The design and synthesis of acrylato and imino derivatives of calix[4]arene for applications in static and dynamic combinatorial libraries

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The synthesis of novel calix[4]arene tetra-acrylates and the potential use of macrocyclic platforms in the development of static and dynamic combinatorial libraries (DCL) using reversible imine formationare described. Using such a macrocyclic platform in DCL formation results in a large number of library members while keeping the number of building blocks in the library to a minimum number.

Keywords: calixarenes, supramolecular chemistry, host–guest systems, self-assembly

We have recently reported the use of calix[4]arene macrocycles as useful platforms for the development of static and dynamic macrocyclic libraries.[1,2] A synthetic receptor should bind to a given guest with a high binding constant and high selectivity. The binding sites for the receptor need to be identified efficiently, necessitating the development of novel combinatorial methodology for the synthesis of libraries of macrocycles.[3,4] This methodology can either be directed towards the generation of static libraries.[5,6] or towards dynamic combinatorial libraries (DCL) as proposed by Lehn, Sanders and co-workers.[7–13] For the development of static combinatorial libraries, reactions and reaction conditions need to be identified that are reliable, tolerate a wide variety of chemically diverse building blocks and yield products in good yields.

Achieving this target is notoriously difficult in macrocyclic chemistry with multiple reaction products frequently possible and with the requirement for multiple functional group transformations to be achieved in a single synthetic operation. For a DCL, reactions need to be identified that are reversible and allow, in the presence of a guest, a shift of the distribution of possible reaction products by establishing a new equilibrium involving guest molecule and product. When designing such a dynamic combinatorial library we would like to argue that it might be beneficial to obtain a maximum number of components of the library while using a minimum amount of building blocks. With this concept a larger number of possible library members can be generated in a single step and an optimisation of the chemical space covered by the DCL can be achieved. In this paper, we report the expansion of this novel approach. By modifying the upper rim of a calix[4]arene with several functionalities suitable for further derivatisation, we can utilise a reversible reaction with a series of structurally diverse reagents suitable for static and dynamic libraries. We communicated our success in developing imine libraries and carcerands earlier.[1,2] Furthermore, a series of static cyclopeptide macrocyclic libraries have been reported.[14–17]

Results and discussion

Synthesis of static libraries

With the aim of enhancing our novel synthetic methodology for macrocyclic library synthesis we used Heck coupling to obtain the deep cavity calix[4]arene acrylates **2**, **3**, **4**, **5**, **6** and **7** from tetraiodo compound **1** and the corresponding acrylate using palladium acetate and 1,3-bis-(diphenylphosphino)prop ane as a coligand (Scheme 1).[18] Acrylates comprising both a carbonyl and an olefinic moiety, which must be considered as the two synthetically most versatile functional groups in organic chemistry, were chosen to allow a maximum scope and versatility for further functionalisations.

The coupling proceeded as expected to give the novel deep cavity calix[4]arenes **2–4** and **6** in good yields as the all-*trans* isomers, **5** and **7** having been reported earlier (see Table 1).[1] All spectroscopic data were in full agreement with the structure. The ^{1}H NMR chemical shifts of the calix[4]arene methylene protons provided evidence for the deep cavity nature of the compounds.[18,19]

For example, the ^{1}H NMR spectrum for **4** (see Fig. 1) clearly shows the β-*trans* olefinic protons and the well-separated methylene signals at 3.2 ppm and 4.4 ppm, which are characteristic of a cone conformational structure.

With a view to chiral recognition, the synthesis of an enantiomerically pure deep cavity calix[4]arene was attempted. The acrylate derived from *L*-menthol was synthesised and subsequently coupled to the tetraiodocalix[4]arene. The desired target compound was obtained after reactions over a period of 150h in 40% yield using $Pd(OAc)_2$/DPPP (10%) in DMF with Et_3N. An inspection of the ^{1}H NMR spectra of the crude reaction mixture over the reaction time suggests rapid formation (64h) of a mixture in which the triolefinic calixarene predominates and there is a comparatively slow (86h) progression of the reaction to the tetra-olefinic product **6**.

Ungaro and co-workers have shown that, in the case of *L*-alanine substituted broader rim calix[4]arenes, a stereogenic centre close to the aromatic calix[4]arene protons gives rise to non equivalent aromatic protons.[20] In our system, the two aromatic protons are diastereotopic, with the aromatic rings of the calixarene acting as a stereogenic plane, similar to the alanine derivatives of Ungaro. This is supported by the ^{13}C NMR spectrum for **6**, which shows additional aromatic signals at around 130ppm. This effect is solvent independent and, in the case of **6** the two ^{1}H NMR aromatic signals (shown in Fig. 2 at 6.89ppm and 6.80ppm) were observed in both $CDCl_3$ and d_6-DMSO. This observation is rather surprising since the stereogenic centre of the menthol residue is separated from the stereogenic aromatic ring by eight chemical bonds.

The next stage involved the reaction of **5** to give tetracondensation products **8–22** (see Scheme 2). A range of amines were selected to demonstrate the scope of this approach for the formation of a static combinatorial library and included amines comprising of electron rich/deficient aromatic systems and amines possessing hydrogen bonding acceptors and donors *e.g.* e, k, l and m. Imine formation was carried out with an excess of eight equivalents of the amine in chloroform in the presence of molecular sieves.

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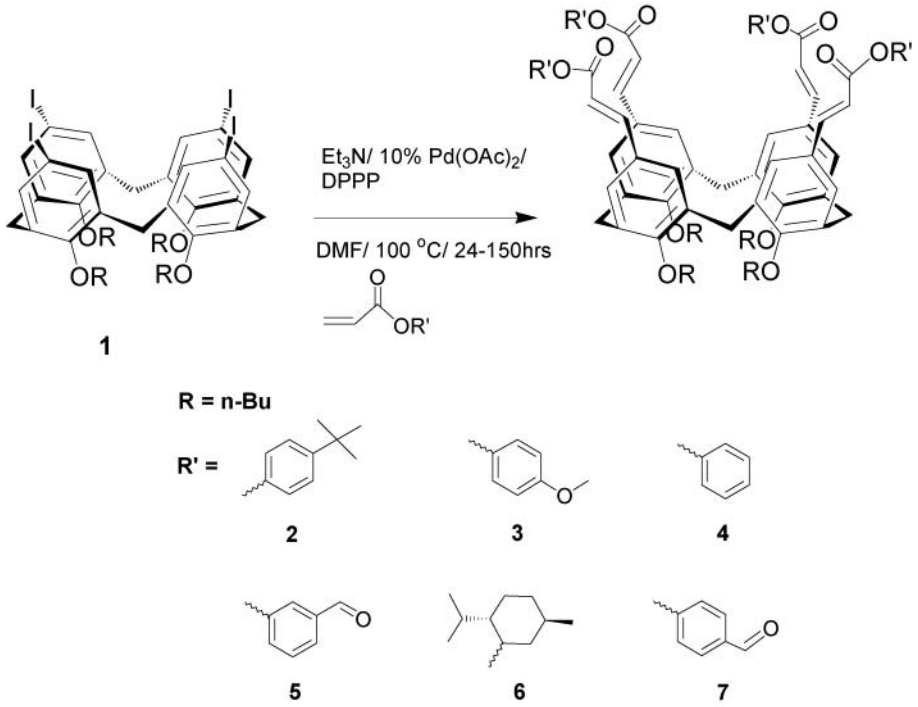


Scheme 1

Table 1 Selected data on the acrylate coupling reactions

Acrylate	Yield/ %	Reaction time/ h	^{1}H NMR chemical shift calix[4]arene ArH/ ppm
2	68	24	6.92
3	50	48	6.85
4	75	48	6.93
5	73	36	6.93
6	40	150	6.87 and 6.76
7	32	12	6.93

The tetra-imines (with the exception of **11**, **18**, **19** and **20**, which could not be synthesised) were obtained in moderate to good yields and displayed the expected C_{4V} symmetry along with the expected, spectroscopic data, supporting their structures (see Table 2).

