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Synthesis of amine, halide, and pyridinium terminated 2-alkyl-*p*-*tert*-butylcalix[4]arenes

Matthew P. Hertel [a], Andrew C. Behrle [a], Samantha A. Williams [b], Joseph A.R. Schmidt [a,*], Jordan L. Fantini [b,*]

[a] *Department of Chemistry, The University of Toledo, 2801 W. Bancroft St., MS 602, Toledo, OH 43606-3390, USA*
[b] *Department of Chemistry and Biochemistry, Ebaugh Laboratories, Denison University, Granville, OH 43023, USA*

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ABSTRACT

The synthesis of calix[4]arenes with functional groups tethered to a single methylene bridge has been explored. Mono-lithiated calix[4]arenes react with 1,ω-bromochloroalkanes to give 2-(ω-chloroalkyl)-calix[4]arenes, which function as key intermediates in the synthesis of a variety of tether-functionalized calix[4]arenes. Subsequent reactivity of these chloroalkyl species has allowed for successful synthesis of 2-(ω-iodoalkyl)-calix[4]arenes, 2-(ω-pyridiniumalkyl)-calix[4]arenes, and 2-(ω-aminoalkyl)-calix[4]arenes. This latter group of amine-terminated calix[4]arenes are especially significant as they may serve as useful entries to a wide range of subsequent chemistry, including metal coordination or attachment to a solid support. Both alkyl and aryl amines have been incorporated at the end of the tether, and a 2,6-diisopropylaniline derivative has been analyzed by X-ray diffraction.

1. Introduction

Calixarenes are a class of macrocyclic compounds in which a series of phenolic groups are linked to one another through methylene units at their 2- and 6-positions. Calixarenes provide an attractive scaffold for the construction of sophisticated, functional molecular assemblies because this class of molecules exhibits rigidity and well-defined conformations along with ample sites for modification and elaboration.[1–3] The cyclic nature of these compounds provides a natural cavity that can be exploited directly or used in tandem with further functional groups appended to the core structure in such applications as molecular recognition.[4] Further, the phenolic oxygen moieties can be utilized as ligands for the sequestration of metal centers within or directly below these cyclic cavities.[5,6] Through careful design, many calixarene systems have been successfully used in a wide range of applications, including use in sensors, catalysis, and separations; several reviews and books serve to summarize the work in this field.[7–13] Calix[4]arenes exhibit four idealized structural conformations (cone, partial cone, 1,2-alternate, and 1,3-alternate; Fig. 1) and in many cases the calix[4]arene can be forced to adopt a selected conformation through proper choice of substituents.[1] For calix[4]arenes with methyl or sterically smaller groups attached to the phenolic oxygen atoms, the different conformations rapidly equilibrate at ambient temperature due to the ability of the aryl rings to flip via passage of the phenolic group through the center of the macrocycle.[14] Calix[4]arenes with ethyl substituents attached to the phenolic oxygen atoms favor the partial cone conformation upon synthesis at room temperature, but exhibit fluxional behavior at temperatures as low as 50 °C.[14–16] Sterically larger substituent groups exist in a locked conformation, preventing interconversion in solution.[14–16] The equilibrium interconversion of conformers results in fluxional NMR spectra that are often very challenging to interpret. It has been shown that calix[4]arenes have a high affinity for the sodium cation, with preferential formation of 1:1 calix[4]arene/Na^+ complexes.[17] Thus, by collecting the NMR spectra of these species in solvent with a high concentration of NaI, the calix[4]arene is forced to adopt the cone conformation through coordination to sodium, producing simple and readily interpretable NMR spectra that are quite useful in characterizing reaction products.[18]

Considering the cone conformation of a typical calix[4]arene, the wide rim (further from the methylene bridges) has been designated the upper rim, while the narrow rim (nearer to the methylene bridges) is designated the lower rim (Fig. 2). In the cone conformation, the two protons of each methylene bridge are spatially arranged in axial and equatorial positions similar to that of a cyclohexane ring (Fig. 2).[19] Many methods are known for the modification of the calixarene at its upper and lower rims.[20–22] In contrast, there are very few reports of functionalization at the methylene bridge region (the

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* Corresponding authors. Fax: +1 419 530 4033 (J.A.R.S.).
E-mail addresses: joseph.schmidt@utoledo.edu (J.A.R. Schmidt), fantinij@denison.edu (J.L. Fantini).

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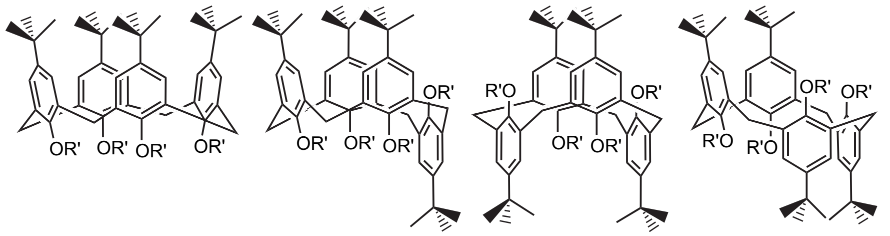


Figure 1. Calix[4]arenes have four primary conformations, related to each other by flipping of the aryl units.

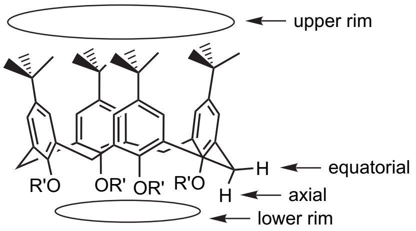


Figure 2. The wide rim of the calix[4]arene is designated the upper rim, while the narrow rim formed by the phenolic oxygens is called the lower rim. In the cone conformation, the methylene bridge protons reside in axial and equatorial positions.

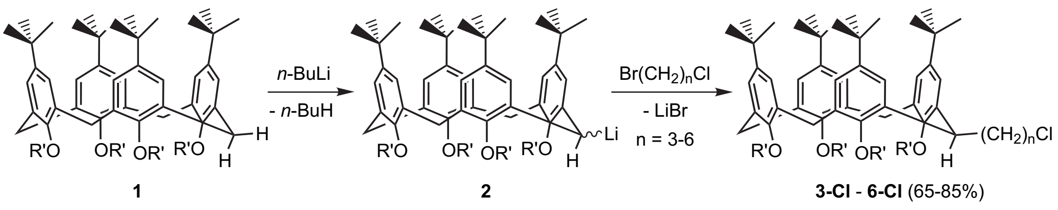
2-, 8-, 14-, and 20-positions) of the calix[4]arene. Reports in the mid-1990s of methylene bridge functionalized calixarenes were of those created by fragment condensation, either condensation of two 2-ring units, or bridging of a 3-ring unit by a fourth ring.[19,23–27] In later studies, substituents were added by direct reaction of the fully formed calixarene, employing methods such as anionic *ortho* Fries reaction[28] or oxidation of the calixarene to a spirodienone intermediate.[29–33] Calixarenes with substituents at all four methylene bridges have been achieved by radical bromination, followed by substitution reactions,[34–36] or nucleophilic attack on a ketocalix[4]arene.[37] Recently, early metal complexes of calix[4]arenes have been shown to oxidatively add to the C–H bond of the methylene bridge *intra*molecularly, producing 2-metalated calixarene complexes and subsequent reaction products.[38,39] Modifications at the methylene bridge present a significant opportunity to expand the range of structural motifs available in calixarene chemistry. While substituents on the upper and lower rims of calixarenes in the cone conformation are generally oriented parallel to its central axis, substituents attached to the methylene bridge are likely to favor the equatorial position and thus extend nearly perpendicular to the axis passing through the calixarene cavity (Fig. 2).[19,40]

Previous work in the Fantini[41] group described a new method for the production of calix[4]arenes functionalized at a single methylene bridge position.[18] This was achieved by mono-lithiation of tetramethoxy-*p*-*tert*-butylcalix[4]arene (**1**), followed by reaction of this lithiated species with an electrophile. The initial report described the attachment of a methyl, ethyl, benzyl, or carboxy group to a single methylene bridge of the calix[4]arene.[18] The aim of the current work is to develop a synthesis for the installation of secondary amines at the end of an alkyl tether at the methylene bridge position. The incorporation of tethered amines would yield compounds retaining properties associated with calix[4]arenes, while the tethered amines allow for subsequent coordination to a metal center or covalent attachment to a solid support. Attachment to a surface or bead could be achieved in one step by amide bond formation upon reaction with a functionalized solid support.[42] Additionally, dehydrogenation of the secondary amine would provide a route to the related imine,[43] which could be further elaborated using the wide range of reaction chemistry associated with imines.[44–50] Herein, we report the attachment of halide (chloro and iodo), amine, and pyridinium moieties at the end of a single alkyl tether of three to six carbons in length attached to the methylene bridge position of tetramethoxy-*p*-*tert*-butylcalix[4]arene **1**.

2. Results and discussion

Utilizing the previously reported synthesis, treatment of tetramethoxy-*p*-*tert*-butylcalix[4]arene (**1**) with *n*-butyllithium gave the mono-lithiated product (**2**), in which a single methylene group was deprotonated (Scheme 1).[18] Due to quenching of the lithiated species in the presence of amines, installation of an alkyl-tethered amine at the 2-position required a two-step synthesis—addition of a linker unit followed by amination. Reaction of **2** with 6-bromohexanenitrile as a means to produce a tethered nitrile was unsuccessful due to proton abstraction from this reagent and concomitant quenching to give the unsubstituted calix[4]arene **1**. An alternate strategy for the formation of an amino tether involved the use of an α,ω-dihaloalkane, such as 1,4-dibromobutane. Unfortunately, the use of symmetrically substituted alkanes of this sort led to complicated mixtures of products under a wide range of conditions. After quenching with water, the resulting mixture contained unreacted calix[4]arene (**1**), the desired 2-(ω-bromoalkyl)-calix[4]arene, and a bis-calix[4]arene species spanned by the alkyl group, which had been substituted on both ends. Separation of these three products was generally challenging and isolated product yields were unacceptably low for further applications.

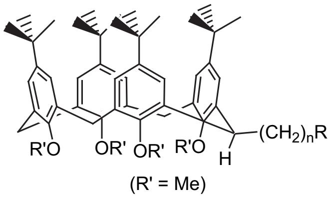
Successful synthesis of 2-(ω-haloalkyl)-calix[4]arenes was achieved by reaction of the lithiated species **2** with 1 equiv of a 1-bromo-ω-chloroalkane of 3–6 methylene units in length. The lithiated calix[4]arene reacted preferentially at the brominated end of the alkyl tether to produce the 2-(ω-chloroalkyl)-calix[4]arenes



Scheme 1. Lithiation of the calix[4]arene **1**, followed by reaction with a 1-bromo-ω-chloroalkane gives 2-(ω-chloroalkyl)-calix[4]arenes ***n*-Cl** (n=3–6, where the number indicates the length of the alkyl tether; R'=Me).

with nearly quantitative conversion (**3-Cl** to **6-Cl**, where 3–6 refers to number of methylene units in the alkyl tether; Scheme 1). The products were then isolated by recrystallization from pentane at −25 °C (Table 1). Alternatively, a traditional organic workup utilizing extraction into methylene chloride, washing with brine, and crystallization from methanol also yielded pure product as a slightly sticky microcrystalline material. As noted above, calix[4]arenes with methoxy groups at the lower rim have been shown to be quite fluxional in solution, with four different conformations accessible (Fig. 1).[14] Likewise, solutions of compounds **3-Cl** to **6-Cl** exhibited significant fluxionality by ^{1}H NMR spectroscopy. To eliminate this fluxionality, the NMR spectra were collected in solvent that had been presaturated with NaI.[18] The interaction of the calix[4]arene with the sodium cation in solution forced these species to adopt the full cone conformation,[18] and the NMR spectra of **3-Cl** to **6-Cl** were successfully obtained in CD_3CN saturated with NaI.

