenes 15–20. – *General Procedure:* To a mixture of the appropriate aminocalix[4]arene and thiophosgene (0.33 equiv. per amino group) in dry toluene was carefully added NEt_3 and the reaction mixture was refluxed for 2 h. After evaporation until dryness, the crude product was dissolved in CH_2Cl_2 (50 ml) and washed with 1 N HCl (25 ml), H_2O (25 ml), and brine (25 ml) and subsequently dried with Na_2SO_4 . Recrystallization of the crude mixture from MeOH/ CH_2Cl_2 gave isothiocyanate-functionalized calix[4]arenes **15–20**.

5-Isothiocyanto-25,26,27,28-tetrapropoxycalix[4]arene (15): The reaction was carried out using **7** (0.50 g, 0.82 mmol), thiophosgene (68 μl , 0.89 mmol), and NEt_3 (0.13 ml, 0.89 mmol) in toluene (50 ml). Yield 0.41 g (77%), m.p. 143–144°C ($\text{CH}_2\text{Cl}_2/\text{MeOH}$). – ^1H NMR: $\delta = 6.9\text{--}6.7$ (m, 6 H, ArH), 6.42 (t, 1 H, $J = 8.0 \text{ Hz}$, ArH), 6.23 (d, 2 H, $J = 13.5 \text{ Hz}$, ArH), 6.04 (s, 2 H, ArHNCS), 4.38, 4.32, 3.08 and 3.0 (4 d, 8 H, $J = 13.5 \text{ Hz}$, ArCH₂Ar), 3.9–3.75 (m, 4 H, OCH₂), 3.7–3.6 (m, 4 H, OCH₂), 1.9–1.7 (m, 8 H, OCH₂CH₂), 0.97 (t, 6 H, $J = 7.3 \text{ Hz}$, CH₃), 0.84 (t, 6 H, $J = 7.4 \text{ Hz}$, CH₃). – ^{13}C NMR: $\delta = 157.3, 155.8, 155.4, 136.5, 136.0, 135.2, 129.8, 129.2, 128.4, 124.2, 122.2, 122.0, 77.2$ (OCH₂), 76.8 (OCH₂), 76.6 (OCH₂), 31.0 (ArCH₂Ar), 30.9 (ArCH₂Ar), 23.4, 23.1, 10.6, 10.0. – IR (KBr): $\tilde{\nu} = 2130 \text{ cm}^{-1}$ (N≡C). – MS-FAB; m/z : 649.3 [M^+], calcd. 649.3. – $\text{C}_{41}\text{H}_{47}\text{NO}_4\text{S}$ (649.9): calcd. C 75.85, H 7.54, N 2.02; found C 75.77, H 7.29, N 2.16.

5,17-Bis(isothiocyanto)-25,26,27,28-tetrapropoxycalix[4]arene (16): The reaction was carried out using **8** (1.00 g, 1.61 mmol), thiophosgene (0.37 ml, 4.85 mmol), and NEt_3 (0.68 ml, 4.90 mmol) in toluene (100 ml). Yield 0.63 g (55%), m.p. 167–169°C ($\text{CH}_2\text{Cl}_2/\text{MeOH}$). – ^1H NMR: $\delta = 6.8\text{--}6.7$ (m, 6 H, ArH), 6.38 (s, 4 H, ArHNCS), 4.40 and 3.11 (AB q, 8 H, $J = 13.4 \text{ Hz}$, ArCH₂Ar), 3.87 (t, 4 H, $J = 7.6 \text{ Hz}$, OCH₂), 3.78 (t, 4 H, $J = 7.2 \text{ Hz}$, OCH₂), 1.95–1.85 (m, 8 H, OCH₂CH₂), 1.02 (t, 6 H, $J = 7.3 \text{ Hz}$, CH₃), 0.94 (t, 6 H, $J = 7.5 \text{ Hz}$, CH₃). – ^{13}C NMR: $\delta = 156.6, 156.5, 136.2, 134.8, 128.7, 125.0, 124.7, 122.7, 77.0$ and 76.7 (OCH₂), 30.9 (ArCH₂Ar), 23.3 and 23.1 (OCH₂CH₂), 10.4 and 10.1 (CH₃). – IR (KBr): $\tilde{\nu} = 2121 \text{ cm}^{-1}$ (N≡C). – MS-FAB; m/z : 706.6 [M^+], calcd. 706.9. – $\text{C}_{42}\text{H}_{46}\text{N}_2\text{O}_4\text{S}_2 \cdot 0.25 \text{H}_2\text{O}$ (711.4): calcd. C 70.90, H 6.59, N 3.94; found C 70.51, H 6.50, N 4.07.

5,11-Bis(isothiocyanto)-25,26,27,28-tetrapropoxycalix[4]arene (17): The reaction was carried out using **9** (1.00 g, 1.61 mmol), thiophosgene (0.37 ml, 4.85 mmol), and NEt_3 (0.70 ml, 5.04 mmol) in toluene (100 ml). Yield 0.59 g (52%), m.p. 178–180°C ($\text{CH}_2\text{Cl}_2/\text{MeOH}$). – ^1H NMR: $\delta = 6.7\text{--}6.6$ (m, 6 H, ArH), 6.48 and 6.43 (2 br. s, 4 H, ArH), 4.45–4.35 (m, 4 H, ArCH₂Ar), 3.2 and 3.0 (2 d, 4 H, $J = 13.3 \text{ Hz}$, ArCH₂Ar), 3.85–3.75 (m, 8 H, OCH₂), 1.9–1.8 (m, 8 H, OCH₂CH₂), 1.0–0.95 (m, 12 H, CH₃). – ^{13}C NMR: $\delta = 156.5, 156.0, 137.2, 135.8, 135.4, 134.0, 132.5, 128.7, 128.0, 125.6, 125.0, 124.5, 122.3, 76.9$ and 76.8 (OCH₂), 31.0, 30.9 and 30.8 (ArCH₂Ar), 23.2, 10.3. – IR (KBr): $\tilde{\nu} = 2127 \text{ cm}^{-1}$

(N≡C). — MS-FAB; m/z : 706.4 [M^+], calcd. 706.4. — $C_{42}H_{46}N_2O_4S_2$ (706.9): calcd. C 71.36, H 6.56, N 3.96; found C 71.16, H 6.46, N 3.72.