Dynamic combinatorial library

After the successful synthesis of a static imine library, we considered a dynamic library based on the imine condensation reaction of tetra-formyl compound **5**. Imine formation is a reversible reaction therefore allowing the exploitation of thermodynamic control in a highly modular approach. The two basic advantages of using a macrocyclic scaffold in a DCL should be emphasised here. Firstly the macrocyclic scaffold presents a pre-formed binding site for the potential guest hence making the host guest interactions entropically favourable. Secondly, and more importantly, the use of a macrocyclic scaffold allows the maximisation of possible reaction products while using a minimum of building blocks and required reaction steps. Additionally, the four amine building blocks used are unable to react with themselves allowing selectivity advantages in the library. We have only used achiral amines.

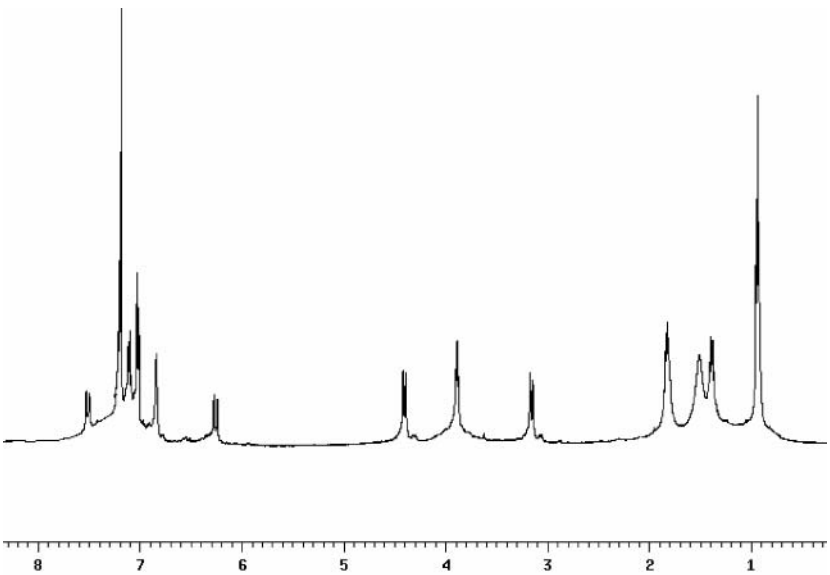
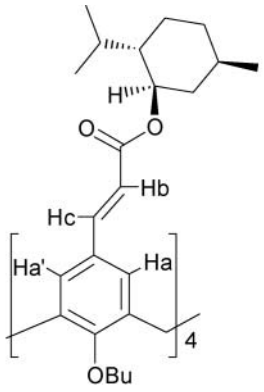


Fig. 1 ^{1}H NMR spectrum of 4 (270MHz, $CDCl_3$, 25 °C). Broad signals are characteristic of anisotropy associated with slow tumbling of calixarene.[16]



6

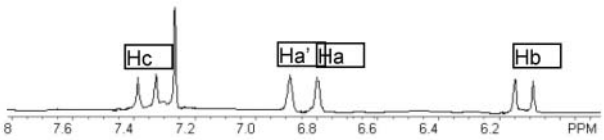


Fig. 2 The aromatic region of the ^{1}H NMR spectrum of 6 ($CDCl_3$ referenced to solvent, 270MHz, 298K).

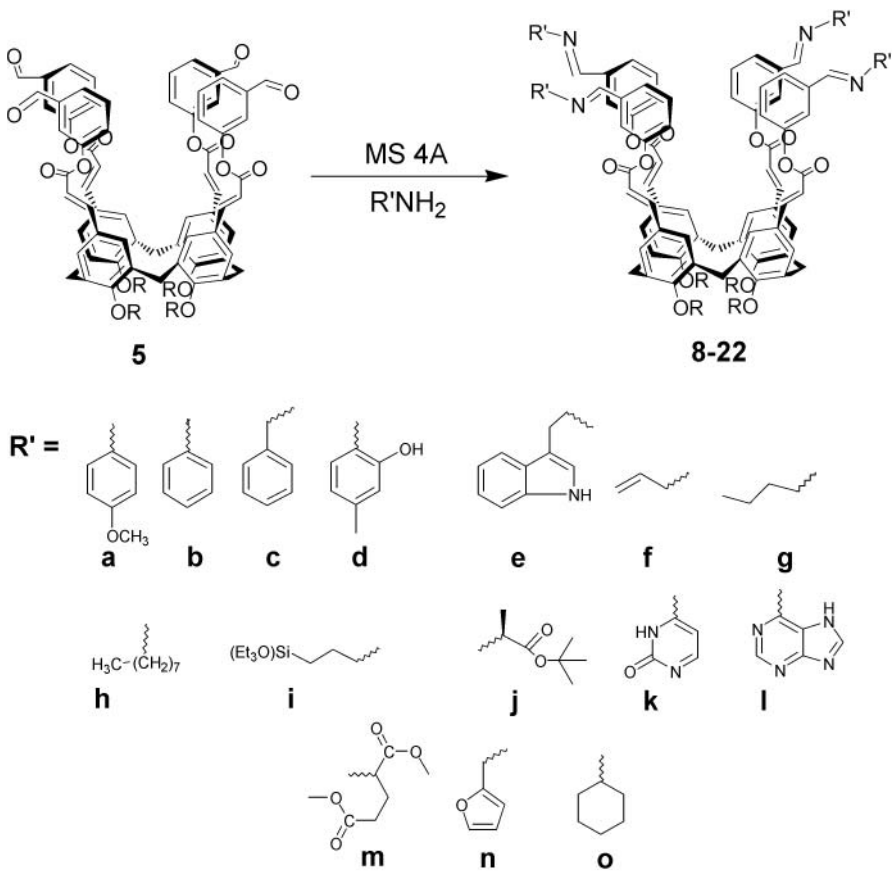
However, combination of the inherent stereoisomerism of the calix with the imine permutations possible with a single racemic amine add an additional 157 possible stereoisomers to the library. Therefore such a DCL composed of a macrocyclic scaffold and additional building blocks cover a large range of chemical space.

Table 2 Yields and selected spectroscopic data for tetra-imines **8–22**

Tetra-imine	Amine	Yield/ %	Reaction time/ h	^{1}H NMR chemical shift N = *CH*/ ppm	LSIMS *m/z*
8	**a**	75	10	8.19	1768
9	**b**	72	11	8.16	1646
10	**c**	68	10	8.17	1703
11	**d**	–	–	–	–
12	**e**	59	12	7.90	1917
13	**f**	83	7	8.05	1502
14	**g**	77	11	8.06	1564
15	**h**	75	10	8.06	1792
16	**i**	45	12	8.01	2162
17	**j**	38	15	8.01	1856
18	**k**	–	–	–	–
19	**l**	–	–	–	–
20	**m**	–	–	–	–
21	**n**	78	10	8.12	1663
22	**o**	49	8	8.02	1671

In a DCL, the potential number of unique calix[4]arene compounds possible when **5** is reacted with four different amines could comprise 158 different imines in the cone conformation (including mono-, di-, tri- and tetra-imines, regioisomers and possible stereoisomers).