Table 1
Summary of new compounds

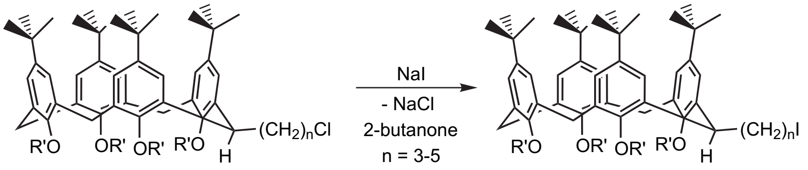


Compound	Tether length (n)	R	Isolated yield (%)
3-Cl	3	Cl	68
4-Cl	4	Cl	79
5-Cl	5	Cl	85
6-Cl	6	Cl	83
3-I	3	I	67
4-I	4	I	37
5-I	5	I	50
[3-py]Cl	3	$NC_5H_5^+$	97
[4-py]Cl	4	$NC_5H_5^+$	98
[5-py]Cl	5	$NC_5H_5^+$	97
3-NCy	3	NHC_6H_{11}	44
5-NCy	5	NHC_6H_{11}	49
5-N^{i}Pr	5	$NHCHMe_2$	31
3-N^{iPr}	3	NH-2,6-^{i}Pr$_2$C$_6$H$_3$	82
4-N^{H}	4	NHPh	82
4-N^{Me}	4	NH-2,6-Me$_2$C$_6$H$_3$	68
4-N^{Et}	4	NH-2,6-Et$_2$C$_6$H$_3$	89
4-N^{iPr}	4	NH-2,6-^{i}Pr$_2$C$_6$H$_3$	86
5-N^{H}	5	NHPh	60
5-N^{Me}	5	NH-2,6-Me$_2$C$_6$H$_3$	86
5-N^{Et}	5	NH-2,6-Et$_2$C$_6$H$_3$	74
5-N^{iPr}	5	NH-2,6-^{i}Pr$_2$C$_6$H$_3$	90
6-N^{Me}	6	NH-2,6-Me$_2$C$_6$H$_3$	89
6-N^{Et}	6	NH-2,6-Et$_2$C$_6$H$_3$	82
6-N^{iPr}	6	NH-2,6-^{i}Pr$_2$C$_6$H$_3$	86
3-N^{Cl}	3	NH-2,5-Cl$_2$C$_6$H$_3$	60
4-N^{Cl}	4	NH-2,5-Cl$_2$C$_6$H$_3$	60
5-N^{Cl}	5	NH-2,5-Cl$_2$C$_6$H$_3$	73

The NMR spectra of **3-Cl** to **6-Cl** have some common notable features. First, the spectra reveal that only a single coordinated species is present in solution. In the full cone conformation, the two positions on the methylene bridges of the calix[4]arene can be considered as axial and equatorial, with the axial position pointed toward the lower rim and the equatorial position extending into the solvent. The two protons have been well characterized with the low-field resonances indicative of the axial position and the higher field resonances diagnostic of the equatorial position.[19] Examination of the spectra for **3-Cl** to **6-Cl** reveals that the tertiary proton at the functionalized methylene group is located exclusively in the axial position for each compound, indicating that the tether is extending away from the calix[4]arene in the equatorial position, as expected based on energetic considerations.[19] Additionally, the NMR spectra show approximate mirror symmetry in solution, although for the longer tethers the methoxy groups are inequivalent in the ^{13}C NMR spectra. This is most likely due to slight deviations from a true mirror plane at the sodium coordination center. The remaining resonances are all found at typical chemical shifts. When each bulk synthetic product (**3-Cl** to **6-Cl**) was recrystallized from pentane, elemental analysis (C,H,N) percentages consistent with cocrystallized lithium bromide (the reaction byproduct) were observed. In almost every case, 4/3 equiv of LiBr was calculated to be present in the microcrystalline material. Given that the preferred coordination number for lithium is four and each calix[4]arene has four accessible oxygen donor atoms, we hypothesize that each lithium is coordinated by one bromide anion and three calix[4]arene oxygen atoms, requiring 4/3 equiv of salt to utilize all donor atoms. Thus far, we have been unable to successfully isolate X-ray quality single crystals to confirm this assertion.

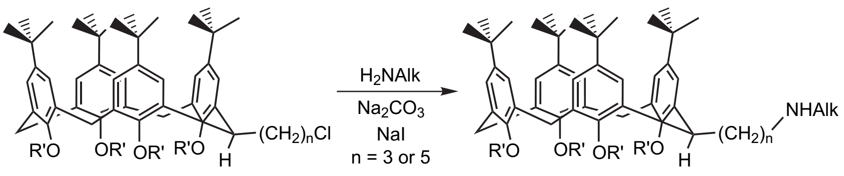
The 2-(ω-chloroalkyl)-calix[4]arenes were converted to 2-(ω-iodoalkyl)-calix[4]arenes by utilization of the Finkelstein reaction.[51] This reaction was accomplished by treating **3-Cl** to **5-Cl** with NaI in refluxing 2-butanone. After approximately 6 days, the reaction was complete and the 2-(ω-iodoalkyl)-calix[4]arenes (**3-I** to **5-I**) were isolated in moderate yield by recrystallization from methanol (Scheme 2; Table 1). These compounds were readily identified by ^{13}C NMR spectroscopy, with the diagnostic resonance for the methylene group at the end of the tether (attached to the iodine) appearing at 6.5 ppm in all cases. The NMR spectroscopic data for these compounds in the presence of NaI again showed a cone conformation with the iodo tether located in an equatorial position. Mass spectroscopy further confirmed the synthesis of these compounds with the observation of $[M+Na]^+$ ions in all cases (electrospray ionization from a methanol solution with NaI as an internal standard).

The chlorotethers (**3-Cl** to **6-Cl**) were investigated as precursors to amine-tethered calix[4]arene species. Initial investigations utilized a variety of standard organic (S_N2-type) synthetic methodologies with a wide range of bases, such as hydroxide, carbonate, and phosphate, etc. It was found that sodium carbonate was most effective for these reactions, although the overall conversion was quite modest and the resulting compounds proved to be rather difficult to isolate effectively due to their high solubility in most organic solvents and their oily nature. Although we successfully isolated three alkylamine-tethered calix[4]arene products (Scheme 3; Table 1), we ultimately shifted our focus to aryl amines, which proved to be much more readily isolated. Specifically, we made two calix[4]arenes tethered to cyclohexylamine (**3-NCy** and **5-NCy**; tether lengths of 3 and 5 methylene units) and a calix[4]arene



3-Cl - 5-Cl **3-Cl - 5-I** (35-70%)

Scheme 2. The Finkelstein reaction was utilized to produce 2-(ω-iodoalkyl)-calix[4]arenes (**3-I** to **5-I**; the number indicates the length of the alkyl tether; R′=Me).



3-Cl or **5-Cl** → **3-NCy**, **5-NCy**, or **5-N^{i}Pr** (30-50%)

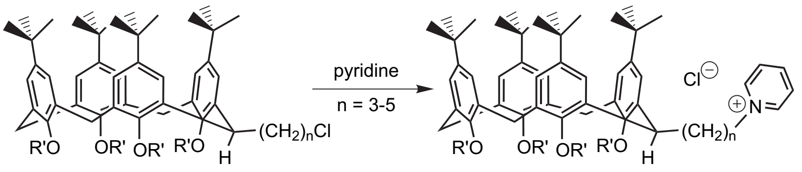
Scheme 3. Functionalization of the alkyl tether with an alkylamine resulted in moderate isolated yields for a limited number of substrates (the number indicates the length of the alkyl tether; R′=Me; Alk=Cy or ^{i}Pr).

tethered to isopropylamine through a 5-carbon tether (**5-N^{i}Pr**). For each of these alkylamine-functionalized compounds, the calix[4]-arene bridgehead proton was found near 4.6–4.7 ppm, indicative of its axial orientation. Thus, the amino-terminated alkyl tether was located in the equatorial position, as with the precursor chloride compounds. The most notable resonances in the NMR spectra of these compounds were the ^{13}C peaks attributed to the carbon atoms adjacent to the amino nitrogen atom. For the two cyclohexyl derivatives, the cyclohexyl methine carbon was found near 57 ppm and the methylene carbon at the terminus of the linker group resonated at nearly 44 ppm. For the isopropylamine derivative, these two carbon atoms were at 50.6 and 44.3 ppm, respectively. Although the carbon at the end of the tether was only slightly shifted, the appearance of the new low-field peak was diagnostic for formation of these alkylamine-functionalized compounds. As with the other compounds included herein, high-resolution mass spectra also confirmed the formation of these compounds.

Although various substituted aniline derivatives could be produced using the amination methodology described above, these compounds were obtained in very low yields, even under the optimized conditions. In an effort to utilize pyridine as base for this reaction, we found that the amine-terminated tether was not produced, but rather the pyridinium functionalized calix[4]arene was formed instead. Thus, **3-Cl** to **5-Cl** were treated with neat pyridine at reflux to convert these species to the pyridinium salts **[3-py]Cl** to **[5-py]Cl** in excellent yields (97–98%; Scheme 4; Table 1). These species were fully characterized and showed spectroscopic features somewhat similar to **3-Cl** to **5-Cl** (in NaI-saturated CD_3CN). The compounds again showed approximate mirror symmetry. The pyridinium resonances were observed in the usual region (^{1}H: 8.0–9.2 ppm). The most significant difference in the ^{1}H NMR spectra of these compounds was the appearance of a resonance at ~4.7–4.9 ppm, which integrated as two protons and was assigned to the methylene unit at the end of the alkyl tether (directly attached to the pyridinium nitrogen atom). This was accompanied by a disappearance of the peak at ~3.4–3.6 ppm, which had previously been observed for the $–CH_2Cl$ protons at the end of the alkyl chain. In the ^{13}C NMR spectrum, the terminal methylene group, which had resonated near 45 ppm in the chlorotethered precursors shifted upfield upon formation of the pyridinium salts, and was found in the midst of the other alkyl carbon resonances. These compounds were further identified by high-resolution electrospray mass spectra, where $[M-Cl]^{+}$ peaks were observed in all three cases.

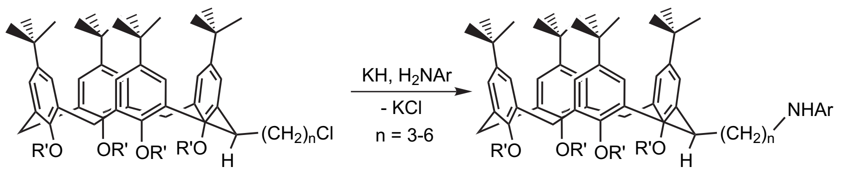
Overall, we found that installation of aniline derivatives as secondary amines at the tether's end in 2-functionalized calix[4]-arenes required relatively forcing conditions. A more practical synthesis of this class of compounds was accomplished by reaction of aniline or a 2,6-dialkylaniline (H_2N-2,6-$R_2C_6H_3$; R=Me, Et, ^{i}Pr) with KH in THF. The potassium salt of the aniline derivative was then treated immediately with **3-Cl** to **6-Cl**. This reaction was observed as a slow progression of color changes from yellow, to orange, to red, to eventually a dark brown color. Upon completion, the product was quenched with water to destroy any residual hydride and protonate any product deprotonated by excess KH in the reaction. An organic workup was used to remove the leftover salts from the product 2-(ω-anilinoalkyl)-calix[4]arenes (**3-N^{R}** to **6-N^{R}**; R represents the 2,6-substituents of the aniline; Scheme 5). Residual excess aniline was removed from the product by vacuum distillation to yield the products as glassy solids upon cooling (Table 1). Again, the use of NaI-saturated NMR solvent revealed spectra with approximate mirror symmetry. The signal at ~3.4–3.6 ppm assigned to the $–CH_2Cl$ protons at the end of the tether in **3-Cl** to **6-Cl** was no longer present. This methylene group was now observed at higher field as an apparent quartet (due to coupling to a methylene group and the N–*H* proton), although it overlapped with resonances from other methylene units in the alkyl chain in several cases. The most diagnostic peak in each NMR spectrum was the N–*H* proton, which was nearly always observed as a triplet, coupling to the terminal methylene unit with $^{3}J_{HH}$=7–8 Hz. ^{1}H NMR resonances readily attributed to the aryl group from the aniline moieties were also identified in the isolated products (**3-N^{R}** to **6-N^{R}**). Consistent with **3-Cl** to **6-Cl** and **[3-py]Cl** to **[5-py]Cl**, the calix[4]arene methylene proton at the bridgehead of the tether was located at low-field, indicative of its axial orientation and equatorially oriented amine-terminated alkyl tether. Further confirmation of aniline installation was achieved by high-resolution mass spectra, in which the $[M+H]^{+}$ peak was observed in all cases.