5,11,17,23-Tetrakis(isothiocyanato)-25,26,27,28-tetrapropoxycalix[4]arene (18): The reaction was carried out using **10** (1.00 g, 1.52 mmol), thiophosgene (0.48 ml, 6.40 mmol), and NEt_3 (0.90 ml, 6.50 mmol) in toluene (100 ml). Yield 1.33 g (> 95%), m.p. > 300°C ($CH_2Cl_2/MeOH$). — 1H NMR: δ = 6.56 (s, 8 H, ArHNCS), 4.35 and 3.19 (AB q, 8 H, J = 13.5 Hz, $ArCH_2Ar$), 3.81 (t, 8 H, J = 7.5 Hz, OCH_2), 1.9–1.8 (m, 8 H, OCH_2CH_2), 0.98 (t, 12 H, J = 7.4 Hz, CH_3). — ^{13}C NMR: δ = 155.5, 135.8, 134.2, 125.5, 77.2 (OCH_2), 30.7 ($ArCH_2Ar$), 23.1 (OCH_2CH_2), 10.2 (CH_3). — IR (KBr): $\tilde{\nu}$ = 2109 cm^{-1} (N≡C). — MS-FAB; m/z : 821.0 [$M + H$] $^+$, calcd. 821.2. — $C_{44}H_{44}N_4O_4S_4 \cdot 0.25 H_2O$ (825.6): calcd. C 64.02, H 5.40, N 6.79; found C 63.83, H 5.48, N 6.79.

5,17-Diiodo-11,23-bis(isothiocyanato)-25,26,27,28-tetrapropoxycalix[4]arene (19): The reaction was carried out using **11** (0.75 g, 0.86 mmol), thiophosgene (0.14 ml, 1.90 mmol), and NEt_3 (0.26 ml, 1.90 mmol) in toluene (100 ml). The product was purified by column chromatography (SiO_2 , CH_2Cl_2 /hexane, 30:70 v/v). Yield 0.64 g (79%), m.p. 288–289°C ($CH_2Cl_2/MeOH$). — 1H NMR: δ = 7.16 (s, 4 H, ArHI), 6.37 (s, 4 H, ArHNCS), 4.32 and 3.05 (AB q, 8 H, J = 13.5 Hz, $ArCH_2Ar$), 3.85 (t, 4 H, J = 7.4 Hz, OCH_2), 3.75 (t, 4 H, J = 7.2 Hz, OCH_2), 1.9–1.8 (m, 8 H, OCH_2CH_2), 1.05–0.9 (m, 12 H, CH_3). — ^{13}C NMR: δ = 156.8, 155.2, 137.4, 135.4, 125.2, 86.3 (ArI), 77.3 and 76.9 (OCH_2), 30.6 ($ArCH_2Ar$), 23.2, 23.0, 10.4, 10.0. — IR (KBr): $\tilde{\nu}$ = 2111 cm^{-1} (N≡C). — MS-FAB; m/z : 958.3 [M^+], calcd. 958.1. — $C_{42}H_{44}I_2N_2O_4S_2$ (958.8): calcd. C 52.62, H 4.63, N 2.92; found C 52.82, H 4.53, N 2.92.

5,17-Bis(isothiocyanato)-11,23-dinitro-25,26,27,28-tetrapropoxycalix[4]arene (20): The reaction was carried out using **12** (0.70 g, 0.98 mmol), thiophosgene (0.17 ml, 2.24 mmol), and NEt_3 (0.30 ml, 2.24 mmol) in toluene (100 ml). Yield 0.64 g (82%) (in 2 crops), m.p. > 300°C ($CH_2Cl_2/MeOH$). — 1H NMR: δ = 7.59 (s, 4 H, ArHNO₂), 6.54 (s, 4 H, ArHNCS), 4.43 and 3.23 (AB q, 8 H, J = 13.8 Hz, $ArCH_2Ar$), 3.95 (t, 4 H, J = 7.4 Hz, OCH_2), 3.82 (t, 4 H, J = 7.4 Hz, OCH_2), 1.9–1.8 (m, 8 H, OCH_2CH_2), 0.98 (t, 12 H, J = 7.4 Hz, CH_3). — ^{13}C NMR: δ = 162.0, 155.3, 142.8, 135.3, 125.7, 123.8, 77.4 (OCH_2), 30.9 ($ArCH_2Ar$), 23.2 and 23.1 (OCH_2CH_2), 10.2 and 10.1 (CH_3). — IR (KBr): $\tilde{\nu}$ = 2125 (N≡C) cm^{-1} . — MS-FAB; m/z : 798.0 [$M + H$] $^+$, calcd. 798.0. — $C_{44}H_{44}N_4O_4S_4 \cdot 0.25 H_2O$ (801.5): calcd. C 64.02, H 5.40, N 6.79; found C 63.83, H 5.48, N 6.79.

5,17-Bis(methoxycarbonylamino)-25,26,27,28-tetrapropoxycalix[4]arene (21): To a solution of **13** (0.34 g, 0.48 mmol) in toluene (15 ml) was added MeOH (50 μ l, 1.2 mmol) and the reaction mixture was refluxed for 15 h. After evaporation of the solvents, the residue was triturated with hexane/ CH_2Cl_2 (ca. 3:1) to give pure **21**, yield 0.23 g (66%), m.p. > 295°C. — 1H NMR: δ = 6.95–6.9 (m, 4 H, ArH), 6.81–6.78 (m, 2 H, ArH), 6.22 (s, 4 H, ArHNH), 6.19 (s, 2 H, NH), 4.42 and 3.11 (AB q, 8 H, J = 13.4 Hz, $ArCH_2Ar$), 3.94 (t, 4 H, J = 7.9 Hz, OCH_2), 3.69 (t, 4 H, J = 7.0 Hz, OCH_2), 3.62 (s, 6 H, OCH_3), 1.9–1.8 (m, 8 H, J = 7.2 Hz, OCH_2CH_2), 1.05 (t, 6 H, J = 7.5 Hz, CH_3), 0.90 (t, 6 H, J = 7.5 Hz, CH_3). — ^{13}C NMR: δ = 164.3 (C=O), 157.5, 152.4, 136.1, 134.5, 131.4, 128.8, 122.1, 119.1, 76.9 (OCH_2), 52.0 (OCH_3), 31.1 ($ArCH_2Ar$), 23.4, 23.0 (OCH_2CH_2), 10.7, 10.0 (CH_2CH_3). — IR (KBr): $\tilde{\nu}$ = 3387 cm^{-1} (NH), 1739 (C=O), 1541 (NH). — MS-FAB; m/z : = 738.2 [M^+], calcd. 738.4. — $C_{44}H_{54}N_2O_8 \cdot 1.8 H_2O$ (771.4): calcd. C 68.52, H 7.53, N 3.63; found C 68.54, H 7.20, N 3.68.