The inclusion of an additional amine adds another 133 possible permutations of imine reaction products to the dynamic library, clearly illustrating the immense diversity covered with our approach. The possibility of exerting thermodynamic control via a guest and the subsequent predominance of one (or significantly fewer than 158) compounds would certainly illustrate the potential value of the method described. If compared to a chemical library comprising four amino acid building blocks, which comprises a maximum number of 120 members



Scheme 2

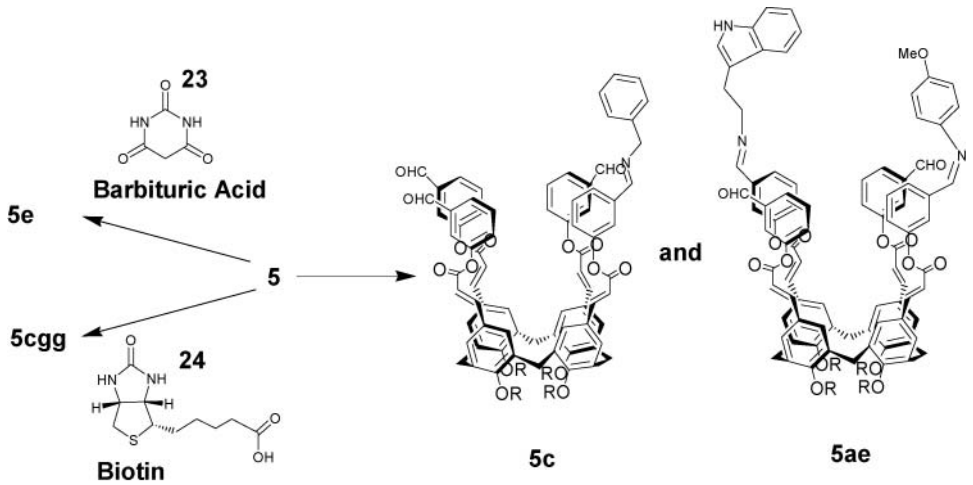


Fig. 3 Scheme showing tentative major product imines formed (as judged by the intensities of peaks in LSIMS mass spectra) in the presence and absence of a guest molecule.

(70 cyclic tetrapeptides + 40 tripeptides + 10 dipeptides) the advantage of using a macrocyclic scaffold becomes evident.

A representative example of this thermodynamic preference was given by LSIMS–MS analysis of the products, when **5** was mixed with stoichiometric (4:1 amine/calixarene) amounts of amines **5a**, **5c**, **5e** and **5g**. After 12 h reaction time a statistical mixture of at least 30 imines with distinct *m/z* values (as judged by the intensity of the molecular ions in the LSIMS-MS) was observed (See Table 3). After a prolonged reaction time of 64 h, there was strong evidence for equilibration under thermodynamic control as illustrated by the predominance of a hetero-condensation product **5c** (*m/z* 1434) with smaller amounts of **5a**, **5ae** and **5g** as judged by the relative intensities of the molecular ions in the LSIMS-MS. Longer reaction times did not change the composition of the DCL significantly.

It cannot be excluded that one of the amines acts as a templating guest to induce the formation of the four most stable tetra-imines. As a control experiment we added two non-amine templates (barbituric acid **23** and biotin **24**) to the dynamic library described above. Again LSIMS-MS allowed us to identify the major components of the library after 48 h of equilibration.

FAB-MS spectra of representative equimolar mixtures of imines revealed differences of relative intensities of the molecular ions within 20%, indicating that LSIMS-MS is in this case a valid technique for the analysis of structurally closely related compounds of comparable molecular weight.[21] It is furthermore worth noting that the library components could not be sufficiently resolved by HPLC.

The highest intensity molecular ion when barbituric acid was present corresponds to **5e** with a complete loss of the signal for **5c**. In the case of biotin the highest intensity molecular ion corresponds to the tris-imine **5cgg**.[21] Note that in such a mass spectrometry experiment, the relative intensities of the individual molecular ions are not necessarily a reliable indication of the amount of product formed. However, the experiments presented clearly demonstrate that upon addition of a template guest the composition of the library changes dramatically.

Hence these experiments provide a clear proof of concept of these macrocyclic DCLs. The ^{1}H NMR spectra of the dynamic library support the formation of a major mono-imine **5e** and tris-imine **5ccg**, respectively. The DCL product **5cgg** exists as three possible isomers (regioisomers and enantiomeric stereoisomers) and **5ae** as two possible regioisomers. From the NMR data obtained it is currently not possible to distinguish and unambiguously assign the structure of the major regio/stereoisomers. All attempts to purify the major library component for more detailed binding studies unfortunately failed. Additional evidence for binding of the guest template to a component of the dynamic library comes from diffusion NMR experiments, indicating a reduced diffusion coefficient of barbituric acid and biotin benzyl ammonium salt in the presence of the dynamic library as opposed to the templates in the absence of the dynamic library.[1]

Table 3 Masses and molecular formulas for DCL products

Imine	Molecular formula	Mass peak *m/z*	Intensity/ relative %	Guest
5c	$C_{91}H_{87}O_{15}N$	1434	35	None
5ae	$C_{101}H_{96}O_{15}N_3$	1590	15	None
5a	$C_{91}H_{87}O_{16}N$	1450	10	None
5e	$C_{94}H_{90}O_{15}N_2$	1487	5	None
5e	$C_{84}H_{90}O_{15}N_2$	1487	39	**23**
5cgg	$C_{99}H_{105}O_{13}N_3$	1540	25	**24**

These experiments clearly indicated that when alternative guest templates were introduced to the dynamic library a new equilibrium is established where a thermodynamically more stable host–guest system results in molecular amplification of individual DCL members.

Conclusion

We have demonstrated the ready availability of a series of multi-functionalised macrocyclic species using reliable Heck chemistry. Furthermore we have shown that acrylato-aldehyde substituted calix[4]arenes can be further elaborated into more complex tetra-imine derivatives. Acrylato-aldehyde substituted calix[4]arenes can engage in thermodynamically controlled, reversible reactions with primary amines. Through introduction of four different amines it is statistically possible to form 158 different permutations of mono, di, tri, and tetra functionalised calix[4]arene, yet in our case comparatively few were observed, thereby covering a large amount of chemical space with a minimum number of building blocks. As a proof of principle it was shown that the DCL composed of a macrocyclic scaffold and four amine building blocks induces a new thermodynamic equilibrium by addition of template guest molecules.

Experimental

^{1}H and ^{13}C NMR spectra were recorded on either a JEOL 270MHz, Bruker AC 300MHz or a DRX 500MHz spectrometer. Standard

Bruker 2-D software was used for spectral processing. All coupling constants are quoted in Hz. Elemental analysis were made on a Leeman Labs CE440 Elemental Analyzer. Note that solvent inclusion complexes of calix[4]arenes often influence elemental analysis and this is taken into account for each compound.[22,23] IR spectra were determined on a Perkin Elmer 200 Spectrometer. The mass spectra (*m/z*) were recorded either by the EPSRC National Mass Spectrometry Service Centre, Swansea or a ThermoFinnigan Mat 95 X. All LSIMS data were collected on a ThermoFinnigan Mat 95 X and ESI-MS was recorded on a ThermoFinnigan DECA CQXP Plus. Acrylates were synthesised according to a general experimental shown below. All other chemicals/reagents were purchased from the Aldrich Chemical Company and used without further purification unless stated otherwise. Solvents were dried and purified according to standard procedures. Melting points were determined on a Kofler hot-stage apparatus and are uncorrected. All compounds are named using the simplified IUPAC calixarene nomenclature.

General procedure for preparation of acrylates

K_2CO_3 (0.89 g, 6.45 mmol) and the alcohol (6.40 mmol) were stirred in DCM (75 mL) for 10min at room temperature. Acryloyl chloride (0.52 mL) was slowly added with the room temperature being maintained. Upon completion of the reaction, it was quenched with water (200mL0 and the organic component extracted with DCM (3 × 50 mL). The combined organic extracts were washed with HCl (3 × 20 mL 3M), water (2 × 50 mL) NaOH (3 × 30 mL, 2M) and again with water (2 × 50 mL). The organic extract was dried (Na_2SO_4), filtered and evaporated under reduced pressure. Solid acrylates could be recrystallised from methanol/diethyl ether and all acrylates were stored below 0ºC or used immediately.