To further characterize the amine-tethered 2-functionalized calix[4]arene species, we grew X-ray quality crystals of compound **4-N^{iPr}**. This species crystallized from acetonitrile at −25 °C as colorless rods (Fig. 3). As expected, the amino tether is located in an equatorial position and 1 equiv of acetonitrile resides within the calix[4]arene cavity. Additionally, **4-N^{iPr}** was found to crystallize in the cone conformation exclusively. The metrical parameters within the molecule are all consistent with previous reports,[19,28] and there are no extraordinary intermolecular interactions beyond the usual crystal packing forces. The overall structure compares well with the



3-Cl - **5-Cl** → **[3-py]Cl** - **[5-py]Cl** (>95%)

Scheme 4. Reaction of the 2-(ω-chloroalkyl)-calix[4]arenes with pyridine yields pyridinium-tethered calix[4]arenes (**[3-py]Cl** to **[5-py]Cl**; the number indicates the length of the alkyl tether; R′=Me).



3-Cl - **6-Cl**

3-N^R - **6-N^R** (60-90%)

Scheme 5. Reaction with potassium anilide derivatives results in installation of secondary aryl amines at the tether's end (R=H: Ar=C_6H_5; R=Me: Ar=2,6-$Me_2C_6H_3$; R=Et: Ar=2,6-$Et_2C_6H_3$; R=^{i}Pr: Ar=2,6-$^iPr_2C_6H_3$; R=Cl: Ar=2,5-$Cl_2C_6H_3$; the number indicates the length of the alkyl tether; R′=Me).

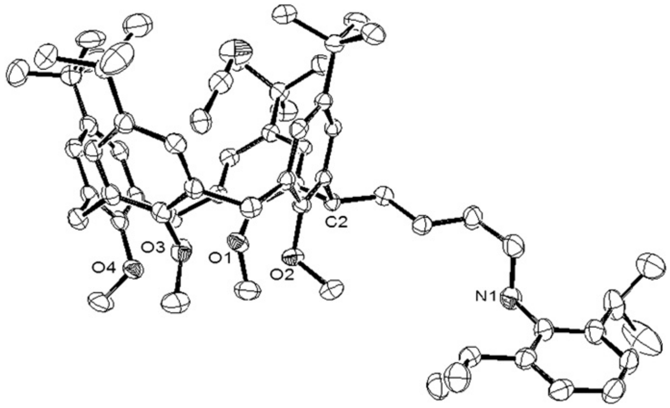


Figure 3. ORTEP diagram (50% thermal ellipsoids) of **4-N^{iPr}**. Hydrogen atoms, disordered *tert*-butyl group, and 1 equiv of acetonitrile are omitted for clarity. Note the acetonitrile solvate present within the calixarene cone.

other crystallographically characterized calix[4]arenes in which a single methylene bridge has been functionalized with an organic group, all of which are also found to crystallize in the cone conformation with an equatorial substituent.[19,28] Substitution of two or more of the methylene bridges can sometimes perturb the conformational preference away from the cone confirmation with large groups opposite to each other,[30,52] while tetrasubstitution proves even more complicated.[36,37]

Finally, we investigated electron-poor aniline derivatives as amine functional groups at the end of the alkyl tethers. Having had some success with reasonably electron-rich alkyl amines and excellent results with the less basic anilines, the use of chloro-substituted anilines was explored as a means to further diversify the amine-tethered calix[4]arenes. Using the reaction conditions described for the anilines above, 2,5-dichloroaniline was attached at the end of the 3–5 methylene unit tethers. These reactions proceeded readily to produce the analogous 2,5-dichloroaniline functionalized species (**3-N^{Cl}** to **5-N^{Cl}**; Scheme 5; Table 1). Interestingly, in this case after the progression of colors during the reaction period, the solution was observed as a vibrant purple color prior to quenching with water. Spectroscopic characterization of the products again showed approximate mirror symmetry for these species in NaI-saturated solution, with the alkyl tether oriented in the equatorial position. The most remarkable change from the aniline derivatives for these compounds involved the chemical shifts observed for the protons of the 2,5-dichlorophenyl groups. These were easily identified in the ^{1}H NMR spectrum in the 6.5–7.2 ppm region with a characteristic coupling pattern representative of protons at the 3-, 4-, and 6-positions of the aryl ring. Additionally, the effects of the electron withdrawing chlorides were evident in the ^{1}H NMR chemical shift observed for the amine protons. The N–*H* resonances appeared more than 1 ppm downfield from the chemical shifts observed for the 2,6-dialkylaniline derivatives. Full spectroscopic characterization and high-resolution mass spectrometry confirmed the formation of **3-N^{Cl}** to **5-N^{Cl}**, completing our series of secondary amine-tethered calix[4]arenes.

3. Conclusion

Herein, we have shown that mono-lithiated calix[4]arene **2** is a useful platform for the attachment of alkyl-tethered functional groups at a single methylene bridge. The chemoselectivity in the reaction of these lithiated species with 1,ω-bromochloroalkanes allows for the clean production of 2-(ω-chloroalkyl)-calix[4]arenes with tether lengths of 3–6 methylene units. These chlorotethered calix[4]arenes can then be further elaborated to produce 2-(ω-iodoalkyl)-calix[4]arenes, 2-(ω-pyridiniumalkyl)-calix[4]arenes, and 2-(ω-aminoalkyl)-calix[4]arenes. The use of both alkyl and aryl amine-functionalized tethers provides a means to potentially metalate these functionalized calix[4]arenes or link them to a solid support without compromising the overall calix[4]arene structure. Efforts to utilize these 2-functionalized calix[4]arenes for advanced applications remain an ongoing area of pursuit in the Fantini and Schmidt laboratories.

4. Experimental section

4.1. General

Compounds **3-I** to **5-I**, **[3-py]Cl** to **[5-py]Cl**, **3-NCy**, **5-NCy**, and **5-N^{i}Pr** were synthesized under ambient atmosphere. Compounds **3-Cl** to **6-Cl** and **3-N^R** to **6-N^R** were synthesized using standard Schlenk and dry box techniques. The following materials were purchased from commercial suppliers and used as received: 1-bromo-3-chloropropane, 1-bromo-4-chlorobutane, 1-bromo-5-chloropentane, 1-bromo-6-chlorohexane, 2-butanone, *n*-butyllithium (1.6 M in hexanes), cyclohexylamine, 2,5-dichloroaniline, dichloromethane, diethylether, isopropylamine, methanol, pentane, potassium hydride, pyridine, sodium carbonate, and sodium iodide. Tetrahydrofuran was purchased from Fisher or VWR and purified by distillation from a purple Na/benzophenone ketyl solution. Aniline, 2,6-dimethylaniline, 2,6-diethylaniline, and 2,6-diisopropylaniline were dried over calcium hydride, freeze–pump–thawed three times, distilled under reduced pressure, and stored in the dark. CD_3CN and $CDCl_3$ were purchased from Cambridge Isotope Laboratories or Acros Organics and used as received. ^{1}H and ^{13}C NMR data were obtained on a 400 MHz Avance or a 600 MHz Inova NMR spectrometer at ambient temperature. Unless otherwise specified, NMR spectra were collected on the 600 MHz Inova spectrometer using CD_3CN that had been presaturated with NaI as solvent. Unless specifically noted, the reported coupling constants are given for $^3J_{HH}$ coupling. The NMR spectra of some compounds were taken in a 3:1 $CDCl_3/CD_3CN$ solution containing NaI (1 g per 80 mL solution) as noted in the individual procedures. ^{1}H NMR shifts are given relative to CD_2HCN (1.96 ppm) or $SiMe_4$ (0.00 ppm) and ^{13}C NMR shifts are given relative to CD_3CN (1.32 ppm) or $CDCl_3$ (77.0 ppm). For IR, liquid samples were taken neat on a Perkin–Elmer XTL FTIR spectrophotometer, while solid samples were prepared by dissolving in CH_2Cl_2, applying a drop to a KBr plate, and allowing the solvent to evaporate. Infrared spectra of some solids were recorded with a Bruker Vector 22 using a Pike Technologies horizontal ATR attachment. High-resolution time-of-flight or quadrupole mass spectra were obtained using electrospray ionization by the Mass Spectrometry Laboratory at the University of Illinois, Urbana, IL or the Campus Chemical Instrument Center—Mass Spectrometry & Proteomics Facility at The Ohio State University, Columbus, OH. Electrospray samples were prepared by dissolving in methanol, and in some cases, a NaI internal standard was used. Elemental analyses were determined by Columbia Analytical Services, Tucson, AZ. The X-ray structure determination was performed at the Ohio Crystallographic Consortium housed at The University of Toledo. Tetrahydroxy-*p-tert*-butylcalix[4]arene[53] and tetramethoxy-*p-tert*-butylcalix[4]arene (**1**)[54] were prepared as previously reported.

4.2. General procedure for the synthesis of 2-(ω-chloroalkyl)-tetramethoxy-*p-tert*-butylcalix[4]arenes (3-Cl to 6-Cl)

To a solution of **1** (1–3 g) in THF (50 mL) was added 1.15 equiv *n*-BuLi (1.53 M in hexanes) via syringe over 5 min at ambient temperature. The solution turned from a clear yellow prior to the addition of *n*-BuLi to blood red by the end of the addition. To this solution was added 1.15 equiv 1-bromo-ω-chloroalkane via syringe at ambient temperature. This solution was allowed to stir for 12 h. Once a yellow solution was observed, a few drops of water were added to quench any unreacted *n*-BuLi. The solution was filtered and all volatiles were removed in vacuo. Workup method A: the colorless solid was crystallized from a mixture of pentane and diethylether. A halide test with silver nitrate confirmed the presence of halides in all cases. Elemental analysis indicated the presence of stoichiometric amounts of LiBr in the crystalline materials. Workup method B: the colorless solids were redissolved in CH_2Cl_2 and washed with brine. After removal of solvent under vacuum, recrystallization from methanol gave a semi-crystalline white powder, which was found to be salt-free.

*4.2.1. 2-(3-Chloropropyl)tetramethoxy-p-tert-butylcalix[4]arene (**3-Cl**).* Reagents: **1** (2.58 g, 3.66 mmol); *n*-BuLi (1.53 M in hexanes, 2.80 mL, 4.28 mmol); 1-bromo-3-chloropropane (0.669 g, 0.420 mL, 4.28 mmol). Yield: 2.15 g (67.6%); ^{1}H NMR: δ 7.24 (m, 6H), 7.20 (d, 2H, $^4J_{HH}$=2 Hz), 4.59 (t, 1H, 8 Hz), 4.17 (d, 3H, $^2J_{HH}$=12 Hz), 4.04 (s, 6H), 4.03 (s, 6H), 3.59 (t, 2H, 6 Hz), 3.45 (m, 3H), 2.24 (m, 2H), 1.73 (m, 2H), 1.12 (m, 36H); ^{13}C{^{1}H} NMR: δ 151.1, 149.6, 149.5, 138.3, 135.5, 135.4, 135.3, 126.9, 126.2, 122.6, 65.1, 64.7, 45.5, 35.8, 34.6, 34.4, 31.9, 30.8, 30.7, 30.6, 30.1; IR (cm^{-1}): 3332 (m), 3251 (m), 2960 (s), 2904 (s), 2862 (m), 1651 (w), 1600 (w), 1582 (w), 1483 (m), 1462 (m), 1436 (m), 1393 (w), 1362 (m), 1300 (w), 1284 (w), 1244 (w), 1203 (m), 1176 (w), 1118 (m), 1000 (m), 971 (w), 947 (w), 806 (w), 736 (w), 701 (w), 646 (w). Elemental analysis calculated for $C_{51}H_{69}O_4Cl\cdot LiBr$: C, 70.54; H, 8.01. Found: C, 70.42; H, 7.99.