5,17-Bis(benzoyloxycarbonylamino)-25,26,27,28-tetrapropoxycalix[4]arene (22): To a solution of **13** (0.56 g, 0.80 mmol) in toluene (25 ml) was added benzyl alcohol (0.25 ml, 2.4 mmol) and the reaction mixture was refluxed for 24 h. After removal of the solvent, the residue was taken up in CH_2Cl_2 (50 ml) and washed with 2 N NaOH (2 $\times$ 20 ml), H_2O (20 ml), and brine (20 ml). After evaporation of the solvent, the residue was treated with 5 ml of $CH_2Cl_2/EtOH/H_2O$ (ca. 1:1:1) and washed with hexane to give pure **22**, yield 0.38 g (54%), m.p. 107–109°C. — 1H NMR: δ = 7.5–7.0 (m, 10 H, $ArHCH_2O$), 6.9–6.7 (m, 6 H, ArH), 6.39 (s, 4 H, NHArH), 6.37 (s, 2 H, NH), 5.05 (s, 4 H, $CHPh$), 4.46 and 3.15 (AB q, 8 H, J = 13.4 Hz, $ArCH_2Ar$), 3.94 (t, 4 H, J = 7.7 Hz, OCH_2CH_2), 3.76 (t, 4 H, J = 7.1 Hz, OCH_2CH_2), 1.95–1.9 (m, 8 H, OCH_2CH_2), 1.06 (t, 6 H, J = 7.4 Hz, CH_3), 0.97 (t, 6 H, J = 7.4 Hz, CH_3). — ^{13}C NMR: δ = 154.0, 157.2, 152.8, 136.5, 135.6, 134.9, 131.3, 128.6, 128.5, 128.1, 122.2, 120.0, 76.9 and 76.6 (OCH_2), 66.6 (OCH_2Ph), 31.1 ($ArCH_2Ar$), 23.3, 23.1 (OCH_2CH_2), 10.6, 10.1 (CH_3). — IR (KBr): $\tilde{\nu}$ = 3331 cm^{-1} (NH), 1711 (C=O), 1530 (NH). — MS-FAB; m/z : 890.4 [M^+], calcd. 890.5. — $C_{56}H_{62}N_2O_8$ (891.1): calcd. C 75.48, H 7.01, N 3.14; found C 75.39, H 7.58, N 3.27.

5,11,17,23-Tetrakis(methoxycarbonylamino)-25,26,27,28-tetrapropoxycalix[4]arene (23): To a solution of **14** (0.44 g, 0.54 mmol) in toluene (20 ml) was added MeOH (0.33 ml, 8.16 mmol) and the reaction mixture was refluxed for 17 h. After evaporation of the solvents the residue was taken up in CH_2Cl_2 (50 ml). The organic layer was washed with 2 N NaOH (20 ml) and brine (20 ml) and dried with $MgSO_4$. After evaporation of the solvent, the residue was triturated with methanol to give pure **23**, yield 0.43 g (78%), m.p. 157–159°C ($CHCl_3/MeOH$). — 1H NMR: δ = 6.60 (s, 8 H, ArH), 6.41 (s, 4 H, NH), 4.38 and 3.07 (AB q, 8 H, J = 13.5 Hz, $ArCH_2Ar$), 3.77 (t, 8 H, J = 7.4 Hz, OCH_2), 3.69 (s, 12 H, OCH_3), 1.9–1.8 (m, 8 H, OCH_2CH_2), 0.95 (t, 12 H, J = 7.4 Hz, CH_3). — ^{13}C NMR: δ = 154.6, 153.1, 135.3, 131.6, 119.7, 76.7 (OCH_2), 52.1 (OCH_3), 31.1 ($ArCH_2Ar$), 23.1 (OCH_2CH_2), 10.3 (CH_3). — IR (KBr): $\tilde{\nu}$ = 3323 cm^{-1} (NH), 1714 (C=O), 1546 (NH). — MS-FAB; m/z : = 884.7 [M^+], calcd. 884.4. — $C_{48}H_{60}N_4O_{12} \cdot 0.6 CHCl_3$ (956.7): calcd. C 61.03, H 6.38, N 5.86; found C 61.07, H 6.55, N 5.72.

5,11,17,23-Tetrakis(ethoxycarbonylamino)-25,26,27,28-tetrapropoxycalix[4]arene (24): To a solution of **14** (0.38 g, 0.46 mmol) in toluene (15 ml) was added EtOH (0.43 ml, 7.36 mmol) and the reaction mixture was refluxed for 20 h. The reaction mixture was concentrated in vacuo and the residue taken up in CH_2Cl_2 (50 ml). The organic layer was washed with 2 N NaOH (20 ml) and brine (20 ml) and subsequently dried with $MgSO_4$. After evaporation of the solvent, the residue was triturated with hexane/ CH_2Cl_2 to give pure **24**, yield 0.30 g (69%), m.p. 239–241°C (MeOH). — 1H NMR: δ = 6.6–6.55 (m, 8 H, ArH), 6.29 (s, 4 H, NH), 4.38 and 3.07 (AB q, 8 H, J = 13.5 Hz, $ArCH_2Ar$), 4.16 (q, 8 H, J = 7.1 Hz, OCH_2CH_3), 3.77 (t, 8 H, J = 7.4 Hz, $OCH_2CH_2CH_3$), 1.9–1.8 (m, 8 H, $OCH_2CH_2CH_3$), 1.26 (t, 12 H, J = 7.1 Hz, OCH_2CH_2), 0.95 (t, 12 H, J = 7.5 Hz, $OCH_2CH_2CH_3$). — ^{13}C NMR: δ = 153.7, 153.1, 135.3, 131.6, 119.9, 76.7 ($ArOCH_2$), 60.9 (OCH_2CH_3), 31.1 ($ArCH_2Ar$), 23.1 (OCH_2CH_2), 14.6 (OCH_2CH_3), 10.3 (CH_3). — IR (KBr): $\tilde{\nu}$ = 3320 cm^{-1} (NH), 1705 (C=O), 1542 (NH). — MS-FAB; m/z : 940.8 [M^+], calcd. 941.1. — $C_{52}H_{68}N_4O_{12} \cdot 0.80 H_2O$ (955.6): calcd. C 65.39, H 7.42, N 5.77; found C 65.37, H 7.34, N 5.86.

5,11,17,23-Tetrakis(benzoyloxycarbonylamino)-25,26,27,28-tetrapropoxycalix[4]arene (25): To a solution of **14** (0.63 g, 0.77 mmol) in toluene (25 ml) was added benzyl alcohol (1.24 ml, 11.5 mmol)