General procedure for preparation of **2–7**

Triethylamine (0.215 mL, 0.156 g, 1.54 mmol) and acrylate (1.54 mmol) were added to a stirred solution of 5,11,17,23-tetraiodocalixarene-25,26,27,28-tetra-n-butylether (0.3 g, 0.27 mmol) **1** in DMF (40 mL). After 10 minutes vigorous stirring at 25 °C palladium acetate (0.006 g, 0.027 mmol) and 1,3-bis(diphenylphosphinopropane) (0.027 g, 0.027 mmol) were added and the mixture heated to 90 °C and stirred for 12–150 h. After addition of diethyl ether (100 mL) the mixture was washed with HCl (3 × 20 mL 3M). The organic extract was dried (Na_2SO_4), filtered and evaporated under reduced pressure. The residue was further dried in a desiccator (SiO_2) under reduced pressure for 12 h and recrystallised from methanol to give the calix[4]arene **2–7**.

5,11,17,23-Tetrakis[(E)-2-(p-tert-butylphenoxycarbonyl)ethenyl]-25,26,27,28-tetrabutoxycalix[4]arene (**2**): M.p. 144–147 °C. IR (Nujol)/cm^{-1}: 1732 (C=O), 1620 (C=C). ^{1}H NMR (270 MHz; $CDCl_3$, 25 °C): δ = 7.58 (d, $^3J_{H,H}$ = 16.0 Hz, 4 H, Ar-CH=), 7.29 (d, $^3J_{H,H}$ = 8.7 Hz, 8 H, ArH), 7.01 (d, $^3J_{H,H}$ = 8.7 Hz, 8 H, ArH), 6.92 (s, 8 H, ArH(calix)), 6.32 (d, $^3J_{H,H}$ = 16.0 Hz, 4 H, CH–C=O), 4.41 (d, $^2J_{H,H}$ = 13.4 Hz, 4 H, C*H*$_A$H$_B$Ar), 3.9 (t, $^3J_{H,H}$ = 6.4 Hz, 8 H, CH_2O), 3.19 (d, $^2J_{H,H}$ = 13.4 Hz, 4 H, CH$_A$*H*$_B$Ar), 1.90 (m, 8 H, C*H*$_2$CH$_2$O), 1.50–1.35 (m, 8 H, OCH$_2$CH$_2$C*H*$_2$), 1.23 (s, 36 H, C(CH$_3$)$_3$) 1.00 (t, $^3J_{H,H}$ = 8.3 Hz, 12 H, C*H*$_3$CH$_2$) ppm. ^{13}C NMR (100 MHz; $CDCl_3$, 25 °C): δ = 164.8, 158.2, 149.4, 143.2, 142.2, 126.6, 125.8, 125.5, 123.4 121.8, 121.4, 116.1, 72.4, 32.3, 31.4, 31.0, 19.3, 14.1; *m/z* (EI) 1458 [M+H]. Found C, 75.49; H, 7.61% $C_{96}H_{112}O_{12} \cdot 4H_2O$ requires C, 75.36; H, 7.91%.

5,11,17,23-Tetrakis[(E)-2-(4-methoxyphenoxycarbonyl)ethenyl]-25,26,27,28-tetrabutoxycalix[4]arene (**3**): M.p. 160–162 °C. IR (Nujol)/cm^{-1}: 1732 (C=O), 1620 (C=C); ^{1}H NMR (270 MHz; $CDCl_3$, 25 °C): δ 7.58 (d, $^3J_{H,H}$ = 16.0 Hz, 4 H, Ar-CH=), 7.00 (d, $^3J_{H,H}$ = 9.0 Hz, 8 H, ArH), 6.85 (s, 8 H, ArH), 6.78 (d, $^3J_{H,H}$ = 9.0 Hz, 8 H, ArH), 6.28 (d, $^3J_{H,H}$ = 16.0 Hz, 4 H, Ar-CH=CH–C=O), 4.43 (d, $^2J_{H,H}$ = 13.4 Hz, 4 H, C*H*$_A$H$_B$Ar), 3.93 (t, $^3J_{H,H}$ = 6.4 Hz, 4 H, CH_2O), 3.76 (s, 12 H, CH_3O), 3.19 (d, $^3J_{H,H}$ = 13.4 Hz, 4 H, CH$_A$*H*$_B$Ar), 1.90 (m, 8 H, C*H*$_2$CH$_2$O), 1.50–1.40 (m, 8 H, OCHCH$_2$C*H*$_2$), 1.00 (t, $^3J_{H,H}$ = 8.3 Hz, 12 H, C*H*$_3$CH$_2$) ppm. ^{13}C NMR (100 MHz; $CDCl_3$, 25 °C): δ = 165.4, 158.8, 156.81, 144.0, 135.1, 129.0, 128.1, 122.8, 122.6, 116.8, 116.4, 74.7, 55.3, 36.8, 32.1, 18.7, 14.1 ppm. *m/z* (EI) 1354 [M+H]. Found C, 72.65; H, 6.88% $C_{84}H_{88}O_{16} \cdot 1.5H_2O$ requires C, 73.08; H, 6.64%.

5,11,17,23-Tetrakis[(E)-2-(phenoxycarbonyl)ethenyl]-25,26,27,28-tetrabutoxycalix[4]arene (**4**): M.p. 92–94 °C. IR (Nujol)/cm^{-1}: 1732 (C=O), 1634 (C=C); ^{1}H NMR (270 MHz; $CDCl_3$, 25 °C): δ = 7.58 (d, $^3J_{H,H}$ = 16.0 Hz, 4 H, Ar-CH=), 7.28 (d, $^3J_{H,H}$ = 7.8 Hz, 8 H, ArH), 7.21 (t, $^3J_{H,H}$ = 7.8 Hz, 4 H, ArH), 7.11 (d, $^3J_{H,H}$ = 7.8 Hz, 8 H, ArH), 6.93 (s, 8 H, ArH), 6.32 (d, $^3J_{H,H}$ = 16.0 Hz, 4 H, Ar-CH=CH–C=O), 4.43 (d, $^2J_{H,H}$ = 13.4 Hz, 4 H, C*H*$_A$H$_B$Ar), 3.93 (t, $^3J_{H,H}$ = 6.4 Hz, 8 H, CH_2O), 3.19 (d, $^2J_{H,H}$ = 13.4 Hz, 4 H, CH$_A$*H*$_B$Ar), 1.90 (m, 8 H, C*H*$_2$CH$_2$O), 1.50–1.40 (m, 8 H, OCHCH$_2$C*H*$_2$), 1.00 (t, $^3J_{H,H}$ = *J* 8.3 Hz, 12 H, C*H*$_3$CH$_2$)ppm. ^{13}C NMR (100 MHz; $CDCl_3$, 25 °C): δ = 165.6, 159.0, 150.8, 146.4, 135.4, 129.8, 129.2, 129.0, 125.9, 122.1, 115.7, 75.6, 32.5, 31.3, 19.5, 14.2 ppm. *m/z* (EI) 1232 [M+]. Found C, 77.65; H, 6.21% $C_{80}H_{80}O_{12}$ requires C, 77.90; H, 6.54%.

5,11,17,23-Tetrakis[(E)-2-(4-carboxyphenoxy)ethenyl]-25,26,27,28-tetrapropoxycalix[4]arene (**5**): M.p. 94–96 °C. IR (Nujol)/cm^{-1}: 1730 (C=O), 1720 (C=O), 1631 (C=C); ^{1}H NMR (270 MHz; $CDCl_3$, 25 °C): δ = 9.81 (s, 4 H, CHO), 7.69–7.64 (m, 8 H, ArH, Ar-CH=), 7.59 (s,4 H, ArH), 7.41–7.35 (m, 8 H, ArH), 6.93 (s, 8 H, ArH), 6.34 (d, $^3J_{H,H}$ = 15.6 Hz, 4 H, CH–C=O), 4.51 (d, $^2J_{H,H}$ = 13.8 Hz, 4 H, C*H*$_A$H$_B$Ar), 3.93 (t, $^3J_{H,H}$ = 6.9 Hz, 8 H, OC*H*$_2$CH$_2$), 3.28 (d, $^2J_{H,H}$ = 13.8 Hz, 4 H, CH$_A$*H*$_B$Ar), 1.98–1.91 (m, 8 H, OCH$_2$C*H*$_2$CH$_3$), 1.07 (t, $^3J_{H,H}$ = 8.3 Hz, 12 H, C*H*$_3$CH$_2$) ppm. ^{13}C NMR (100 MHz; $CDCl_3$, 25 °C): δ = 191.3, 165.4, 151.4, 147.3, 137.6, 135.7, 129.9, 128.9, 128.7, 128.5, 128.1, 126.6, 123.2, 114.6, 77.2, 31.0, 23.4, 10.3 ppm. *m/z* (LSIMS) 1289 [M+]; Found C, 69.94; H 5.58% $C_{80}H_{72}O_{16} \cdot 4H_2O$ requires C, 70.57; H, 5.92%.