*4.2.2. 2-(4-Chlorobutyl)tetramethoxy-p-tert-butylcalix[4]arene (**4-Cl**).* Reagents: **1** (3.00 g, 4.26 mmol); *n*-BuLi (1.53 M in hexanes, 3.10 mL, 4.74 mmol); 1-bromo-4-chlorobutane (0.818 g, 0.550 mL, 4.78 mmol). Yield: 3.06 g (78.8%); ^{1}H NMR: δ 7.29–7.26 (m, 8H), 4.62 (t, 1H, 8 Hz), 4.22 (d, 3H, $^2J_{HH}$=12 Hz), 4.09 (s, 6H), 4.08 (s, 6H), 3.59 (t, 2H, 7 Hz), 3.50–3.46 (m, 3H), 2.17 (m, 2H), 1.84 (pent, 2H, 8 Hz), 1.46 (m, 2H), 1.18 (s, 36H); ^{13}C{^{1}H} NMR: δ 151.2, 149.1, 149.0, 138.5, 135.23, 135.21, 135.1, 126.6, 126.3, 122.9, 65.1, 64.9, 45.4, 36.0, 34.8, 34.6, 33.1, 32.8, 31.2, 31.1, 30.0, 26.3; IR (cm^{-1}): 3847 (w), 3743 (m), 3608 (w), 3338 (s), 3255 (s), 3047 (w), 2944 (s), 2871 (w), 2363 (m), 2238 (w), 1967 (w), 1740 (w), 1652 (m), 1600 (w), 1481 (s), 1362 (m), 1299 (m), 1268 (s), 1200 (s), 1119 (m), 996 (s), 948 (w), 873 (w), 805 (w), 740 (s), 702 (w). Elemental analysis calculated for $C_{52}H_{71}O_4Cl\cdot 4/3LiBr$: C, 68.53; H, 7.85. Found: C, 68.67; H, 7.91.

*4.2.3. 2-(5-Chloropentyl)tetramethoxy-p-tert-butylcalix[4]arene (**5-Cl**).* Reagents: **1** (3.01 g, 4.27 mmol); *n*-BuLi (1.53 M in hexanes, 3.10 mL, 4.74 mmol); 1-bromo-5-chloropentane (0.873 g, 0.620 mL, 4.71 mmol). Yield: 3.34 g (84.6%); ^{1}H NMR: δ 7.24 (s, 4H), 7.22 (d, 2H, $^4J_{HH}$=2 Hz), 7.18 (d, 2H, $^4J_{HH}$=2 Hz), 4.56 (t, 1H, 8 Hz), 4.17 (d, 3H, $^2J_{HH}$=12 Hz), 4.04 (s, 6H), 4.02 (s, 6H), 3.48 (t, 2H, 7 Hz), 3.45 (d, 2H, $^2J_{HH}$=12 Hz), 3.44 (d, 1H, $^2J_{HH}$=12 Hz), 2.09 (q, 2H, 8 Hz), 1.70 (pent, 2H, 7 Hz), 1.46 (pent, 2H, 8 Hz), 1.29 (m, 2H), 1.12 (s, 36H); ^{13}C{^{1}H} NMR: δ 151.7, 149.6, 149.5, 139.1, 135.7, 135.6, 127.2, 127.1, 126.8, 126.7, 123.5, 123.3, 65.6, 65.5, 65.4, 65.3, 46.1, 36.5, 35.2, 35.1, 34.3, 33.0, 31.7, 31.6, 30.5, 30.4, 30.2, 27.7; IR (cm^{-1}): 3413 (w), 3036 (w), 2964 (s), 2874 (m), 2814 (m), 2036 (w), 1749 (w), 1600 (w), 1579 (w), 1481 (s), 1460 (m), 1427 (m), 1388 (w), 1358 (m), 1296 (w), 1281 (w), 1263 (m), 1242 (m), 1203 (m), 1170 (w), 1116 (m), 1021 (m), 946 (w), 872 (m), 806 (w), 797 (w), 737 (w), 704 (w). Elemental analysis calculated for $C_{53}H_{73}O_4Cl\cdot 4/3LiBr$: C, 68.79; H, 7.95. Found: C, 68.09; H, 7.98.

*4.2.4. 2-(6-Chlorohexyl)tetramethoxy-p-tert-butylcalix[4]arene (**6-Cl**).* Reagents: **1** (1.42 g, 2.02 mmol); *n*-BuLi (1.53 M in hexanes, 1.58 mL, 2.42 mmol); 1-bromo-6-chlorohexane (0.495 g, 0.370 mL, 2.48 mmol). Yield: 1.58 g (83.4%); ^{1}H NMR: δ 7.24 (s, 4H), 7.22 (d, 2H, $^4J_{HH}$=2 Hz), 7.19 (d, 2H, $^4J_{HH}$=2 Hz), 4.56 (t, 1H, 8 Hz), 4.17 (d, 3H, $^2J_{HH}$=12 Hz), 4.04 (s, 6H), 4.02 (s, 6H), 3.49 (t, 2H, 7 Hz), 3.45 (d, 2H, $^2J_{HH}$=12 Hz), 3.44 (d, 1H, $^2J_{HH}$=12 Hz), 2.08 (m, 2H), 1.66 (m, 2H), 1.36 (m, 4H), 1.27 (m, 2H), 1.12 (s, 36H); ^{13}C{^{1}H} NMR: δ 152.1, 149.9, 149.8, 139.5, 136.1, 136.0, 127.6, 127.4, 127.2, 127.1, 123.8, 123.7, 66.0, 65.9, 65.8, 65.7, 46.6, 36.9, 35.6, 35.5, 34.8, 33.5, 32.1, 30.9, 30.8, 30.7, 30.0, 29.8, 27.6; IR (cm^{-1}): 3331 (s), 3248 (s), 3048 (w), 2953 (s), 2863 (s), 1651 (m), 1602 (m), 1584 (m), 1482 (s), 1463 (m), 1438 (m), 1393 (w), 1362 (m), 1300 (w), 1263 (w), 1245 (w), 1205 (m), 1176 (m), 1118 (m), 1021 (w), 999 (m), 947 (w), 870 (w), 805 (w), 732 (w), 703 (w), 647 (w), 619 (w), 610 (w), 585 (w), 565 (w). HRMS calculated for: $C_{54}H_{76}O_4Cl$ $[M+H]^+$: 823.5432, found: 823.5399. Elemental analysis calculated for $C_{54}H_{75}O_4Cl\cdot 4/3LiBr$: C, 69.04; H, 8.05. Found: C, 69.60; H, 8.12.

4.3. General procedure for the synthesis of 2-(ω-iodoalkyl)-tetramethoxy-*p-tert*-butylcalix[4]arenes (3-I to 5-I)

To a mixture of **3-Cl** to **5-Cl** and finely powdered sodium iodide was added 2-butanone to afford a homogeneous solution. The reaction mixture was heated at reflux for 6 days with periodic monitoring by ^{1}H NMR spectroscopy on evaporated aliquots. After the reaction was judged to be complete, all volatiles were removed in vacuo, and the resulting solid was dissolved in dichloromethane and washed twice with saturated NaCl solution. The organic solution was dried over $MgSO_4$, filtered, and concentrated to dryness to yield a white solid. Recrystallization from methanol yielded white powders.

*4.3.1. 2-(3-Iodopropyl)tetramethoxy-p-tert-butylcalix[4]arene (**3-I**).* Reagents: **3-Cl** (0.391 g, 0.500 mmol); 2-butanone (10 mL); NaI (0.150 g, 1.00 mmol). Yield: 0.291 g (66.7%); ^{1}H NMR (CD_3CN/$CDCl_3$/NaI, 400 MHz): δ 7.29 (d, 2H, $^4J_{HH}$=2 Hz), 7.25 (s, 4H), 7.24 (d, 2H, $^4J_{HH}$=2 Hz), 4.72 (t, 1H, 8 Hz), 4.30 (d, 3H, $^2J_{HH}$=12 Hz), 4.18 (s, 6H), 4.17 (s, 6H), 3.49 (d, 2H, $^2J_{HH}$=12 Hz), 3.48 (d, 1H, $^2J_{HH}$=12 Hz), 3.32 (t, 2H, 7 Hz), 2.31 (m, 2H), 1.89 (m, 2H), 1.24 (s, 18H), 1.23 (s, 18H); ^{13}C{^{1}H} NMR (CD_3CN/$CDCl_3$/NaI, 100 MHz): δ 149.94, 149.93, 148.1, 148.0, 136.8, 133.90, 133.85, 125.35, 125.33, 125.2, 121.6, 64.2, 63.9, 33.9, 33.6, 33.5, 31.7, 30.23, 30.18, 29.1, 28.9, 6.5; IR (cm^{-1}): 2959 (m), 1479 (s), 1204 (m), 1023 (s), 869 (m), 796 (w). HRMS calculated for $C_{51}H_{69}O_4INa$ $[M+Na]^+$: 895.4138, found: 895.4122.

*4.3.2. 2-(4-Iodobutyl)tetramethoxy-p-tert-butylcalix[4]arene (**4-I**).* Reagents: **4-Cl** (3.356 g, 4.218 mmol); 2-butanone (25 mL); NaI (1.28 g, 8.54 mmol). Yield: 1.375 g (36.7%); ^{1}H NMR (CD_3CN/$CDCl_3$/NaI, 400 MHz): δ 7.24 (d, 2H, $^4J_{HH}$=2 Hz), 7.23 (s, 4H), 7.22 (d, 2H,

$^{4}J_{HH}$=2 Hz), 4.66 (t, 1H, 8 Hz), 4.28 (d, 3H, $^{2}J_{HH}$=12 Hz), 4.15 (s, 6H), 4.14 (s, 6H), 3.48 (d, 2H, $^{2}J_{HH}$=12 Hz), 3.46 (d, 1H, $^{2}J_{HH}$=12 Hz), 3.25 (t, 2H, 7 Hz), 2.17 (m, 2H), 1.92 (m, 2H), 1.47 (m, 2H), 1.21 (s, 18H), 1.20 (s, 18H); $^{13}C\{^{1}H\}$ NMR ($CD_3CN/CDCl_3$/NaI, 100 MHz): δ 150.1, 148.2, 148.1, 137.3, 134.1, 134.0, 125.5, 125.2, 121.8, 64.4, 64.2, 35.0, 33.8, 33.6, 32.6, 32.1, 30.5, 30.4, 29.3, 29.2, 29.0, 6.5; IR (cm^{-1}): 2954 (m), 1480 (s), 1204 (m), 1022 (s), 870 (m), 798 (w). HRMS calculated for $C_{52}H_{71}O_4INa$ $[M+Na]^+$: 909.4295, found: 909.4289.

*4.3.3. 2-(5-Iodopentyl)tetramethoxy-p-tert-butylcalix[4]arene (**5-I**).* Reagents: **5-Cl** (0.404 g, 0.499 mmol); 2-butanone (8 mL); NaI (0.150 g, 1.00 mmol). Yield: 0.224 g (49.8%); ^{1}H NMR ($CD_3CN/CDCl_3$/NaI, 400 MHz): δ 7.24 (m, 6H), 7.21 (d, 2H, $^{4}J_{HH}$=2 Hz), 4.64 (t, 1H, 8 Hz), 4.26 (d, 3H, $^{2}J_{HH}$=12 Hz), 4.14 (s, 6H), 4.12 (s, 6H), 3.48 (d, 2H, $^{2}J_{HH}$=12 Hz), 3.47 (d, 1H, $^{2}J_{HH}$=12 Hz), 3.20 (t, 2H, 7 Hz), 2.14 (m, 2H), 1.83 (m, 2H), 1.52 (m, 2H), 1.38 (m, 2H), 1.205 (s, 18H), 1.202 (s, 18H); $^{13}C\{^{1}H\}$ NMR ($CD_3CN/CDCl_3$/NaI, 100 MHz): δ 150.0, 148.0, 147.9, 137.3, 133.9, 133.7, 126.1, 125.3, 125.0, 121.6, 64.1, 63.9, 34.8, 33.6, 33.4, 32.9, 32.3, 30.24, 30.17, 29.7, 29.1, 28.9, 26.9, 6.5; IR (cm^{-1}): 2952 (m), 1480 (s), 1203 (m), 1021 (s), 870 (m), 796 (w). HRMS calculated for $C_{53}H_{73}O_4INa$ $[M+Na]^+$: 923.4451, found: 923.4430.