and a few drops of NEt_3 and the reaction mixture was refluxed for 17 h. The reaction mixture was concentrated in vacuo and the residue taken up in CH_2Cl_2 (50 ml). The organic layer was washed with 2 N NaOH (20 ml) and brine (20 ml), and subsequently dried with MgSO_4 . After evaporation of the solvent, $\text{EtOH}/\text{H}_2\text{O}$ (5 ml, ca. 1:1) was added to the residue and after filtration the residue was triturated with EtOH to give pure **25**, yield 0.24 g (26%), m.p. 188–190°C. – ^1H NMR: δ = 7.6–7.2 (m, 20 H, OCH_2ArH), 6.6–6.5 (m, 8 H, NHArH), 6.32 (s, 4 H, NH), 5.01 (s, 8 H, ArCH_2O), 4.32 and 3.00 (AB q, 8 H, J = 13.5 Hz, ArCH_2Ar), 3.71 (t, 8 H, J = 7.3 Hz, $\text{OCH}_2\text{CH}_2\text{CH}_3$), 1.8–1.7 (m, 8 H, OCH_2CH_2), 0.89 (t, 12 H, J = 7.3 Hz, CH_3). – ^{13}C NMR: δ = 153.9, 153.2, 136.4, 135.3, 131.5, 128.5, 128.1, 120.0, 76.8 (ArOCH_2), 66.6 (OCH_2Ph), 31.1 (ArCH_2Ar), 23.1 ($\text{ArOCH}_2\text{CH}_2$), 10.3 (CH_3). – IR (KBr): $\tilde{\nu}$ = 3322 cm^{-1} (NH), 1709 ($\text{C}=\text{O}$), 1535 (NH). – MS-FAB; m/z : 1188.4 [M^+], calcd. 1188.4. – $\text{C}_{72}\text{H}_{76}\text{N}_4\text{O}_{12} \cdot 0.75 \text{H}_2\text{O}$ (1202.9): calcd. C 71.98, H 6.71, N 4.82; found C 71.89, H 6.49, N 4.66.

5,17-Bis(*N'*-benzylureido)-25,26,27,28-tetrapropoxycalix[4]-arene (26): To a solution of **13** (0.64 mmol) in toluene (20 ml) was added benzylamine (0.21 ml, 1.92 mmol) and the reaction mixture was refluxed for 17 h. After evaporation of the solvent, CH_2Cl_2 (10 ml) was added and the resulting precipitate was filtered off and washed with CH_2Cl_2 . After concentration of the filtrate the residue was treated with $\text{CH}_2\text{Cl}_2/\text{MeOH}$ (5 ml, 1:1) to give pure **26**, yield 0.30 g (53%), m.p. > 295°C. – ^1H NMR: δ = 7.4–7.2 (m, 10 H, NHCH_2ArH), 6.97 (s, 6 H, ArH), 6.25 [s, 2 H, $\text{NHC}(\text{O})\text{NHCH}_2\text{Ph}$], 5.98 (s, 4 H, NHArH), 5.43 [t, 2 H, J = 5.8 Hz, $\text{NHC}(\text{O})\text{NHCH}_2\text{Ph}$], 4.41 and 3.09 (AB q, 8 H, J = 13.6 Hz, ArCH_2Ar), 4.26 [d, 4 H, J = 5.8 Hz, $\text{NHC}(\text{O})\text{NHCH}_2\text{Ph}$], 3.95 (t, 4 H, J = 8.1 Hz, OCH_2), 3.64 (t, 4 H, J = 6.7 Hz, OCH_2), 2.0–1.8 (m, 8 H, OCH_2CH), 1.07 (t, 6 H, J = 7.4 Hz, CH_3), 0.87 (t, 6 H, J = 7.5 Hz, CH_3). – ^{13}C NMR: δ = 157.3, 156.8, 152.8, 139.5, 136.0, 132.1, 135.0, 128.8, 128.5, 127.3, 122.1, 121.5, 76.9 (OCH_2), 43.9 (ArCH_2NH), 31.0 (ArCH_2Ar), 23.4, 23.1 (OCH_2CH_2), 10.7, 10.0 (CH_3). – IR (KBr): $\tilde{\nu}$ = 3330 cm^{-1} (NH), 1651 ($\text{C}=\text{O}$), 1559 (NH). – MS-FAB; m/z : = 889.1 [M^+], calcd. 889.1. – $\text{C}_{56}\text{H}_{64}\text{N}_4\text{O}_6 \cdot 1.0 \text{H}_2\text{O}$ (907.2): calcd. C 74.15, H 7.33, N 6.18; found: C 74.23, H 7.34, N 6.18.

5,11,17,23-Tetrakis(*N'*-benzylureido)-25,26,27,28-tetrapropoxycalix[4]arene (27): To a solution of **14** (0.31 g, 0.38 mmol) in toluene (15 ml) was added benzylamine (0.33 ml, 3.04 mmol) and the reaction mixture was refluxed for 17 h. After evaporation of the solvent, 5 ml of $\text{CH}_2\text{Cl}_2/\text{MeCN}$ (1:1) was added to the residue. The precipitate was filtered off and triturated with MeOH to give pure **27**, yield 0.27 g (60%), m.p. > 295°C (MeOH). – ^1H NMR ($[\text{D}_6]\text{DMSO}$): δ = 8.13 [s, 4 H, $\text{ArNHC}(\text{O})$], 7.3–7.2 (m, 20 H, CH_2ArH), 6.74 (s, 8 H, ArH), 6.29 (t, 4 H, J = 5.8 Hz, CH_2NH), 4.31 and 3.03 (AB q, 8 H, J = 12.8 Hz, ArCH_2Ar), 4.23 (d, 8 H, J = 5.8 Hz, NHCHAr), 3.75 (t, 8 H, J = 7.4 Hz, OCH_2), 1.95–1.85 (m, 8 H, OCH_2CH_2), 0.96 (t, 12 H, J = 7.5 Hz, CH_3). – ^{13}C NMR ($[\text{D}_6]\text{DMSO}$): δ = 155.2, 150.6, 140.5, 134.1, 134.0, 128.2, 127.0, 126.6, 118.1, 76.4 (OCH_2), 42.6 (NHCH_2Ph), 22.6 (OCH_2CH_2), 10.2 (CH_3). – IR (KBr): $\tilde{\nu}$ = 3332 cm^{-1} (NH), 1646 ($\text{C}=\text{O}$), 1559 (NH). – MS-FAB; m/z : 1185.4 [M^+], calcd. 1185.5. – $\text{C}_{72}\text{H}_{80}\text{N}_8\text{O}_8 \cdot 0.8 \text{H}_2\text{O}$ (1199.9): calcd. C 72.07, H 6.85, N 9.33; found C 72.10, H 6.40, N 8.93.