5,11,17,23-Tetrakis[(E)-2-(L-menthoxycarbonyl)ethenyl]-25,26,27,28-tetrabutoxycalix[4]arene (**6**): M.p. 85–87 °C. IR (Nujol)/cm^{-1}: 1708 (C=O), 1634 (C=C); ^{1}H NMR (270 MHz; $CDCl_3$, 25 ºC): δ = 7.35 (d, $^3J_{H,H}$ = 16.2 Hz, 4 H, Ar-CH=), 6.87(s, 4 H, ArH) 6.76 (s, 4 H, ArH) 6.12 (d, $^3J_{H,H}$ = 16.2 Hz, 4 H, CH–C=O), 4.65 (m, 4 H, C*H*OC=O) 4.43 (d, $^2J_{H,H}$ = 13.4 Hz, 4 H, C*H*$_A$H$_B$Ar), 3.93 (t, $^3J_{H,H}$ = 6.4 Hz, 8 H, CH_2O), 3.19 (d, $^3J_{H,H}$ = 13.4 Hz, 4 H, CH$_A$*H*$_B$Ar), 1.90 (m, 8 H, C*H*$_2$CH$_2$O), 1.67–1.60 (m, 12 H, OCHC*H*$_2$CH and OCHC*H*) 1.50–1.40 (m, 8 H, OCHCH$_2$C*H*$_2$), 1.00 (t, $^3J_{H,H}$ = 8.3 Hz, 12 H, C*H*$_3$CH$_2$) 0.98–0.78 (m, 60 H, (C*H*$_3$)$_2$C*H* and C*H*$_2$C*H*$_2$C*H*CH$_3$) ppm. ^{13}C NMR (100 MHz; $CDCl_3$, 25 °C): δ = 166.7, 158.4, 144.4, 135.2, 130.2, 129.2, 127.5, 116.7, 75.1, 73.8, 47.4, 40.9, 34.4, 32.2, 31.4, 31.3, 30.9, 26.4, 22.1, 20.9, 19.3, 16.4, 14.1 ppm. *m/z* (EI) 1482 [M+]. Found C, 72.40; H, 9.00% $C_{96}H_{136}O_{12} \cdot 6H_2O$ requires C, 72.51; H, 9.38%.

5,11,17,23-Tetrakis[(E)-2-(4-carboxyphenoxycarbonyl)ethenyl]-25,26,27,28-tetrabutoxycalix[4]arene (**7**): M.p. 103–105 °C. IR (Nujol)/cm^{-1}: 1748 (C=O (ester)), 1710 (C=O), 1615 (C=C); ^{1}H NMR (270 MHz; $CDCl_3$, 25 °C): δ = 9.99 (s, 4 H, CHO), 7.79 (d, $^3J_{H,H}$ = 8.6 Hz, 8 H, ArH (benzenaldehyde)), 7.62 (d, $^3J_{H,H}$ = 15.9 Hz, 4 H, Ar-CH=), 7.28 (d, $^3J_{H,H}$ = 8.6 Hz, 8 H, ArH (benzenaldehyde)), 6.93 (s, 8 H, ArH) 6.37 (d, $^3J_{H,H}$ = 15.9 Hz, 4 H, Ar-CH=CH–C=O), 4.50 (d, $^2J_{H,H}$ = 13.2 Hz, 4 H, C*H*$_A$H$_B$Ar), 3.97 (t, $^3J_{H,H}$ = 6.4 Hz, 8 H, CH_2O), 3.19 (d, $^2J_{H,H}$ = 13.2 Hz, 4 H, CH$_A$*H*$_B$Ar), 1.90 (m, 8 H, C*H*$_2$CH$_2$O), 1.50–1.35 (m, 8 H, OCHCH$_2$C*H*$_2$), 1.00 (t, $^3J_{H,H}$ = 8.3 Hz, 12 H, C*H*$_3$CH$_2$) ppm. ^{13}C NMR (100 MHz; $CDCl_3$, 25 °C): δ = 191.5, 165.4, 156.1, 147.2, 142.3, 136.0, 131.7, 131.3, 129.7, 128.8, 123.1, 114.8, 75.6, 32.5, 31.2, 19.7, 14.3 ppm. *m/z* (EI) 1345[M+]. Found C, 68.97; H, 5.92% $C_{84}H_{80}O_{16} \cdot 6H_2O$ requires C, 69.41; H, 6.38%.

General procedure for preparation of **8–22**

To a solution of **5** (50 mg, 0.037 mmol) in $CDCl_3$ (3 mL) was added amines **5a**–**5o** (0.148 mmol) and of 4Å molecular sieves (200 mg). The solution was allowed to react without stirring at RT for 7–15 h. After filtering, the $CDCl_3$ was removed under reduced pressure. Recrystallisation from chloroform/diethyl ether gave **8–10, 12–17, 21** and **22**.

5,11,17,23-Tetrakis[(E)-2-(3-p-anisidineiminophenoxy)ethenyl]-25,26,27,28-tetrabutoxycalix[4]arene (**8**): M.p. 102–107 °C; IR (Nujol)/cm^{-1}: 1720(C=O), 1635(C=N), 1589(C=C); ^{1}H NMR (270 MHz; $CDCl_3$, 25 °C): δ = 8.19 (s, 4 H, CH=N), 7.65–7.61 (m, 12 H, ArH + Ar-CH=), 7.31–7.30 (m, 4 H, ArH), 7.18–7.14 (m, 4 H, ArH), 7.13 (d, $^3J_{H,H}$ = 7.0 Hz, 8 H, ArH, (p-anisidine)), 6.94 (s, 8 H, ArH), 6.87 (d, $^3J_{H,H}$ = 7.0 Hz, 8 H, ArH (p-anisidine)), 6.36 (d, $^3J_{H,H}$ = 16.1 Hz, 4 H, CH–C=O), 4.50 (d, $^2J_{H,H}$ = 13.6 Hz, 4 H, C*H*$_A$H$_B$Ar), 3.98 (t, $^3J_{H,H}$ = 6.3 Hz, 8 H, OC*H*$_2$CH$_2$), 3.77 (s, 12 H, OCH_3), 3.26 (d, $^2J_{H,H}$ = 13.6 Hz, CH$_A$*H*$_B$Ar), 1.94–1.89 (m, 8 H, C*H*$_2$CH$_2$O), 1.50–1.46 (m, 8 H, OCH$_2$CH$_2$C*H*$_2$), 1.02 (t, $^3J_{H,H}$ = 8.4 Hz, 12 H, C*H*$_3$CH$_2$) ppm. ^{13}C NMR (1000 MHz; $CDCl_3$, 25 °C): δ = 165.8, 159.4, 158.6, 157.4, 151.5, 146.9, 144.7, 138.0, 135.8, 129.7, 128.9, 126.6, 125.7, 122.5, 118.7, 117.2, 116.7, 115.3, 75.5, 55.9, 32.5, 31.7, 19.6, 14.0 ppm. *m/z* (LSIMS) 1768 [M+ 4H]; Found C, 71.58; H, 5.96; N, 2.93% $C_{112}H_{108}O_{16}N_4 \cdot CHCl_3$ requires C, 71.98; H, 5.83; N, 2.97%.