*4.3.4. 2-(3-Pyridiniumpropyl)tetramethoxy-p-tert-butylcalix[4]arene chloride **[3-py]Cl**.* A 50-mL round bottom flask equipped with a magnetic stir bar and a water-jacketed condenser was charged with **3-Cl·LiBr** (1.294 g, 1.490 mmol) and 40 mL pyridine. The faint yellow solution was heated to reflux for 12 h at which point the color had changed to a deep reddish-brown. All volatiles were removed in vacuo to produce a brown solid (1.249 g, 97.4%); ^{1}H NMR: δ 9.17 (d, 2H, 6 Hz), 8.56 (t, 1H, 6 Hz), 8.06 (t, 2H, 6 Hz), 7.26 (d, 2H, $^{4}J_{HH}$=2 Hz), 7.23 (s, 4H), 7.22 (d, 2H, $^{4}J_{HH}$=2 Hz), 4.88 (t, 2H, 7 Hz), 4.60 (t, 1H, 8 Hz), 4.16 (d, 1H, $^{2}J_{HH}$=12 Hz), 4.15 (d, 2H, $^{2}J_{HH}$=12 Hz), 4.03 (s, 6H), 4.02 (s, 6H), 3.44 (d, 3H, $^{2}J_{HH}$=12 Hz), 2.31 (m, 2H), 1.97 (m, 2H), 1.15 (s, 18H), 1.12 (s, 18H); $^{13}C\{^{1}H\}$ NMR: δ 150.2, 150.1, 149.9, 149.2, 148.2, 137.5, 137.4, 129.2, 128.6, 128.5, 127.7, 124.9, 124.8, 122.0, 117.6, 69.7, 67.5, 37.5, 33.6, 32.2, 32.0, 25.6, 24.0, 23.0; IR (cm^{-1}): 3396 (br s), 3050 (m), 2956 (s), 2869 (m), 2831 (w), 2818 (w), 2739 (w), 2710 (w), 1635 (m), 1603 (w), 1584 (w), 1482 (s), 1463 (m), 1436 (w), 1394 (w), 1362 (m), 1299 (w), 1264 (w), 1245 (w), 1205 (m), 1177 (m), 1126 (m), 1023 (w), 1000 (m), 944 (w), 890 (w), 871 (w), 807 (w), 773 (w), 735 (w), 684 (w), 645 (w). HRMS calculated for $C_{56}H_{74}NO_4$ $[M-Cl]^+$: 824.5618, found: 824.5598.

*4.3.5. 2-(4-Pyridiniumbutyl)tetramethoxy-p-tert-butylcalix[4]arene chloride **[4-py]Cl**.* A 50-mL round bottom flask equipped with a magnetic stir bar and a water-jacketed condenser was charged with **4-Cl·4/3LiBr** (1.049 g, 1.151 mmol) and 40 mL pyridine. The faint yellow solution was heated to reflux for 12 h at which point the color had changed to a deep reddish-brown color. All volatiles were removed in vacuo to produce a brown solid (0.987 g, 98.0%); ^{1}H NMR: δ 9.08 (d, 2H, 6 Hz), 8.59 (t, 1H, 6 Hz), 8.09 (t, 2H, 6 Hz), 7.34 (s, 4H), 7.32 (d, 2H, $^{4}J_{HH}$=2 Hz), 7.25 (d, 2H, $^{4}J_{HH}$=2 Hz), 4.67 (t, 2H, 7 Hz), 4.55 (t, 1H, 8 Hz), 4.17 (d, 3H, $^{2}J_{HH}$=12 Hz), 4.04 (s, 6H), 4.00 (s, 6H), 3.50 (m, 3H), 2.15 (q, 2H, 8 Hz), 1.41 (pent, 2H, 7 Hz), 1.32 (m, 2H), 1.15 (s, 18H), 1.14 (s, 18H); $^{13}C\{^{1}H\}$ NMR: δ 151.8, 149.7, 149.6, 146.3, 145.3, 138.9, 135.8, 135.6, 128.9, 128.5, 126.7, 126.3, 123.0, 121.8, 117.5, 65.9, 65.4, 36.6, 35.0, 34.9, 34.8, 34.7, 32.8, 32.0, 31.26, 31.20, 31.18, 25.6; IR (cm^{-1}): 3383 (br s), 3046 (m), 2959 (s), 2868 (s), 2822 (m), 2744 (w), 2716 (w), 2591 (w), 2561 (w), 2304 (w), 2039 (w), 1963 (w), 1786 (w), 1740 (w), 1635 (m), 1602 (m), 1583 (m), 1482 (s), 1463 (m), 1434 (m), 1417 (m), 1394 (m), 1362 (m), 1299 (m), 1264 (m), 1245 (m), 1206 (m), 1177 (m), 1123 (m), 1023 (m), 1000 (m), 944 (w), 891 (w), 871 (m), 807 (m), 772 (w), 737 (m), 701 (m), 685 (m), 646 (w). HRMS calculated for $C_{57}H_{76}NO_4$ $[M-Cl]^+$: 838.5774, found: 838.5747.

*4.3.6. 2-(5-Pyridiniumpentyl)tetramethoxy-p-tert-butylcalix[4]arene chloride **[5-py]Cl**.* A 50-mL round bottom flask equipped with a magnetic stir bar and a water-jacketed condenser was charged with **5-Cl·4/3LiBr** (1.372 g, 1.483 mmol) and 40 mL pyridine. The faint yellow solution was heated to reflux for 12 h at which point the color had changed to a deep reddish-brown color. All volatiles were removed in vacuo to produce a brown solid (1.275 g, 96.8%); ^{1}H NMR: δ 9.05 (d, 2H, 6 Hz), 8.59 (t, 1H, 6 Hz), 8.09 (t, 2H, 6 Hz), 7.35 (s, 4H), 7.33 (d, 2H, $^{4}J_{HH}$=2 Hz), 7.27 (d, 2H, $^{4}J_{HH}$=2 Hz), 4.67 (t, 2H, 7 Hz), 4.57 (t, 1H, 8 Hz), 4.20 (d, 3H, $^{2}J_{HH}$=12 Hz), 4.06 (s, 6H), 4.02 (s, 6H), 3.51 (m, 3H), 2.16 (q, 2H, 8 Hz), 2.00 (pent, 2H, 7 Hz), 1.43 (pent, 2H, 8 Hz), 1.34 (m, 2H), 1.16 (s, 36H); $^{13}C\{^{1}H\}$ NMR: δ 151.5, 150.3, 149.9, 148.8, 146.3, 139.1, 135.8, 135.6, 135.5, 128.9, 126.9, 126.8, 126.7, 124.7, 123.0, 65.6, 65.0, 36.6, 35.0, 34.9, 34.8, 33.0, 31.5, 31.4, 31.3, 31.2, 31.1, 28.6, 26.4; IR (cm^{-1}): 3388 (br s), 3048 (m), 2959 (s), 2878 (m), 2820 (w), 2736 (w), 2710 (w), 2033 (w), 1741 (w), 1635 (w), 1603 (w), 1584 (w), 1482 (m), 1463 (m), 1432 (w), 1419 (w), 1393 (w), 1362 (w), 1300 (w), 1262 (w), 1245 (w), 1206 (w), 1176 (w), 1123 (w), 1024 (w), 1001 (w), 870 (w), 807 (w), 774 (w), 735 (w), 684 (w). HRMS calculated $C_{58}H_{78}NO_4$ $[M-Cl]^+$: 852.5931, found: 852.5909.

4.4. General procedure for the synthesis of 2-(ω-alkylamine)-tetramethoxy-*p*-*tert*-butylcalix[4]arenes

To a mixture of finely powdered sodium iodide, sodium carbonate, and **3-Cl** or **5-Cl** was added THF and an excess of the appropriate alkylamine. The heterogeneous reaction mixture was heated at reflux for several days with periodic monitoring by ^{1}H NMR spectroscopy on evaporated aliquots. After the reaction was judged to be complete, all volatiles were removed in vacuo, and the resulting solid was dissolved in dichloromethane and washed twice with saturated NaCl solution. For the cyclohexylamine compounds (**3-NCy** and **5-NCy**), the organic solution was contacted with 12 M HCl, then dried over $MgSO_4$, filtered, and concentrated to dryness to yield the hydrochloride salt as an off-white solid. For the isopropylamine compound (**5-N*ⁱ*Pr**), the organic solution was evaporated to dryness and the residue converted to a powder by treatment with acetonitrile saturated with NaI.

*4.4.1. 2-(3-Cyclohexylaminopropyl)tetramethoxy-p-tert-butylcalix[4]arene (**3-NCy**).* Reagents: **3-Cl** (1.02 g, 1.31 mmol); cyclohexylamine (0.44 mL, 3.8 mmol); NaI (0.452 g, 3.01 mmol); Na_2CO_3 (0.601 g, 5.67 mmol); THF (7 mL). Yield of **[3-NCy]·HCl**: 0.509 g (44%); ^{1}H NMR of **[3-NCy]·HCl** ($CD_3CN/CDCl_3$/NaI, 400 MHz): δ 7.92 (br s, 2H), 7.28 (d, 2H, $^{4}J_{HH}$=2 Hz), 7.22 (s, 4H), 7.21 (d, 2H, $^{4}J_{HH}$=2 Hz), 4.70 (t, 1H, 8 Hz), 4.27 (d, 3H, $^{2}J_{HH}$=12 Hz), 4.16 (s, 6H), 4.13 (s, 6H), 3.47 (d, 2H, $^{2}J_{HH}$=12 Hz), 3.45 (d, 1H, $^{2}J_{HH}$=12 Hz), 3.17 (m, 1H), 3.10 (m, 2H), 2.30 (m, 2H), 2.20 (m, 2H), 1.85 (m, 1H), 1.73 (m, 4H), 1.24 (m, 5H), 1.22 (s, 18H), 1.20 (s, 18H); $^{13}C\{^{1}H\}$ NMR of **[3-NCy]·HCl** ($CD_3CN/CDCl_3$/NaI, 100 MHz): δ 149.9, 148.2, 148.0, 136.7, 133.9, 133.8, 125.4, 125.2, 121.9, 64.4, 63.8, 57.1, 43.8, 34.8, 33.7, 33.5, 30.3, 30.2, 29.9, 29.1, 28.9, 27.8, 24.6, 23.9, 23.6. HRMS calculated for $C_{57}H_{82}NO_4$ $[M+H]^+$: 844.6244, found: 844.6221.

*4.4.2. 2-(5-Cyclohexylaminopentyl)tetramethoxy-p-tert-butylcalix[4]arene (**5-NCy**).* Reagents: **5-Cl** (1.0 g, 1.2 mmol); cyclohexylamine (0.42 mL, 3.6 mmol); NaI (0.45 g, 3.0 mmol); Na_2CO_3 (0.61 g, 5.8 mmol); THF (7 mL). Yield of **[5-NCy]·HCl**: 0.53 g (49%); ^{1}H NMR of **[5-NCy]·HCl** ($CD_3CN/CDCl_3$/NaI, 400 MHz): δ 7.92 (br s, 2H), 7.25 (d, 2H, $^{4}J_{HH}$=2 Hz), 7.23 (s, 4H), 7.21 (d, 2H, $^{4}J_{HH}$=2 Hz), 4.65 (t, 1H, 8 Hz), 4.27 (d, 3H, $^{2}J_{HH}$=12 Hz), 4.13 (s, 6H), 4.12 (s, 6H), 3.474 (d, 2H, $^{2}J_{\mathrm{HH}}$=12 Hz), 3.465 (d, 1H, $^{2}J_{\mathrm{HH}}$=12 Hz), 3.20 (m, 1H), 2.97 (m, 2H), 2.23 (m, 2H), 2.17 (m, 2H), 1.76 (m, 5H), 1.49 (m, 2H), 1.40 (m, 2H), 1.24 (m, 5H), 1.211 (s, 18H), 1.205 (s, 18H); ^{13}C{^{1}H} NMR of **[5-NCy]·HCl** ($CD_3CN/CDCl_3$/NaI, 100 MHz): δ 149.89, 149.87, 137.3, 133.9, 133.8, 133.6, 125.30, 125.26, 124.88, 121.68, 64.1, 63.8, 57.0, 43.7, 34.8, 33.6, 33.4, 32.9, 30.3, 30.1, 29.0, 28.9, 27.7, 27.4, 26.0, 24.7, 23.9, 23.6. HRMS calculated for $C_{59}H_{85}NO_4Na$ [M+Na]$^+$: 894.6376, found: 894.6368.