5,17-Bis(*N'*-butylthioureido)-25,26,27,28-tetrapropoxycalix[4]-arene (28): To a solution of **16** (0.20 g, 0.28 mmol) in CH_2Cl_2 (20 ml) was added *n*-butylamine (59 μl , 0.59 mmol) and the reaction mixture was stirred at room temp. for 4 h. Water was added to the solution and after separation of the layers, the organic layer was

washed with 1 N HCl (10 ml), H_2O (10 ml), and brine (10 ml) and dried with Na_2SO_4 . After evaporation of the solvents and drying in vacuo, the residue was recrystallized from EtOH to give pure **28**, yield 0.20 g (83%), m.p. 188–191°C (EtOH). – ^1H NMR: δ = 7.0–6.95 (m, 4 H, ArH), 6.9–6.85 (m, 4 H, ArH + NH), 6.70 (br. s, 2 H, NH), 6.52 (s, 4 H, ArHNH), 4.42 and 3.14 (AB q, 8 H, J = 13.5 Hz, ArCH_2Ar), 3.96 (t, 4 H, J = 7.9 Hz, OCH_2), 3.71 (t, 4 H, OCH_2), 3.55–3.45 (m, 4 H, CH_2NH), 1.95–1.8 (m, 8 H, OCH_2CH_2), 1.55–1.45 (m, 4 H, $\text{CH}_2\text{CH}_2\text{NH}$), 1.4–1.3 (m, 4 H, $\text{CH}_2\text{CH}_2\text{CH}_2\text{NH}$), 1.08 (t, 4 H, CH_3), 1.05–0.85 (m, 12 H, CH_3). – ^{13}C NMR: δ = 180.7 ($\text{C}=\text{S}$), 157.5, 154.2, 136.4, 135.3, 131.0, 129.0, 123.7, 122.5, 45.0 (CH_2NH), 31.1 and 31.0 (ArCH_2Ar), 23.5, 22.9, 20.2, 13.8, 10.7, 9.8. – IR (KBr): $\tilde{\nu}$ = 3380, 3170 cm^{-1} (NH stretch), 1580, 1520 (NH bend). – MS-FAB; m/z : 854.2 [M^+], calcd. 854.6. – $\text{C}_{50}\text{H}_{70}\text{N}_4\text{O}_4\text{S}_2 \cdot 0.1 \text{H}_2\text{O}$ (857.1): calcd. C 70.07, H 8.26, N 6.64; found C 69.78, H 8.06, N 6.54.

5,17-Bis(*N'*-benzylthioureido)-25,26,27,28-tetrapropoxycalix[4]-arene (29): To a solution of **16** (0.15 g, 0.21 mmol) in CH_2Cl_2 (15 ml) was added benzylamine (0.51 μl , 0.47 mmol) and the reaction mixture was stirred at room temp. for 4 h. Water was added to the solution and after separation of the layers, the organic layer was washed with 1 N HCl (5 ml), H_2O (5 ml), and brine (10 ml) and dried with Na_2SO_4 . After evaporation of the solvents and drying in vacuo, the residue was recrystallized from $\text{CH}_2\text{Cl}_2/\text{MeOH}$ to give pure **29**, yield 0.18 g (72%), m.p. 226–228°C ($\text{CH}_2\text{Cl}_2/\text{MeOH}$). – ^1H NMR: δ = 7.35–7.3 (m, 10 H, ArH), 7.15 (s, 2 H, NH), 6.95–6.9 (m, 4 H, ArH), 6.8–6.75 (m, 4 H, ArH + NH), 6.02 (s, 4 H, ArHNH), 4.75 (d, 4 H, J = 5.3 Hz, CH_2NH), 4.40 and 3.10 (AB q, 8 H, J = 13.5 Hz, ArCH_2Ar), 3.94 (t, 4 H, J = 8.0 Hz, OCH_2), 3.69 (t, 4 H, J = 6.8 Hz, OCH_2), 1.95–1.8 (m, 8 H, OCH_2CH_2), 1.06 (t, 6 H, J = 7.4 Hz, CH_3), 0.87 (t, 6 H, J = 7.4 Hz, CH_3). – ^{13}C NMR: δ = 157.4, 154.3, 137.5, 136.2, 135.4, 129.0, 127.8, 127.6, 123.7, 122.6, 49.1 (CH_2NH), 31.0 (ArCH_2Ar), 23.5, 23.4, and 22.9 (OCH_2CH_2), 10.7, 9.8. – IR (KBr): $\tilde{\nu}$ = 3380, 3170 cm^{-1} (NH stretch), 1560, 1520 (NH bend). – MS-FAB; m/z : 921.8 [$\text{M} + \text{H}$] $^+$, calcd. 921.4. – $\text{C}_{56}\text{H}_{64}\text{N}_4\text{O}_4\text{S}_2 \cdot 0.5 \text{H}_2\text{O}$ (930.3): calcd. C 72.30, H 7.04, N 6.02; found C 72.14, H 6.88, N 6.02.

5,11,17,23-Tetrakis(*N'*-butylthioureido)-25,26,27,28-tetrapropoxycalix[4]arene (30): To a solution of **17** (0.20 g, 0.24 mmol) in CH_2Cl_2 (20 ml) was added benzylamine (0.11 ml, 1.02 mmol) and the reaction mixture was stirred at room temp. for 4 h. Water was added to the reaction mixture and after separation of the layers, the organic layer was washed with 1 N HCl (10 ml), H_2O (10 ml), and brine and dried with Na_2SO_4 . After evaporation of the solvents and drying in vacuo, the residue was recrystallized from $\text{CH}_2\text{Cl}_2/\text{EtOH}$ to give pure **30**, yield 0.16 g (59%), m.p. 188–191°C ($\text{CH}_2\text{Cl}_2/\text{EtOH}$). – ^1H NMR ($[\text{D}_6]\text{DMSO}$): δ = 9.01 (s, 4 H, NH), 7.25 (s, 4 H, NH), 6.70 (s, 8 H, ArH), 4.32 and 3.13 (AB q, 8 H, J = 12.7 Hz, ArCH_2Ar), 3.82 (t, 8 H, OCH_2 , J = 5.8 Hz), 3.41 (m, 8 H, CH_2NH), 1.95–1.85 (m, 8 H, OCH_2CH_2), 1.5–1.4 (m, 8 H, $\text{CH}_2\text{CH}_2\text{NH}$), 1.35–1.2 (m, 8 H, $\text{CH}_2\text{CH}_2\text{CH}_2\text{NH}$), 1.0–0.95 (m, 12 H, CH_3), 0.9–0.85 (m, 12 H, CH_3). – ^{13}C NMR: δ = 179.7 ($\text{C}=\text{S}$), 152.9, 134.4, 132.7, 123.2, 76.4 (OCH_2), 43.6 (CH_2NH), 30.6 (ArCH_2Ar), 22.7, 19.6, 13.7, 10.1. – IR (KBr): $\tilde{\nu}$ = 3370, 3240 cm^{-1} (NH stretch), 1530 (NH bend). – MS-FAB; m/z : 1113.9 [$\text{M} + \text{H}$] $^+$, calcd. 1113.6. – $\text{C}_{60}\text{H}_{88}\text{N}_8\text{O}_4\text{S}_4 \cdot 1.0 \text{H}_2\text{O}$ (1131.7): calcd. C 63.68, H 8.02, N 9.90; found C 63.24, H 8.05, N 9.85.