5,11,17,23-Tetrakis[(E)-2-(3-anilineiminophenoxy)ethenyl]-25,26,27,28-tetrabutoxycalix[4]arene (**9**): M.p. 91–94 °C. IR (Nujol)/cm^{-1}: 1730 (C=O), 1640 (C=N), 1634 (C=C); ^{1}H NMR (270 MHz; $CDCl_3$,

25 °C): δ = 8.16 (s, 4 H, CH=N), 7.60–7.15 (m, 12 H, Ar-CH=, ArH), 7.32–7.11 (m, 28 H, ArH + ArH(aniline)), 6.93 (s, 8 H, ArH), 6.28 (d, $^3J_{H,H}$ = 14.9 Hz, 4 H, CH–C=O), 4.50 (d, $^2J_{H,H}$ = 12.8 Hz, 4 H, CH_AH_BAr), 3.98–3.96 (m, $^3J_{H,H}$ = 8.3 Hz, 8 H, OCH_2CH_2), 3.27 (d, $^2J_{H,H}$ = 12.8 Hz, 4 H, CH_AH_BAr), 1.98–1.91 (m, 8 H, CH_2CH_2O), 1.50–1.35 (m, 8 H, $OCH_2CH_2CH_2$), 1.00 (t, $^3J_{H,H}$ = 8.3 Hz, 12 H, CH_3CH_2) ppm. ^{13}C NMR (100 MHz; $CDCl_3$, 25 °C): δ = 165.8, 159.6, 151.9, 159.4, 147.1, 137.8, 135.7, 129.6, 129.3, 126.2, 125.8, 125.1, 124.9, 122.6, 121.1, 121.1, 118.7, 115.3, 75.6, 31.5, 31.3, 19.5, 14.1 ppm. *m/z* (LSIMS) 1646 [M+2H]; Found C, 73.80; H, 6.11; N, 3.1 $C_{108}H_{100}O_{12}N_4 \cdot CHCl_3$ requires C, 74.16; H, 5.77; N, 3.17

5,11,17,23-Tetrakis[(E)-2-(3-benzyliminophenoxy)ethenyl]-25, 26,27,28-tetrabutoxycalix[4]arene (**10**): M.p. 89–93 °C; IR (Nujol) /cm^{-1}: 1732 (C=O), 1640 (C=N), 1635 (C=C); ^{1}H NMR (270 MHz; $CDCl_3$, 25 °C): δ = 8.17 (s, 4 H, CH=N), 7.61 (d, $^3J_{H,H}$ = 7.3 Hz, 4 H, ArH), 7.60–7.15 (m, 36 H, Ar-CH=, ArH, ArH (benzylamine)), 6.92 (s, 8 H, ArH), 6.28 (d, $^3J_{H,H}$ = 15.2 Hz, 4 H, CH–C=O), 4.83 (s, 8 H, CH_2N=), 4.50 (d, $^2J_{H,H}$ = 12.8 Hz, 4 H, CH_AH_BAr), 3.97 (q, $^3J_{H,H}$ = 8.3 Hz, 8 H, OCH_2CH_2), 3.25 (d, $^2J_{H,H}$ = 12.8 Hz, 4 H, CH_AH_BAr), 1.92–1.90 (m, 8 H, CH_2CH_2O), 1.50–1.35 (m, 8 H, $OCH_2CH_2CH_2$), 1.00 (t, $^3J_{H,H}$ = 8.3 Hz, 12 H, CH_3CH_2) ppm. *m/z* (LSIMS) 1703 [M+2H]; Found C, 72.12; H, 6.13; N, 3.18% $C_{112}H_{108}N_4O_{12} \cdot 1.5CHCl_3$ requires C, 72.47; H, 5.87; N, 2.98%

5,11,17,23-Tetrakis[(E)-2-(3-tryptiminophenoxy)ethenyl]-25,26, 27,28-tetrabutoxycalix[4]arene (**12**): M.p. 94–97 °C. IR (Nujol)/cm^{-1} 1645 (C=N) 1680 (C=O), 1620(C=C); ^{1}H NMR (270 MHz; $CDCl_3$, 25 °C): δ = 7.90 (s, 4 H, CH=N), 7.83, (s, 4 H, ArH (tryptamine) 7.62–7.58 (m, 16 H, ArH (tryptamine) + Ar-CH= + ArH), 7.34–7.32 (m, 8 H, ArH), 7.18–7.07 (m, 12 H, ArH (tryptamine)), 6.93 (s, 8 H, ArH), 6.31 (d, $^3J_{H,H}$ = 15.5 Hz, 4 H, CH–C=O) 4.50 (d, $^2J_{H,H}$ = 13.5 Hz, 4 H, CH_AH_BAr), 3.97 (t, $^3J_{H,H}$ = 7.3 Hz, 8 H, OCH_2CH_2), 3.80 (m, 8 H, CH_2–N=), 3.26 (d, $^2J_{H,H}$ = 13.5 Hz, 4 H, CH_AH_BAr), 3.07 (t, $^3J_{H,H}$ = 6.23 Hz, 8 H, CH_2CH_2-Ar (tryptamine), 1.91–1.90 (m, 8 H, CH_2CH_2O), 1.50–1.35 (m, 8 H, $OCH_2CH_2CH_2$), 1.00 (t, $^3J_{H,H}$ = 8.3 Hz, 12 H, CH_3CH_2) ppm. ^{13}C NMR (100MHz; $CDCl_3$, 25 °C): δ = 165.5, 160.5, 159.8, 153.8, 151.2, 148.2, 146.7, 137.7, 136.2, 135.5, 129.4, 128.7, 124.9, 124.0, 122.5, 121.7, 121.6, 119.1, 118.8, 115.1, 113.6, 111.2, 75.3, 61.6, 32.2, 30.9, 26.5, 19.3, 14.0 ppm. *m/z* (LSIMS) 1917 [M+3H]; Found C, 69.32; H, 6.37; N, 5.06% $C_{124}H_{120}O_{12}N_8 \cdot 2.3 CHCl_3$ requires C, 69.19; H, 5.62; N, 5.11%.

5,11,17,23-Tetrakis[(E)-2-(3-allyliminophenoxy)ethenyl]-25,26, 27,28-tetrabutoxycalix[4]arene (**13**):M.p. 86–89 °C. IR (Nujol)/cm^{-1}: 1732 (C=O), 1646 (C=C),1640 (C=N),1634 (C=C); ^{1}H NMR (270 MHz; $CDCl_3$, 25 °C): δ = 8.05 (s, 4 H, CH=N), 7.59 (m, 8 H, ArH, Ar-CH=), 7.46 (s, 4 H, ArH), 7.35–7.18 (m, 8 H, ArH), 6.92 (s, 8 H, ArH), 6.30 (d, $^3J_{H,H}$ = 15.8 Hz, 4 H, CH–C=O), 6.10–5.90 (m, 4 H, CH_C=CH_D), 5.19 (d, $^3J_{H,H}$ = 15.0 Hz, 4 H, CH_C=CH_D), 5.12 (d, $^3J_{H,H}$ = 10.9 Hz, 4 H, CH_C=CH_D), 4.49 (d, $^2J_{H,H}$ = 13.7 Hz, 4 H, CH_AH_BAr), 4.17 (d, $^3J_{H,H}$ = 4.9 Hz, 8 H, CH_2-N=), 3.96 (t, $^3J_{H,H}$ = 7.0 Hz, 8 H, OCH_2CH_2), 3.25 (d, $^2J_{H,H}$ = 13.7 Hz, 4 H, CH_AH_BAr), 1.91–1.89 (m, 8 H, CH_2CH_2O), 1.50–1.45 (m, 8 H, $OCH_2CH_2CH_2$), 1.05 (t, $^3J_{H,H}$ = 8.3 Hz, 12 H, CH_3CH_2) ppm. ^{13}C NMR (100 MHz; $CDCl_3$, 25 °C): δ = 160.5, 150.6, 146.1, 139.2, 136.9, 136.1, 135.2, 134.8, 128.8, 128.1, 124.2, 123.6, 123.1, 121.4, 115.5, 114.4, 75.6, 44.0, 31.5, 31.3, 19.5, 14.1 ppm. *m/z* (LSIMS) 1502 [M+H]; Found C, 69.06, H, 6.89, 5.72% $C_{96}H_{100}O_{12}N_4 \cdot 1.5CHCl_3$ requires C, 69.67, H, 6.09%, N 3.33%.