*4.4.3. 2-(5-Isopropylaminopentyl)tetramethoxy-p-tert-butylcalix[4]arene (**5-N^{i}Pr**).* Reagents: **5-Cl** (1.0 g, 1.2 mmol); isopropylamine (0.35 mL×12, 4.1 mmol each); NaI (0.45 g, 3.0 mmol); Na_2CO_3 (0.61 g, 5.8 mmol); THF (7 mL). Over the course of 12 days, 0.35 mL of isopropylamine was added each day. Yield: 0.323 g (31%); ^{1}H NMR ($CD_3CN/CDCl_3$/NaI, 400 MHz):[55] δ 7.25 (d, 2H, $^{4}J_{\mathrm{HH}}$=2 Hz), 7.23 (s, 4H), 7.21 (d, 2H, $^{4}J_{\mathrm{HH}}$=2 Hz), 4.65 (t, 1H, 8 Hz), 4.27 (d, 3H, $^{2}J_{\mathrm{HH}}$=12 Hz), 4.13 (s, 6H), 4.12 (s, 6H), 3.51 (sept, 1H, 7 Hz), 3.47 (d, 2H, $^{2}J_{\mathrm{HH}}$=12 Hz), 3.46 (d, 1H, $^{2}J_{\mathrm{HH}}$=12 Hz), 2.96 (m, 2H), 2.17 (m, 2H), 1.93 (m, 2H), 1.55 (m, 2H), 1.48 (d, 6H, 7 Hz), 1.40 (m, 2H), 1.21 (s, 18H), 1.20 (s, 18H); ^{13}C{^{1}H} NMR ($CD_3CN/CDCl_3$/NaI, 100 MHz): δ 150.0, 148.1, 148.0, 137.4, 134.0, 133.9, 133.7, 125.42, 125.39, 125.0, 121.8, 64.2, 63.9, 50.6, 44.3, 34.8, 33.7, 33.5, 33.0, 30.3, 30.2, 29.2, 29.0, 27.5, 26.1, 25.0, 17.9. HRMS calculated for $C_{56}H_{81}NO_4Na$ [M+Na]$^+$: 854.6063, found: 854.6056.

4.5. General procedure for the synthesis of aniline derivatives (3-N^{R} to 6-N^{R})

To a nitrogen-filled Schlenk tube was added **3-Cl** to **6-Cl**, which was then placed under vacuum for several hours. To the Schlenk tube was added ∼4 equiv KH in a glovebox. After purging back onto a Schlenk line, THF (15 mL) and ∼4 equiv aniline or substituted aniline were added. The yellow suspension immediately began to evolve H_2 and started a slow color transformation to an eventual dark brown colored solution after 12 h. Several drops of water were added to quench the unreacted KH and convert any deprotonated product back to the protio species. All volatiles were removed in vacuo prior to extraction into pentane. Filtration yielded a light to dark brown solution, which again had all volatiles removed in vacuo. Excess aniline was removed by vacuum distillation producing beige to dark brown colored glassy solids.

*4.5.1. 2-(3-(2,6-Diisopropylanilino)propyl)tetramethoxy-p-tert-butylcalix[4]arene (**3-N^{iPr}**).* Reagents: **3-Cl·LiBr** (1.052 g, 1.211 mmol); KH (0.190 g, 4.74 mmol); 2,6-diisopropylaniline (0.84 g, 0.89 mL, 4.7 mmol). Yield: 0.913 g (81.7%); ^{1}H NMR: δ 7.35 (s, 4H), 7.34 (d, 2H, $^{4}J_{\mathrm{HH}}$=2 Hz), 7.27 (d, 2H, $^{4}J_{\mathrm{HH}}$=2 Hz), 7.01 (d, 2H, 7 Hz), 6.94 (t, 1H, 7 Hz), 4.61 (t, 1H, 8 Hz), 4.19 (d, 2H, $^{2}J_{\mathrm{HH}}$=12 Hz), 4.18 (d, 1H, $^{2}J_{\mathrm{HH}}$=12 Hz), 4.05 (s, 6H), 4.04 (s, 6H), 3.51 (m, 3H), 3.26 (sept, 2H, 7 Hz), 3.04 (t, 1H, 7 Hz), 2.84 (q, 2H, 7 Hz), 2.24 (q, 2H, 8 Hz), 1.59 (m, 2H), 1.15 (s, 18H), 1.14 (s, 18H), 1.10 (d, 12H, 7 Hz); ^{13}C{^{1}H} NMR: δ 151.9, 151.8, 149.7, 149.6, 143.8, 142.0, 139.2, 135.9, 132.9, 127.2, 127.1, 126.7, 124.3, 123.4, 118.6, 65.3, 65.0, 53.0, 32.3, 31.55, 31.53, 31.50, 30.4, 30.3, 24.7, 23.3, 14.4; IR (cm^{-1}): 3387 (w), 3045 (m), 2957 (s), 2929 (s), 2868 (m), 2820 (m), 2743 (w), 2713 (w), 2035 (w), 1751 (w), 1620 (w), 1602 (w), 1585 (w), 1481 (m), 1463 (m), 1448 (m), 1392 (w), 1384 (w), 1362 (m), 1300 (w), 1286 (w), 1262 (m), 1247 (w), 1206 (m), 1174 (w), 1124 (w), 1026 (m), 951 (w), 935 (w), 922 (w), 913 (w), 871 (w), 801 (w), 740 (w), 705 (w). HRMS calculated for $C_{63}H_{88}NO_4$ [M+H]$^+$: 922.6713, found: 922.6721.

*4.5.2. 2-(4-Anilinobutyl)tetramethoxy-p-tert-butylcalix[4]arene (**4-N^{H}**).* Reagents: **4-Cl·4/3LiBr** (0.917 g, 1.01 mmol); KH (0.160 g, 3.99 mmol); aniline (0.378 g, 0.370 mL, 4.06 mmol). Yield: 0.701 g (81.7%); ^{1}H NMR: δ 7.35 (s, 4H), 7.33 (d, 2H, $^{4}J_{\mathrm{HH}}$=2 Hz), 7.30 (d, 2H, $^{4}J_{\mathrm{HH}}$=2 Hz), 7.06 (t, 2H, 8 Hz), 6.56 (d, 2H, 8 Hz), 6.54 (t, 1H, 8 Hz), 4.62 (t, 1H, 8 Hz), 4.50 (t, 1H, 7 Hz), 4.21 (d, 3H, $^{2}J_{\mathrm{HH}}$=12 Hz), 4.07 (s, 6H), 4.05 (s, 6H), 3.51 (d, 2H, $^{2}J_{\mathrm{HH}}$=12 Hz), 3.50 (d, 1H, $^{2}J_{\mathrm{HH}}$=12 Hz), 3.04 (q, 2H, 7 Hz), 2.20 (m, 2H), 1.66 (m, 2H), 1.40 (m, 2H), 1.18 (s, 18H), 1.17 (s, 18H); ^{13}C{^{1}H} NMR: δ 151.5, 151.4, 149.7, 149.3, 149.2, 139.0, 135.5, 135.4, 129.5, 126.9, 126.5, 123.3, 116.6, 112.8, 65.2, 65.1, 65.0, 64.9, 43.6, 36.3, 34.9, 34.8, 31.2, 30.0, 29.8, 27.0; IR (cm^{-1}): 3048 (w), 3017 (w), 2958 (s), 2928 (s), 2866 (m), 2820 (m), 2377 (w), 2323 (w), 1603 (w), 1506 (w), 1481 (w), 1463 (w), 1430 (w), 1392 (w), 1361 (w), 1314 (w), 1300 (w), 1286 (w), 1260 (w), 1246 (w), 1206 (w), 1176 (w), 1118 (w), 1024 (w), 871 (w), 797 (w), 747 (w), 691 (w). HRMS calculated for $C_{58}H_{78}NO_4$ [M+H]$^+$: 852.5931, found: 852.5930.

*4.5.3. 2-(4-(2,6-Dimethylanilino)butyl)tetramethoxy-p-tert-butylcalix[4]arene (**4-N^{Me}**).* Reagents: **4-Cl·4/3LiBr** (0.997 g, 1.09 mmol); KH (0.176 g, 4.39 mmol); 2,6-dimethylaniline (0.531 g, 0.540 mL, 4.39 mmol). Yield: 0.656 g (68.1%); ^{1}H NMR: δ 7.36–7.31 (m, 8H), 6.92 (d, 2H, 7 Hz), 6.72 (t, 1H, 7 Hz), 4.63 (t, 1H, 8 Hz), 4.23 (d, 3H, $^{2}J_{\mathrm{HH}}$=12 Hz), 4.08 (s, 6H), 4.05 (s, 6H), 3.51 (d, 2H, $^{2}J_{\mathrm{HH}}$=12 Hz), 3.50 (d, 1H, $^{2}J_{\mathrm{HH}}$=12 Hz), 3.23 (t, 1H, 7 Hz), 2.96 (q, 2H, 7 Hz), 2.20 (m, 8H), 1.62 (pent, 2H, 8 Hz), 1.40 (m, 2H), 1.19 (s, 36H); ^{13}C{^{1}H} NMR: δ 151.1, 149.0, 148.9, 138.6, 135.2, 135.0, 129.4, 129.3, 129.0, 128.7, 126.7, 126.4, 126.0, 123.1, 122.8, 121.4, 64.8, 64.7, 64.6, 64.5, 48.1, 36.0, 34.5, 34.4, 33.7, 31.0, 30.9, 30.8, 29.7, 18.2; IR (cm^{-1}): 3382 (w), 3044 (m), 2957 (s), 2866 (s), 2820 (m), 2034 (w), 1751 (w), 1596 (m), 1582 (m), 1480 (s), 1464 (s), 1432 (m), 1392 (m), 1361 (m), 1300 (m), 1286 (m), 1260 (m), 1247 (m), 1206 (m), 1174 (m), 1124 (m), 1100 (m), 1023 (m), 951 (w), 922 (w), 871 (m), 800 (m), 764 (m), 739 (m), 704 (w), 643 (w), 614 (w). HRMS calculated for $C_{60}H_{82}NO_4$ [M+H]$^+$: 880.6244, found: 880.6246. Elemental analysis calculated for $C_{60}H_{81}NO_4$: C, 81.86; H, 9.27; N, 1.59. Found: C, 80.63; H, 9.02; N, 1.60.