5,11,17,23-Tetrakis(*N'*-benzylthioureido)-25,26,27,28-tetrapropoxycalix[4]arene (31): To a solution of **17** (0.20 g, 0.24 mmol) in CH_2Cl_2 (20 ml) was added benzylamine (0.10 ml, 1.02 mmol) and the reaction mixture was stirred at room temp. for 4 h. Water was added to the solution and after separation of the layers, the organic

layer was washed with 1 N HCl (10 ml), H₂O (10 ml), and brine (10 ml) and dried with Na₂SO₄. After evaporation of the solvents and drying in vacuo, the residue was recrystallized from CH₂Cl₂/MeOH to give pure **31**, yield 0.18 g (60%), m.p. 214–216°C (CH₂Cl₂/MeOH). – ¹H NMR ([D₆]DMSO): δ = 9.21 (s, 4 H, NHAr), 7.79 (s, 4 H, CH₂NH), 7.35–7.20 (m, 20 H, ArH), 6.71 (s, 8 H, ArH), 4.71 (d, 8 H, *J* = 4.8 Hz, CH₂NH), 4.32 and 3.12 (AB q, 8 H, *J* = 12.3 Hz, ArCH₂Ar), 3.82 (t, 8 H, *J* = 5.8 Hz, OCH₂), 1.95–1.85 (m, 8 H, OCH₂CH₂), 1.0–0.95 (m, 12 H, CH₃). – ¹³C NMR: δ = 180.3 (C=S), 153.1, 139.1, 134.3, 132.5, 128.2, 127.3, 126.8, 123.5, 76.4 (OCH₂), 47.2 (CH₂NH), 30.6 (ArCH₂Ar), 22.7, 10.1. – IR (KBr): $\tilde{\nu}$ = 3370, 3205 cm^{−1} (NH stretch), 1560, 1520 (NH bend). – MS-FAB; *m/z*: 1249.6 [M + H]⁺, calcd. 1249.5. – C₇₂H₈₀N₈O₄S₄·2 H₂O (1285.8): C 67.26, H 6.58, N 8.71; found C 67.09, H 6.26, N 8.68.

1,3-Bis(acetoxymethyl)-2,4-bis(phthalimidomethyl)cavitand (37): A solution of 1,3-bis(bromomethyl)-2,4-bis(phthalimidomethyl)cavitand (**36**) (250 mg, 189 μmol) and NaOAc (46 mg, 0.63 mmol) in acetonitrile (25 ml) was stirred at room temp. overnight. After evaporation of the solvent, the residue was redissolved in CH₂Cl₂ (20 ml) and the organic layer was washed with water (3 × 10 ml) and dried with Na₂SO₄. Purification with flash column chromatography (SiO₂, hexanes/EtOAc, gradient 60:40–40:60) afforded **37** as a white foam, 155 mg (64%), m.p. 154–156°C (hexanes/EtOAc). – MS-FAB; *m/z*: 1279.0 [M⁺]. – ¹H NMR: δ = 7.80–7.75 and 7.70–7.65 (2 m, 4:4 H, phthalimido), 7.16, 7.08 (2 s, 2:2 H, ArH), 5.88 (d, 4 H, *J* = 7.1 Hz, outer OCH₂O), 5.07 [s, 4 H, ArCH₂OC(O)CH₃], 4.73 [t, 4 H, *J* = 6.6 Hz, CH(CH₂)₄], 4.62 (s, 4 H, ArCH₂phth), 4.39 (d, 4 H, *J* = 7.2 Hz, inner OCH₂O), 2.45–2.15, 2.15–1.95 (2 m, 4:4 H, CHCH₂), 2.05 [s, 6 H, ArCH₂OC(O)CH₃], 1.45–1.20 [m, 24 H, CHCH₂(CH₂)₃], 0.87 (t, 12 H, *J* = 6.8 Hz, CH₃). – ¹³C NMR: δ = 170.4 (s, OC=O), 167.9 [s, NC(O)], 154.5, 153.6 (s, ArCOCH₂O), 138.4, 137.9 (s, ArCCH), 133.9, 132.1, 123.3 (d, s, d, phthalimido), 121.8, 121.6 (s, ArCCH₂), 121.3, 120.1 (d, ArCH), 99.7 (t, OCH₂O), 57.5 (t, CH₂OAc), 36.9 (d, ArCHAR), 21.2 [q, C(O)CH₃]. – C₇₆H₈₂N₂O₁₆ (1279.5): calcd. C 71.34, N 2.19, H 6.46; found: C 71.11, N 2.07, H 6.14.

1,3-Bis(aminomethyl)-2,4-bis(hydroxymethyl)cavitand (38): A solution of 1,3-bis(acetoxymethyl)-2,4-bis(phthalimidomethyl)cavitand **37** (124 mg, 96.8 μmol) and hydrazine hydrate (0.31 ml, 2.58 mmol) in a 9:1 mixture of EtOH (9 ml) and THF (1 ml) was refluxed for 3.5 h. After the addition of concentrated HCl (0.43 ml, 5.2 mmol), the reaction mixture was refluxed for an additional half an hour. The solvents were removed in vacuo and the precipitate dissolved in CH₂Cl₂ (20 ml). The solution was washed with 2 N NaOH (2 × 10 ml), demi water (2 × 10 ml) and the solvent evaporated. The residue was redissolved and concentrated from CH₂Cl₂ (3 × 10 ml) to give **38** as a white foam, 76 mg (84%), m.p. 170–172°C (dec.) (CH₂Cl₂/hexanes). – MS-FAB; *m/z*: 933.0 [M⁺]. – ¹H NMR (CDCl₃/MeOD, 9:1): δ = 7.04, 7.03 (2 s, 2:2 H, ArH), 5.86 (d, 4 H, *J* = 7.2 Hz, outer OCH₂O), 4.71 [t, 4 H, *J* = 6.6 Hz, CH(CH₂)₄], 4.48 (s, 4 H, ArCH₂OH), 4.33 (d, 4 H, *J* = 7.2 Hz, inner OCH₂O), 3.63 (s, 4 H, ArCH₂NH₂), 2.2–2.05 (m, 8 H, CHCH₂), 1.40–1.15 [m, 24 H, CHCH₂(CH₂)₃], 0.84 (t, 12 H, *J* = 6.9 Hz, CH₃). – ¹³C NMR (CDCl₃/MeOD, 9:1): δ = 155.1, 154.7 (s, ArCOCH₂O), 139.7, 139.4 (s, ArCCH), 128.8 (s, ArCCH₂NH₂), 126.5 (s, ArCCH₂OH), 121.8, 121.3 (d, ArCH), 101.4 (t, OCH₂O), 55.3 (t, ArCH₂OH), 38.3 (d, ArCHAR), 36.1 (t, ArCH₂NH₂).

1:1 Calix[4]arene[(thioureido)methyl]cavitand (39): A mixture of **15** (80 mg, 90 μmol) and **32** (40 mg, 62 μmol) in CHCl₃ (10 ml) was refluxed for 24 h. After evaporation of the solvent, the crude mixture was purified by column chromatography (SiO₂, CH₂Cl₂).