5,11,17,23-Tetrakis[(E)-2-(3-n-butyliminophenoxy)ethenyl]-25, 26,27,28-tetrabutoxycalix[4]arene (**14**): M.p. 101–104 °C. IR (Nujol) /cm^{-1}: 1731 (C=O), 1633 (C=N), 1584 (C=C); ^{1}H NMR (270 MHz; $CDCl_3$, 25 °C): δ = 8.06 (s, 4 H, CH=N), 7.61–7.55 (m, 8 H, ArH + Ar-CH=), 7.46 (s, 4 H, ArH), 7.21–7.20 (m, 4 H, ArH), 7.14 (d, $^3J_{H,H}$ = 8.3 Hz, 4 H, ArH), 6.92 (s, 8 H, ArH), 6.33 (d, $^3J_{H,H}$ = 15.7 Hz, 4 H, CH–C=O), 4.50 (d, $^2J_{H,H}$ = 13.3 Hz, 4 H, CH_AH_BAr), 3.97 (t, $^3J_{H,H}$ = 6.8 Hz, 8 H, OCH_2CH_2), 3.53 (t, $^3J_{H,H}$ = 6.9 Hz, 8 H, N–CH_2), 3.25 (d, $^2J_{H,H}$ = 13.3 Hz, 4 H, CH_AH_BAr), 1.92–1.90 (m, 8 H, CH_2CH_2O), 1.67–1.62 (m, 8 H, NCH_2CH_2), 1.50–1.35 (m, 8 H, $OCH_2CH_2CH_2$), 1.38–1.33 (m, 8 H, $NCH_2CH_2CH_2$), 1.00 (t, $^3J_{H,H}$ = 8.3 Hz, 12 H, CH_3CH_2), 0.91 (t, $^3J_{H,H}$ = 6.2 Hz, 12H, $NCH_2CH_2CH_2CH_2$) ppm. ^{13}C NMR (100 MHz; $CDCl_3$, 25 °C): δ = 165.5, 159.9, 159.7, 151.2, 146.3, 137.7, 135.4, 129.4, 128.6, 124.7, 124.0, 121.8, 120.2, 116.3, 75.3, 61.3, 32.9, 32.2, 31.2, 20.4, 19.3, 14.1, 13.8 ppm. *m/z* (LSIMS) 1564 [M+]; Found C, 71.74; H, 7.24; N, 2.96% $C_{100}H_{116}O_{12}N_4 \cdot CHCl_3$ requires C, 71.98; H, 7.00; N 3.32%.

5,11,17,23-Tetrakis[(E)-2-(3-n-octyliminophenoxy)ethenyl]-25, 26,27,28-tetrabutoxycalix[4]arene (**15**): M.p. 107–101 ºC. IR (Nujol) /cm^{-1}: 1732 (C=O), 1640 (C=N), 1634 (C=C); ^{1}H NMR (270 MHz; $CDCl_3$, 25 °C): δ = 8.06 (s, 4 H, CH=N), 7.61–7.56 (m, 8 H, ArH + Ar-CH=), 7.44 (s, 4 H, ArH), 7.23–7.20 (m, 4 H, ArH), 7.15–7.13 (m, 4 H, ArH), 6.93 (s, 8 H, ArH), 6.32 (d, $^3J_{H,H}$ = 15.5 Hz, 4 H, CH–C=O), 4.50 (d, $^2J_{H,H}$ = 13.5 Hz, 4 H, CH_AH_BAr), 3.97 (t, $^3J_{H,H}$ = 6.7 Hz, 8 H, OCH_2CH_2), 3.55 (t, $^3J_{H,H}$ = 6.7 Hz, 8 H, N–CH_2), 3.25 (d, $^3J_{H,H}$ = 13.5 Hz, 4 H, CH_AH_BAr), 1.92–1.90 (m, 8 H, CH_2CH_2O), 1.65–1.62 (m, 8 H, NCH_2CH_2), 1.50–1.35 (m, 8 H, $OCH_2CH_2CH_2$), 1.38–1.33 (m, 40 H, $NCH_2CH_2(CH_2)_5CH_3$), 1.00 (t, $^3J_{H,H}$ = 8.3 Hz, 12 H, CH_3CH_2), 0.87 (t, $^3J_{H,H}$ = 6.2 Hz, 12 H, $NCH_2CH_2(CH_2)_5CH_3$) ppm. ^{13}C NMR (100 MHz; $CDCl_3$, 25 °C): δ = 165.4, 161.1, 159.9, 157.3, 151.1, 146.6, 137.7 135.5, 129.6, 129.4, 128.7, 124.7, 124.0, 117.8, 75.2, 61.7, 32.2, 31.8, 30.9, 29.4, 29.3, 27.4, 26.7, 23.1, 22.6, 19.3, 14.1 ppm. *m/z* (LSIMS) 1792 [M+2H]; Found C, 72.12; H, 8.32; N, 2.87% $C_{116}H_{148}O_{12}N_4 \cdot 1.3CHCl_3$ requires C, 72.30; H, 7.72; N, 2.87%.

5,11,17,23-Tetrakis[(E)-2-(3-(3-triethoxysilylpropyliminophenoxy))ethenyl]-25,26,27,28-tetrabutoxycalix[4]arene (**16**): M.p. 97–101 °C. IR (Nujol)/cm^{-1}: 1732 (C=O), 1640 (C=N), 1630 (C=C); ^{1}H NMR (270 MHz; $CDCl_3$, 25 °C): δ = 8.01 (s, 4 H, CH=N), 7.49–7.48 (m, 8 H, ArH + Ar-CH=), 7.35 (s, 4 H, ArH), 7.20–7.18 (m, 4 H, ArH), 7.06 (d, $^3J_{H,H}$ = 7.7 Hz, 4 H, ArH), 6.85 (s, 8 H, ArH), 6.26 (d, $^3J_{H,H}$ = 15.5 Hz, 4 H, CH–C=O), 4.42 (d, $^2J_{H,H}$ = 13.4 Hz, 4 H, CH_AH_BAr), 3.90 (t, $^3J_{H,H}$ = 7.2 Hz, 8 H, OCH_2CH_2), 3.52 (t, $^3J_{H,H}$ = 7.2 Hz, 8 H, NCH_2), 3.20 (d, $^2J_{H,H}$ =13.4 Hz, 4 H, CH_AH_BAr), 1.85–1.82 (m, 8 H, CH_2CH_2O), 1.60–1.57 (m, 8 H, NCH_2CH_2), 1.42–1.37 (m, 8 H, $OCH_2CH_2CH_2$), 1.31–1.13 (m, 60 H, Si–OCH_2CH_3 + OCH_2CH_3), 1.00 (t, $^3J_{H,H}$ = 8.4 Hz, 12 H, CH_3CH_2), 0.79 (m, 8 H, CH_2Si) ppm. ^{13}C NMR (100 MHz; $CDCl_3$, 25 °C): δ = 165.1, 159.7, 152.01, 146.4, 137.3, 135.1, 129.0, 128.2, 124.2, 123.5, 121.0 117.2, 115.6, 114.1, 74.7, 63.6, 57.7, 31.6, 29.1, 18.6, 17.6, 13.5, 7.3, 0.4 ppm. *m/z* (LSIMS) 2162 [M+5H] 2116 [M+4H-OCH_2CH_3]; Found C, 61.86; H, 6.87; N, 2.14 $C_{120}H_{164}O_{24}N_4Si_4 \cdot 1.75CHCl_3$ requires C, 61.76; H, 7.06; N, 2.37%.