*4.5.4. 2-(4-(2,6-Diethylanilino)butyl)tetramethoxy-p-tert-butylcalix[4]arene (**4-N^{Et}**).* Reagents: **4-Cl·4/3LiBr** (0.842 g, 0.924 mmol); KH (0.170 g, 4.24 mmol); 2,6-diethylaniline (0.634 g, 0.700 mL, 4.25 mmol). Yield: 0.745 g (88.8%); ^{1}H NMR: δ 7.36–7.30 (m, 8H), 6.97 (d, 2H, 8 Hz), 6.85 (t, 1H, 8 Hz), 4.63 (t, 1H, 8 Hz), 4.23 (d, 3H, $^{2}J_{\mathrm{HH}}$=12 Hz), 4.08 (s, 6H), 4.06 (s, 6H), 3.51 (d, 2H, $^{2}J_{\mathrm{HH}}$=12 Hz), 3.50 (d, 1H, $^{2}J_{\mathrm{HH}}$=12 Hz), 3.14 (t, 1H, 7 Hz), 2.89 (q, 2H, 7 Hz), 2.58 (q, 4H, 8 Hz), 2.20 (m, 2H), 1.66 (m, 2H), 1.41 (m, 2H), 1.19 (s, 18H), 1.18 (s, 18H), 1.13 (t, 6H, 8 Hz); ^{13}C{^{1}H} NMR: δ 151.6, 149.4, 149.3, 146.1, 139.0, 136.9, 135.6, 135.5, 127.3, 127.0, 126.9, 126.7, 126.6, 123.4, 123.3, 122.9, 65.2, 65.0, 50.5, 36.4, 35.0, 34.9, 34.2, 32.3, 31.6, 30.1, 30.0, 27.2, 24.8, 15.2; IR (cm^{-1}): 3041 (w), 2960 (s), 2932 (m), 2869 (m), 2820 (w), 1481 (m), 1460 (w), 1392 (w), 1361 (w), 1301 (w), 1285 (w), 1245 (w), 1206 (w), 1174 (w), 1124 (w), 1024 (w), 870 (w). HRMS calculated for $C_{62}H_{86}NO_4$ [M+H]$^+$: 908.6557, found 908.6530. Elemental analysis calculated for $C_{62}H_{85}NO_4$: C, 81.98; H, 9.43; N, 1.54. Found: C, 80.22; H, 9.34; N, 1.50.

*4.5.5. 2-(4-(2,6-Diisopropylanilino)butyl)tetramethoxy-p-tert-butylcalix[4]arene (**4-N^{iPr}**).* Reagents: **4-Cl·4/3LiBr** (0.869 g, 0.953 mmol); KH (0.178 g, 4.44 mmol); 2,6-diisopropylaniline (0.77 g, 0.82 mL, 4.4 mmol). Yield: 0.770 g (86.2%); ^{1}H NMR: δ 7.36–7.29 (m, 8H), 7.02 (d, 2H, 8 Hz), 6.96 (t, 1H, 8 Hz), 4.64 (t, 1H, 8 Hz), 4.22 (d, 3H, $^{2}J_{\mathrm{HH}}$=12 Hz), 4.07 (s, 12H), 3.52 (d, 2H, $^{2}J_{\mathrm{HH}}$=12 Hz), 3.50 (d, 1H, $^{2}J_{\mathrm{HH}}$=12 Hz), 3.26 (sept, 2H, 7 Hz), 3.06 (t, 1H, 8 Hz), 2.80 (q, 2H, 7 Hz), 2.20 (m, 2H), 1.69 (pent, 2H, 7 Hz), 1.42 (m, 2H), 1.18 (s, 18H), 1.17 (s, 18H), 1.12 (d, 12H, 7 Hz); ^{13}C{^{1}H} NMR: δ 151.54, 151.50, 151.4, 149.4, 149.3, 143.3, 139.0, 135.8, 135.6, 135.4, 126.9, 126.8, 126.3, 124.2, 124.0, 123.1, 65.0, 64.8, 52.4, 36.3, 34.9, 34.8, 34.2, 31.3, 31.2, 30.1, 29.9, 27.8, 27.2, 24.3; IR (cm^{-1}): 3049 (m), 2939 (s), 2863 (s), 2820 (m), 2742 (w), 2713 (w), 2035 (w), 1751 (w), 1619 (m), 1602 (m), 1584 (m), 1480 (s), 1462 (s), 1446 (s), 1392 (w), 1384 (m), 1362 (m), 1300 (m), 1286 (m), 1265 (m), 1246 (m), 1205 (m), 1174 (m), 1123 (m), 1025 (m), 951 (w), 934 (w), 923 (w), 871 (m), 800 (m), 740 (m), 705 (w), 645 (w), 614 (w). HRMS calculated for $C_{64}H_{90}NO_4$ $[M+H]^+$: 936.6870, found: 936.6840.

*4.5.6. 2-(5-Anilinopentyl)tetramethoxy-p-tert-butylcalix[4]arene (**5-N^{H}**).* Reagents: **5-Cl·4/3LiBr** (0.994 g, 1.07 mmol); KH (0.201 g, 5.01 mmol); aniline (0.460 g, 0.450 mL, 4.93 mmol). Yield: 0.562 g (60.4%); ^{1}H NMR: δ 7.36–7.31 (m, 8H), 7.09–7.06 (m, 2H), 6.57–6.54 (m, 3H), 4.63 (t, 1H, 8 Hz), 4.42 (t, 1H, 7 Hz), 4.22 (d, 3H, $^{2}J_{HH}$=12 Hz), 4.08 (s, 6H), 4.06 (s, 6H), 3.51 (d, 2H, $^{2}J_{HH}$=12 Hz), 3.50 (d, 1H, $^{2}J_{HH}$=12 Hz), 3.02 (q, 2H, 7 Hz), 2.19 (m, 2H), 1.59 (pent, 2H, 8 Hz), 1.49 (pent, 2H, 8 Hz), 1.36 (m, 2H), 1.19 (s, 36H); ^{13}C{^{1}H} NMR: δ 151.6, 149.4, 149.3, 139.1, 135.6, 135.5, 129.8, 129.6, 127.1, 126.9, 126.7, 126.5, 123.5, 123.3, 116.8, 116.7, 113.0, 112.9, 65.3, 65.13, 65.08, 64.9, 43.8, 36.4, 35.0, 34.9, 34.2, 31.3, 31.1, 30.1, 29.3, 29.2; IR (cm^{-1}): 3412 (m), 3049 (m), 3020 (m), 2955 (s), 2927 (s), 2864 (s), 2820 (m), 2739 (w), 2708 (w), 2034 (w), 1755 (w), 1603 (w), 1506 (w), 1481 (w), 1463 (w), 1431 (w), 1392 (w), 1362 (w), 1301 (w), 1263 (w), 1246 (w), 1206 (w), 1177 (w), 1125 (w), 1024 (w), 871 (w), 799 (w), 740 (w), 692 (w). HRMS calculated for $C_{59}H_{80}NO_4$ $[M+H]^+$: 866.6087, found: 866.6060.

*4.5.7. 2-(5-(2,6-Dimethylanilino)pentyl)tetramethoxy-p-tert-butylcalix[4]arene (**5-N^{Me}**).* Reagents: **5-Cl·4/3LiBr** (5.063 g, 5.471 mmol); KH (0.880 g, 21.9 mmol); 2,6-dimethylaniline (2.66 g, 2.70 mL, 21.9 mmol). Yield: 4.19 g (85.7%); ^{1}H NMR: δ 7.36–7.30 (m, 8H), 6.93 (d, 2H, 7 Hz), 6.73 (t, 1H, 7 Hz), 4.64 (t, 1H, 8 Hz), 4.24 (d, 3H, $^{2}J_{HH}$=12 Hz), 4.09 (s, 6H), 4.06 (s, 6H), 3.52 (d, 2H, $^{2}J_{HH}$=12 Hz), 3.51 (d, 1H, $^{2}J_{HH}$=12 Hz), 3.21 (t, 1H, 7 Hz), 2.91 (q, 2H, 7 Hz), 2.23–2.16 (m, 8H), 1.55 (pent, 2H, 7 Hz), 1.47 (pent, 2H, 8 Hz), 1.35 (m, 2H), 1.20 (s, 18H), 1.19 (s, 18H); ^{13}C{^{1}H} NMR: δ 151.7, 151.6, 149.5, 149.4, 147.4, 147.3, 139.2, 135.7, 135.5, 129.93, 129.87, 129.3, 127.1, 126.7, 123.4, 122.0, 65.3, 65.2, 65.1, 65.0, 48.6, 48.5, 36.4, 35.1, 35.0, 34.2, 31.4, 31.3, 31.1, 31.0, 30.0, 29.3, 27.7, 18.7; IR (cm^{-1}): 3044 (m), 2956 (s), 2928 (s), 2865 (m), 2820 (m), 2035 (w), 1751 (w), 1597 (m), 1584 (w), 1481 (s), 1463 (s), 1432 (m), 1392 (m), 1361 (m), 1299 (m), 1286 (m), 1265 (m), 1245 (m), 1206 (m), 1174 (m), 1124 (m), 1101 (m), 1024 (s), 950 (w), 922 (w), 871 (m), 798 (w), 763 (m), 739 (m), 705 (w), 644 (w), 614 (w). HRMS calculated for $C_{61}H_{84}NO_4$ $[M+H]^+$: 894.6400, found: 894.6389. Elemental analysis calculated for $C_{61}H_{83}NO_4$: C, 81.92; H, 9.35; N, 1.57. Found: C, 80.10; H, 9.07; N, 1.61.

*4.5.8. 2-(5-(2,6-Diethylanilino)pentyl)tetramethoxy-p-tert-butylcalix[4]arene (**5-N^{Et}**).* Reagents: **5-Cl·4/3LiBr** (0.995 g, 1.08 mmol); KH (0.208 g, 5.19 mmol); 2,6-diethylaniline (0.734 g, 0.810 mL, 4.92 mmol). Yield: 0.730 g (73.6%); ^{1}H NMR: δ 7.35–7.28 (m, 8H), 6.96 (d, 2H, 8 Hz), 6.83 (t, 1H, 8 Hz), 4.61 (t, 1H, 7 Hz), 4.21 (d, 3H, $^{2}J_{HH}$=12 Hz), 4.07 (s, 6H), 4.05 (s, 6H), 3.51 (d, 2H, $^{2}J_{HH}$=12 Hz), 3.50 (d, 1H, $^{2}J_{HH}$=12 Hz), 3.11 (t, 1H, 7 Hz), 2.83 (q, 2H, 7 Hz), 2.57 (q, 4H, 7 Hz), 2.16 (m, 2H), 1.57 (pent, 2H, 7 Hz), 1.46 (m, 2H), 1.34 (m, 2H), 1.17 (s, 18H), 1.16 (s, 18H), 1.12 (t, 6H, 7 Hz); ^{13}C{^{1}H} NMR: δ 151.4, 149.2, 149.1, 146.1, 138.9, 136.8, 135.5, 135.4, 127.1, 126.9, 126.8, 126.5, 126.4, 123.2, 123.1, 122.7, 65.1, 65.0, 64.9, 64.8, 50.3, 36.2, 34.9, 34.7, 31.2, 30.8, 30.0, 29.8, 29.1, 27.5, 24.6, 15.1; IR (cm^{-1}): 3392 (w), 3042 (m), 2936 (s), 2863 (s), 2820 (m), 2035 (w), 1751 (w), 1619 (w), 1602 (m), 1594 (m), 1584 (m), 1480 (s), 1459 (m), 1392 (m), 1300 (m), 1286 (m), 1265 (m), 1245 (m), 1204 (s), 1174 (m), 1124 (m), 1023 (m), 950 (w), 871 (m), 798 (m), 739 (m), 705 (w), 645 (w), 615 (w). HRMS calculated for $C_{63}H_{88}NO_4$ $[M+H]^+$: 922.6713, found: 922.6690.

*4.5.9. 2-(5-(2,6-Diisopropylanilino)pentyl)tetramethoxy-p-tert-butylcalix[4]arene (**5-N^{iPr}**).* Reagents: **5-Cl·4/3LiBr** (0.999 g, 1.08 mmol); KH (0.202 g, 5.04 mmol); 2,6-diisopropylaniline (0.87 g, 0.93 mL, 4.9 mmol). Yield: 0.921 g (89.8%); ^{1}H NMR: δ 7.34–7.27 (m, 8H), 7.02 (d, 2H, 8 Hz), 6.93 (t, 1H, 8 Hz), 4.61 (t, 1H, 8 Hz), 4.20 (d, 3H, $^{2}J_{HH}$=12 Hz), 4.06 (s, 6H), 4.05 (s, 6H), 3.50 (d, 2H, $^{2}J_{HH}$=12 Hz), 3.49 (d, 1H, $^{2}J_{HH}$=12 Hz), 3.24 (sept, 2H, 7 Hz), 3.02 (t, 1H, 7 Hz), 2.74 (q, 2H, 7 Hz), 2.16 (m, 2H), 1.59 (m, 2H), 1.47 (m, 2H), 1.34 (m, 2H), 1.17 (s, 18H), 1.16 (s, 18H), 1.12 (d, 12H, 7 Hz); ^{13}C{^{1}H} NMR: δ 151.4, 144.4, 143.2, 138.9, 135.5, 135.4, 127.0, 126.7, 126.6, 126.4, 124.1, 123.8, 123.3, 123.0, 65.1, 65.0, 64.9, 64.8, 52.3, 36.2, 34.9, 34.7, 31.2, 31.1, 31.0, 29.9, 29.8, 27.8, 27.7, 24.4, 24.3, 24.2, 24.0; IR (cm^{-1}): 3483 (w), 3400 (w), 3044 (m), 2959 (s), 2927 (s), 2867 (m), 2819 (m), 1750 (m), 1619 (w), 1602 (w), 1585 (w), 1482 (m), 1460 (w), 1444 (w), 1392 (w), 1382 (w), 1361 (w), 1300 (w), 1286 (w), 1262 (w), 1246 (w), 1206 (w), 1174 (w), 1124 (w), 1024 (w), 871 (w), 800 (w), 743 (w). HRMS calculated for $C_{65}H_{92}NO_4$ $[M+H]^+$: 950.7026, found: 950.7024. Elemental analysis calculated for $C_{65}H_{91}NO_4$: C, 82.14; H, 9.65; N, 1.47. Found: C, 80.82; H, 9.42; N, 1.66.