Yield 50 mg (53%), m.p. 188–190°C. – ¹H NMR: δ = 7.0–6.7 [m, 10 H, ArH (calix) + ArH (cavitand)], 6.45–6.3 (m, 3 H, ArH + ArNH), 7.20 (d, 1 H, *J* = 7.4 Hz, ArH), 5.89 (s, 2 H, ArHNH), 5.82 and 5.35 [2 d, 4 H, *J* = 7.1 Hz, OCH₂O (outer)], 4.7–4.3 (m, 6 H, CH₂NH + CHC₅H₁₁), 4.32 and 4.06 [2 d, 4 H, *J* = 7.2 Hz, OCH₂O (inner)], 4.45–4.3 and 3.1–3.0 (m, 8 H, ArCH₂Ar), 3.95–3.75 (m, 4 H, OCH₂), 3.75–3.55 (m, 4 H, OCH₂), 2.1–2.0 (m, 8 H, CHCH₂), 1.88 (s, 9 H, CH₃), 2.0–1.75 (m, 8 H, OCH₂CH₂), 1.5–1.15 (m, 24 H, CH₂), 1.1–1.0 (s, 6 H, CH₃), 0.95–0.6 (m, 18 H, CH₃). – ¹³C NMR: δ = 157.4, 153.5, 153.3, 153.2, 153.1, 138.1, 137.8, 137.2, 136.7, 136.6, 135.3, 133.8, 127.7, 123.6, 122.3, 117.3, 98.8 (OCH₂O), 77.2 (OCH₂), 37.0, 32.1 and 31.0 (ArCH₂Ar), 27.7, 23.4, 23.0, 22.7, 14.1, 10.7, 10.5, 10.3, 10.0. – MS-FAB; *m/z*: 1538.3 [M + H]⁺, calcd. 1538.2. – C₉₇H₁₂₀N₂O₁₂S·CH₂Cl₂ (1623.0): calcd. C 72.52, H 7.58, N 1.73; found C 72.34, H 7.52, N 1.55.

4:1 Calix[4]arene-[(thioureido)methyl]cavitand (40): A mixture of **15** (139 mg, 0.21 mmol) and **35** (50 mg, 54 μmol) in CHCl₃ (10 ml) was refluxed for 9 h. After evaporation of the solvent the crude reaction mixture was purified by column chromatography (SiO₂, EtOAc/CH₂Cl₂, 5:95). Yield 0.13 g (87%) (40 mg calix[4]arene **15** recovered), m.p. 215–218°C (CHCl₃/MeOH). – ¹H NMR: δ = 7.05 (s, 4 H, ArH), 7.0–6.85 [m, 12 H, ArH (calix) + ArH (cavitand)], 6.8–6.65 (m, 8 H, ArH), 6.5–6.35 (m, 3 H, ArH + ArNH), 6.22 (d, 8 H, *J* = 7.4 Hz, ArH), 5.93 (s, 8 H, ArHNH), 5.59 [d, 2 H, *J* = 7.2 Hz, OCH₂O (outer)], 4.75 [d, 2 H, *J* = 7.9 Hz, OCH₂O (outer)], 4.62 (s, 8 H, CH₂NH), 4.40 and 3.12 (AB q, 32 H, *J* = 13.2 Hz, ArCH₂Ar), 4.25 [d, 4 H, *J* = 7.2 Hz, OCH₂O (inner)], 4.1–3.9 (m, 16 H, OCH₂), 3.85–3.65 (m, 16 H, OCH₂), 2.3–2.1 (m, 8 H, CHCH₂), 2.0–1.8 (m, 32 H, OCH₂CH₂), 1.5–1.3 (m, 32 H, CH₂), 1.2–1.05 (m, 24 H, CH₃), 1.0–0.9 (m, 18 H, CH₃). – ¹³C NMR: δ = 157.4, 138.1, 136.3, 133.7, 129.2, 127.6, 122.3, 77.2 (OCH₂), 30.9 (ArCH₂Ar), 23.4, 23.0, 22.7, 14.1, 10.7, 9.9. – MS-FAB; *m/z*: 3531.5 [M – H]⁺, calcd. 3531.8. – C₂₂₀H₂₆₄N₈O₂₄S₄·CHCl₃ (3652.2): calcd. C 72.68, H 7.31, N 3.07; found C 72.26, H 7.51, N 2.89.

2:2 5,17-H-calix[4]arene-11,23-[(thioureido)methyl]cavitand (42): Solutions of **16** (59 mg, 83 μmol) in CHCl₃ (15 ml) and **34** (75 mg, 83 μmol) in CHCl₃ (15 ml) were simultaneously added dropwise (10 μl/min) to CHCl₃ (20 ml) at reflux temp. After the addition, the reaction mixture was refluxed for another 48 h and subsequently concentrated to dryness. The crude mixture was purified by column chromatography (SiO₂, EtOAc/CH₂Cl₂, 0:100–15:95). Yield 50 mg (37%), m.p. > 300°C (258–260°C phase transition) (CHCl₃/MeOH). – ¹H NMR: δ = 7.12 (d, 4 H, *J* = 7.3 Hz, ArH), 7.0 and 6.88 [2s, 8 H, ArH (cavitand)], 6.85–6.7 (m, 8 H, ArH), 6.31 (br. s, 4 H, ArNH), 5.90 (br. s, 8 H, CH₂NH), 5.62 [d, 4 H, *J* = 6.7 Hz, OCH₂O (outer)], 4.65 (t, 8 H, *J* = 7.7 Hz, CHC₅H₁₁), 4.52 (br. s, 4 H, NH), 4.38 and 3.10 (AB q, 8 H, *J* = 13.4 Hz, ArCH₂Ar), 4.27 [d, 8 H, *J* = 7.0 Hz, OCH₂O (inner)], 3.63 (t, 16 H, *J* = 6.4 Hz, OCH₂), 2.1–2.0 (m, 8 H, CHCH₂), 2.02 (s, 12 H, ArCH₃), 2.0–1.75 (m, 16 H, OCH₂CH₂), 1.3–1.15 (m, 48 H, CH₂), 1.04 (t, 12 H, *J* = 7.3 Hz, CH₃), 0.95–0.8 (m, 36 H, CH₃). – ¹³C NMR: δ = 157.6, 153.4 (2 ×), 138.3, 137.5, 136.5, 129.4, 123.7, 77.2 (OCH₂), 37.0 (CH₂NH), 32.0 and 31.0 (ArCH₂Ar), 30.2, 27.7, 23.5, 22.9, 22.7, 14.1, 10.8, 10.7, 9.8. – MS-FAB; *m/z*: 3218.8 [M – H]⁺, calcd. 3219.3. – C₁₉₆H₂₄₀N₈O₂₄S₄·2 CHCl₃ (3459.1): calcd. C 68.75, H 7.05, N 3.24; found C 68.81, H 6.35, N 3.27.