5,11,17,23-Tetrakis[(E)-2-(3-(t-butyl-L-alanineiminophenoxy)ethe nyl]-25,26,27,28-tetrabutoxycalix[4]arene (**17**): M.p. 89–94 °C. IR (CH_2Cl_2)/cm^{-1}: 1633 broad (C=N) and (C=C), 1710 broad (C=O) and (C=O); ^{1}H NMR (270 MHz; $CDCl_3$, 25 °C): δ = 8.01 (s, 4 H, CH=N), 7.63–7.59 (m, 8 H, ArH + Ar-CH=), 7.49 (s, 4 H, ArH), 7.18–7.16 (m, 8 H, ArH), 6.90 (s, 8 H, ArH), 6.42 (d, $^3J_{H,H}$ = 15.4 Hz, 4 H, CH–C=O), 4.49 (d, $^2J_{H,H}$ = 13.4 Hz, 4 H, CH_AH_BAr), 3.97 (m, 12 H, OCH_2CH_2 + $CHCH_3$), 3.25 (d, $^2J_{H,H}$ = 13.4 Hz, 4 H, CH_AH_BAr), 1.95–1.91 (m, 8 H, CH_2CH_2O), 1.55–1.39 (m, 56 H, $OCH_2CH_2CH_2$ + $(CH_3)_3$C+ $CHCH_3$), 1.00 (t, $^3J_{H,H}$ = 8.3 Hz, 12 H, CH_3CH_2) ppm. ^{13}C NMR (100 MHz; $CDCl_3$, 25 °C): δ = 171.6, 165.5, 161.5, 159.2, 151.1, 146.7, 137.3, 136.8, 129.3, 128.6, 128.1, 125.2, 124.6, 122.1, 115.0, 81.1, 75.3, 68.4, 32.3, 31.0, 28.1, 28.0, 19.4, 14.0 ppm. *m/z* (LSIMS) 1856 [M+2H] 1728 [M+2H–$(CH_3)_3COOCCH(CH_3)$N]; Found C, 66.99; H, 6.77; N, 2.50% $C_{112}H_{132}O_{20}N_4$ 1.5$CHCl_3$ requires C, 67.04%, H, 6.62%, N, 2.76.

5,11,17,23-Tetrakis[(E)-2-(3-furfuryliminophenoxy)ethenyl]-25, 26,27,28-tetrabutoxycalix[4]arene (**21**): M.p. 96–99 °C. IR (Nujol) /cm^{-1}: 1727 (C=O), 1632 (C=N), 1590 (C=C), ^{1}H NMR (270 MHz; $CDCl_3$, 25 °C): δ = 8.12 (s, 4 H, CH=N), 7.63–7.55 (m, 8 H, ArH + Ar-CH=), 7.47 (s, 4 H, ArH), 7.37–7.32 (m, 4 H, ArH(furfurylamine)), 7.26–7.25 (m, 4 H, ArH), 7.18–7.13 (m, 4 H,H ArH), 6.92 (s, 8 H, ArH), 6.37–6.25 (m, 8 H, ArH(furfurylamine),+ CH–C=O), 6.25–6.20 (m, 4 H, ArH(furfurylamine)), 4.78–4.69 (m, 8 H, CH_2N=), 4.50 (d, $^2J_{H,H}$ = 13.5 Hz, 4 H, CH_AH_BAr), 4.01–3.92 (m, 8 H, OCH_2CH_2), 3.25 (d, $^2J_{H,H}$ = 13.5 Hz, 4 H, CH_AH_BAr), 1.98–1.84 (m, 8 H, CH_2CH_2O), 1.56–1.35 (m, 8 H, $OCH_2CH_2CH_2$), 1.01–0.97 (m, 12 H, CH_3CH_2) ppm. ^{13}C NMR (100 MHz; $CDCl_3$, 25 °C): δ = 165.4, 162.1, 159.2, 152.2, 151.1, 146.7, 142.1, 137.2, 135.3, 130.5, 129.4, 128.6, 125.1, 124.5, 122.1, 115.0, 110.3, 107.5, 75.2, 57.1, 32.3, 31.0, 19.3, 14.0 ppm. *m/z* (LSIMS) 1663 [M+2H]; Found C, 67.84; H, 5.34; N, 3.16% $C_{104}H_{100}O_{16}N_4$ 1.75 $CHCl_3$ requires C, 67.89; H, 5.48; N, 2.99%.

5,11,17,23-Tetrakis[(E)-2-(3-cyclohexyliminophenoxy)ethenyl]- 25,26,27,28-tetrabutoxycalix[4]arene (**22**): M.p. 97–101 °C. IR (Nujol)/cm^{-1}: 1732 (C=O), 1640 (C=N), 1634 (C=C); ^{1}H NMR (270 MHz; $CDCl_3$, 25 °C): δ = 8.02 (s, 4 H, CH=N), 7.52 (d, $^3J_{H,H}$ = 15.4 Hz, 4 H, Ar-CH=), 7.49 (d, $^3J_{H,H}$ = 7.7 Hz, 4 H, ArH), 7.38 (s, 4 H, ArH), 7.21–7.19 (m, 4 H, ArH), 7.12–7.11 (m, 4 H, ArH), 6.85 (s, 8 H,

ArH), 6.25 (d, $^{3}J_{H,H}$ = 15.4 Hz, 4 H, CH–C=O), 4.42 (d, $^{2}J_{H,H}$ = 13.5 Hz, 4 H, CH_AH_BAr), 3.91 (t, $^{3}J_{H,H}$ = 7.2 Hz, 8 H, OCH_2CH_2), 3.52–3.50 (m, 4 H, CHN=CH), 3.21 (d, $^{2}J_{H,H}$ = 13.5 Hz, 4 H, CH_AH_BAr), 1.90–1.85 (m, 8 H, CH_2CH_2O), 1.82–1.72 (m, 16 H, $(CH)_2CHN$), 1.61–1.59 (16H, m, $(CH_2)_2CH_2$), 1.27–1.24 (8H, m, $(CH_2)_2CH_2$), 1.50–1.35 (m, 8 H, $OCH_2CH_2CH_2$), 1.00 (t, $^{3}J_{H,H}$ = 8.3 Hz, 12 H, CH_3CH_2) ppm. ^{13}C NMR (270 MHz; $CDCl_3$, 25 °C): δ = 164.5, 158.1, 156.7, 150.1, 145.6, 137.0, 134.4, 128.3, 127.6, 124.5, 123.9, 122.9, 120.7, 114.1 74.3, 68.8, 33.3, 31.2, 30.0, 24.6, 23.7, 18.3, 14.3 ppm. *m/z* (LSIMS) 1671 [M+2H]; Found C, 68.70; H, 7.36; N, 3.16% $C_{108}H_{124}O_{12}N_4 \cdot 2CHCl_3$ requires C, 69.21; H, 6.65; N, 2.94%.

General experimental for DCL experiments

To a solution of 7.7mmol of **5** in $CDCl_3$ (2.0mL) was added 30.1mmol of each of the amines **5a**, **5c**, **5e** and **5g**. After 64h at room temperature in the absence of stirring, the distribution of imine products was determined via LSIMS-MS (see general experimental for equipment details).

To determine a shift in imine product distribution in the presence of a guest the above equilibration was repeated and after 64h 7.7mmol of either **23** or **24** was added and the system allowed to equilibrate for a further 48h at room temperature in the absence of stirring. The distribution of imine products was then determined via LSIMS-MS.

LSIMS-MS data are available in supporting information.

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