2:2 5,17-I-calix[4]arene-11,23-[(thioureido)methyl]cavitand (43): Solutions of **19** (74 mg, 77 μmol) in CHCl₃ (15 ml) and **34** (70 mg, 77 μmol) in CHCl₃ (15 ml) were simultaneously added

dropwise (20 µl/min) to CHCl₃ (20 ml) at reflux temp. After the addition, the reaction mixture was refluxed for another 15 h and subsequently concentrated to dryness. The crude mixture was purified by column chromatography (SiO₂, EtOAc/CH₂Cl₂ 0:100–15:95). Yield 64 mg (42%), m.p. > 300 °C (255–260 °C phase transition) (CHCl₃/MeOH). – ¹H NMR: δ = 7.45 (s, 8 H, ArH), 7.00 and 6.88 [2s, 8 H, ArH (cavitand)], 6.22 (br. s, 4 H, CH₂NH), 5.97 (s, 8 H, ArHNH), 5.74 [d, 4 H, *J* = 7.0 Hz, OCH₂O (outer)], 4.65 (t, 8 H, *J* = 7.7 Hz, CHC₅H₁₁), 4.53 (br. s, 4 H, ArNH), 4.35–4.25 [m, 24 H, ArCH₂Ar + CH₂NH + OCH₂O (inner)], 3.95 (t, 8 H, *J* = 7.9 Hz, OCH₂), 3.57 (t, 8 H, *J* = 6.4 Hz, OCH₂), 3.05 (d, 8 H, *J* = 13.7 Hz, ArCH₂Ar), 2.1–2.0 (m, 8 H, CHCH₂), 2.06 (s, 12 H, ArCH₃), 1.95–1.7 (m, 16 H, OCH₂CH₂), 1.5–1.15 (m, 48 H, CH₂), 1.02 (t, 12 H, *J* = 7.3 Hz, CH₃), 0.95–0.75 (m, 36 H, CH₃). – ¹³C NMR: δ = 157.6, 154.0, 153.5, 153.4, 139.0, 138.4, 137.7, 137.5, 134.2, 124.0, 122.6, 120.3, 116.9, 99.5 (OCH₂O), 86.1 (ArCl), 77.2 (OCH₂), 37.0 (CH₂NH), 32.1 and 30.7 (ArCH₂Ar), 30.2, 27.7, 23.5, 22.8, 22.7, 14.1, 11.0, 10.8, 9.7. – MS-FAB; *m/z*: 3723.4 [M⁺], calcd. 3723.9. – C₁₉₆H₂₃₆I₄N₈O₂₄S₄·CHCl₃ (3843.4): calcd. C 61.57, H 6.22, N 2.92; found C 61.40, H 6.40, N 2.93.

2:2 5,17-NO₂-calix[4]arene-11,23-[(thioureido)methyl]cavitand (44): Solutions of **20** (44 mg, 55 µmol) in CHCl₃ (10 ml) and **34** (50 mg, 55 µmol) in CHCl₃ (10 ml) were simultaneously added dropwise (10 µl/min) to CHCl₃ (20 ml) at reflux temp. After the addition, the reaction mixture was refluxed for another 15 h and subsequently concentrated to dryness. The crude mixture was purified by column chromatography (SiO₂, EtOAc/CH₂Cl₂, 0:100–15:95). Yield 33 mg (35%), m.p. > 300 °C (CHCl₃/MeOH). – ¹H NMR: δ = 8.05 (br. s, 8 H, ArHNO₂), 6.98 and 6.83 [s, 2 H, ArH (cavitand)], 6.18 (br. s, 8 H, ArHNH + CH₂NH), 5.62 [br. s, 4 H, OCH₂O (outer)], 4.65 (t, 8 H, *J* = 7.5 Hz, CHC₅H₁₁), 4.6–4.4 (m, 16 H, ArCH₂Ar + CH₂NH), 4.19 [d, 4 H, *J* = 7.0 Hz, OCH₂O (inner)], 4.20–4.05 (m, 8 H, OCH₂), 3.67 (br. t, 8 H, OCH₂), 3.22 (d, 8 H, *J* = 13.4 Hz, ArCH₂Ar), 2.3–2.05 (m, 16 H, CHCH₂), 1.96 (s, 12 H, ArCH₃), 2.0–1.75 (m, 16 H, OCH₂CH₂), 1.55–1.15 (m, 48 H, CH₂), 1.06 (t, 12 H, *J* = 7.3 Hz, CH₃), 1.0–0.75 (m, 36 H, CH₃). – ¹³C NMR: δ = 153.2, 142.7, 138.4, 137.6, 137.2, 99.3 (OCH₂O), 77.2 (OCH₂), 37.0 (CH₂NH), 32.1 and 31.0 (ArCH₂Ar), 30.0, 27.7, 23.2, 22.7, 14.1, 10.8, 10.4, 9.7. – MS-FAB; *m/z*: 3400.1 [M⁺], calcd. 3400.3. – C₁₉₆H₂₃₆N₁₂O₃₂S₄·1.5 CHCl₃ (3579.4): calcd. C 66.28, H 6.69, N 4.70; found C 66.19, H 6.70, N 4.54.

2:2 5,11-H-calix[4]arene-11,23-[(thioureido)methyl]bis(hydroxymethyl)cavitand (45): A solution of **18** (25 mg, 35 µmol) in CHCl₃ (15 ml) was added dropwise (20 µl/min) to a solution of **38** (33 mg, 35 µmol) in CHCl₃ (35 ml) at reflux temp. After the addition, the reaction mixture was refluxed for another 24 h and subsequently concentrated to dryness. The crude mixture was purified by column chromatography (SiO₂, EtOAc/CH₂Cl₂, 0:100–15:95). Yield 24 mg (35%), m.p. > 300 °C. – ¹H NMR: δ = 7.2–6.9 [m, 20 H, ArH (calix) + ArH (cavitand)], 6.41 (br. s, 4 H, CH₂NH), 6.02 (br. s, 8 H, ArHNH), 6.31 [d, 4 H, *J* = 7.5 Hz, OCH₂O (outer)], 4.82 (t, 8 H, *J* = 7.6 Hz, CHC₅H₁₁), 4.62 (d, 8 H, *J* = 5.0 Hz, CH₂NH), 4.6–4.4 [m, 24 H, ArCH₂Ar + OCH₂O (inner) + CH₂OH], 3.95 (t, 8 H, *J* = 7.9 Hz, OCH₂), 3.69 (t, *J* = 7.8 Hz, OCH₂), 3.09 (d, 8 H, *J* = 13.4 Hz, ArCH₂Ar), 2.35–2.15 (m, 16 H, CHCH₂), 2.05–1.8 (m, 16 H, OCH₂CH₂), 1.55–1.2 (m, 48 H, CH₂), 1.05 (t, 12 H, *J* = 7.3 Hz, CH₃), 1.05–0.7 (m, 36 H, CH₃). – MS-FAB; *m/z*: 3282.8 [M – H]⁺, calcd. (C₁₉₆H₂₄₀N₈O₂₈S₄) 3283.3. No satisfactory elemental analysis could be obtained.

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