*4.5.10. 2-(6-(2,6-Dimethylanilino)hexyl)tetramethoxy-p-tert-butylcalix[4]arene (**6-N^{Me}**).* Reagents: **6-Cl·4/3LiBr** (0.971 g, 1.03 mmol); KH (0.160 g, 3.99 mmol); 2,6-dimethylaniline (0.502 g, 0.510 mL, 4.13 mmol). Yield: 0.832 g (88.6%); ^{1}H NMR: δ 7.36 (s, 4H), 7.34 (d, 2H, $^{4}J_{HH}$=2 Hz), 7.31 (d, 2H, $^{4}J_{HH}$=2 Hz), 6.93 (d, 2H, 7 Hz), 6.74 (t, 1H, 7 Hz), 4.64 (t, 1H, 8 Hz), 4.24 (d, 3H, $^{2}J_{HH}$=12 Hz), 4.08 (s, 6H), 4.06 (s, 6H), 3.51 (d, 2H, $^{2}J_{HH}$=12 Hz), 3.50 (d, 1H, $^{2}J_{HH}$=12 Hz), 3.23 (br s, 1H), 2.92 (t, 2H, 7 Hz), 2.21 (s, 6H), 2.18 (m, 2H), 1.55 (m, 2H), 1.47 (m, 2H), 1.39–1.26 (m, 4H), 1.20 (s, 18H), 1.19 (s, 18H); ^{13}C{^{1}H} NMR: δ 151.44, 151.42, 149.2, 149.1, 146.1, 138.9, 136.8, 135.5, 135.4, 127.1, 126.90, 126.87, 126.84, 126.54, 126.48, 123.2, 123.1, 122.7, 65.0, 64.9, 50.3, 36.2, 34.9, 34.7, 34.0, 31.2, 30.0, 29.9, 29.8, 29.1, 27.5, 24.6, 15.0; IR (cm^{-1}): 3855 (m), 3746 (m), 3674 (w), 3386 (w), 3045 (m), 2975 (s), 2823 (m), 2362 (m), 2034 (w), 1598 (m), 1477 (s), 1362 (m), 1263 (s), 1207 (s), 1119 (m), 1023 (s), 873 (m), 802 (m), 738 (s). HRMS calculated for $C_{62}H_{86}NO_4$ $[M+H]^+$: 908.6557, found: 908.6557.

*4.5.11. 2-(6-(2,6-Diethylanilino)hexyl)tetramethoxy-p-tert-butylcalix[4]arene (**6-N^{Et}**).* Reagents: **6-Cl·4/3LiBr** (0.968 g, 1.03 mmol); KH (0.160 g, 3.99 mmol); 2,6-diethylaniline (0.616 g, 0.680 mL, 4.13 mmol). Yield: 0.791 g (82.0%); ^{1}H NMR: δ 7.36 (s, 4H), 7.34 (d, 2H, $^{4}J_{HH}$=2 Hz), 7.30 (d, 2H, $^{4}J_{HH}$=2 Hz), 6.97 (d, 2H, 7 Hz), 6.85 (t, 1H, 7 Hz), 4.62 (t, 1H, 8 Hz), 4.23 (d, 3H, $^{2}J_{HH}$=12 Hz), 4.08 (s, 6H), 4.06 (s, 6H), 3.51 (d, 2H, $^{2}J_{HH}$=12 Hz), 3.50 (d, 1H, $^{2}J_{HH}$=12 Hz), 3.14 (br s, 1H), 2.87 (q, 2H, 8 Hz), 2.62 (q, 4H, 8 Hz), 2.16 (q, 2H, 8 Hz), 1.53 (pent, 2H, 8 Hz), 1.40 (m, 4H), 1.33 (m, 2H), 1.19 (s, 18H), 1.18 (s, 18H), 1.14 (t, 6H, 8 Hz); ^{13}C{^{1}H} NMR: δ 151.6, 151.5, 149.4, 149.3, 146.3, 146.2, 139.1, 137.0, 136.9, 135.5, 127.3, 127.0, 126.6, 123.3, 122.89, 122.87, 65.2, 65.0, 50.6, 36.4, 35.0, 34.9, 34.1, 31.30, 31.27, 30.1, 29.9, 29.3, 27.4, 27.3, 24.8, 24.7 15.2; IR (cm^{-1}): 3390 (m), 3183 (w), 3041 (m), 2958 (s), 2820 (s), 2742 (w), 2713 (w), 2681 (w), 2628 (w), 2562 (w), 2304 (w), 2035 (w), 1914 (w), 1851 (w), 1751 (w), 1621 (w), 1593 (m), 1481 (s), 1458 (s), 1392 (m), 1361 (s), 1299 (m), 1285 (m), 1261 (s), 1244 (s), 1205 (s), 1174 (m), 1124 (s), 1115 (s), 1059 (m), 1024 (s), 951 (w), 922 (w), 914 (w), 871 (m), 799 (w), 756 (m), 740 (m), 705 (m), 644 (w), 614 (w). HRMS calculated for $C_{64}H_{90}NO_4$ $[M+H]^+$: 936.6870, found: 936.6869.

*4.5.12. 2-(6-(2,6-Diisopropylanilino)hexyl)tetramethoxy-p-tert-butylcalix[4]arene (**6-N^{iPr}**).* Reagents: **6-Cl·4/3LiBr** (0.967 g, 1.03 mmol); KH (0.160 g, 3.99 mmol); 2,6-diisopropylaniline (0.73 g, 0.78 mL, 4.1 mmol). Yield: 0.856 g (86.2%); ^{1}H NMR: δ 7.36 (s, 4H), 7.34 (d, 2H, $^{4}J_{HH}$=2 Hz), 7.30 (d, 2H, $^{4}J_{HH}$=2 Hz), 7.05 (d, 2H, 8 Hz), 6.99 (t, 1H, 8 Hz), 4.63 (t, 1H, 8 Hz), 4.23 (d, 3H, $^{2}J_{HH}$=12 Hz), 4.08 (s, 6H), 4.06 (s, 6H), 3.51 (d, 2H, $^{2}J_{HH}$=12 Hz), 3.50 (d, 1H, $^{2}J_{HH}$=12 Hz), 3.28 (sept, 2H, 8 Hz), 3.05 (br s, 1H), 2.78 (m, 2H), 2.17 (q, 2H, 8 Hz), 1.56 (pent, 2H, 8 Hz), 1.42 (m, 4H), 1.34 (m, 2H), 1.19 (s, 18H), 1.18 (s, 18H), 1.15 (d, 12H, 8 Hz); ^{13}C{^{1}H} NMR: δ 151.58, 151.57, 149.4, 149.3, 144.6, 143.4, 143.3, 139.1, 135.6, 135.5, 127.0, 126.6, 124.23, 124.20, 124.1, 123.3, 65.2, 65.0, 52.4, 36.4, 35.0, 34.9, 34.1, 31.31, 31.29, 31.1, 30.1, 30.0, 29.3, 27.9, 27.4, 27.3, 24.4, 24.3; IR (cm^{-1}): 3383 (w), 3183 (w), 3045 (m), 2957 (s), 2925 (s), 2866 (s), 2820 (s), 2741 (w), 2713 (w), 2594 (w), 2559 (w), 2035 (w), 1918 (w), 1858 (w), 1751 (w), 1601 (m), 1585 (m), 1481 (s), 1463 (s), 1445 (s), 1392 (m), 1383 (m), 1362 (s), 1300 (m), 1286 (m), 1262 (s), 1246 (s), 1205 (s), 1175 (m), 1148 (m), 1124 (m), 1114 (m), 1055 (m), 1024 (s), 950 (w), 935 (w), 871 (m), 800 (m), 755 (m), 739 (m), 705 (m), 669 (w), 644 (w), 614 (w). HRMS calculated for $C_{66}H_{94}NO_4$ [M+H]$^+$: 964.7183, found: 964.7180.

*4.5.13. 2-(3-(2,5-Dichloroanilino)propyl)tetramethoxy-p-tert-butylcalix[4]arene (**3-N^{Cl}**).* Reagents: **3-Cl·LiBr** (0.200 g, 0.230 mmol); KH (0.041 g, 1.0 mmol); 2,5-dichloroaniline (0.165 g, 1.11 mmol). Yield: 0.125 g (59.9%); ^{1}H NMR: δ 7.11 (d, 2H, $^4J_{HH}$=2 Hz), 7.09–7.04 (m, 6H), 7.01 (d, 1H, 8 Hz), 6.66 (d, 1H, $^4J_{HH}$=2 Hz), 6.49 (dd, 1H, $^3J_{HH}$=8 Hz, $^4J_{HH}$=2 Hz), 4.55 (t, 1H, 8 Hz), 4.36 (m, 1H), 4.15 (d, 3H, $^2J_{HH}$=12 Hz), 4.02 (s, 6H), 4.01 (s, 6H), 3.49 (m, 2H), 3.32 (d, 3H, $^2J_{HH}$=12 Hz), 2.17 (m, 2H), 1.74 (m, 2H), 1.07 (s, 36H); ^{13}C{^{1}H} NMR: δ 150.5, 148.7 148.5, 145.8, 144.9, 137.3, 134.40, 134.36, 134.3, 129.5, 127.8, 125.82, 125.80, 125.6, 125.2, 122.1, 116.2, 64.7, 64.4, 45.0, 44.8, 43.2, 34.8, 34.2, 31.0, 30.8, 22.3; IR (cm^{-1}): 3422 (m), 2962 (s), 1764 (m), 1596 (s), 1481 (s), 1362 (s), 1296 (s), 1245 (s), 1206 (s), 1178 (m), 1120 (s), 1005 (s), 872 (s), 807 (s), 738 (s), 703 (m).

*4.5.14. 2-(4-(2,5-Dichloroanilino)butyl)tetramethoxy-p-tert-butylcalix[4]arene (**4-N^{Cl}**).* Reagents: **4-Cl·4/3LiBr** (1.093 g, 1.199 mmol); KH (0.144 g, 3.59 mmol); 2,5-dichloroaniline (0.583 g, 3.60 mmol). Yield: 0.662 g (60.0%); ^{1}H NMR: δ 7.35–7.33 (m, 6H), 7.28 (d, 2H, $^4J_{HH}$=2 Hz), 7.15 (d, 1H, 8 Hz), 7.00 (d, 1H, $^4J_{HH}$=2 Hz), 6.67 (dd, 1H, $^3J_{HH}$=8 Hz, $^4J_{HH}$=2 Hz), 4.73 (m, 1H), 4.60 (t, 1H, 8 Hz), 4.19 (d, 3H, $^2J_{HH}$=12 Hz), 4.04 (s, 12H), 3.60 (m, 2H), 3.53 (d, 3H, $^2J_{HH}$=12 Hz), 2.19 (m, 2H), 1.83 (m, 2H), 1.43 (m, 2H), 1.16 (s, 36H); ^{13}C{^{1}H} NMR: δ 151.54, 151.52, 149.51, 149.50, 149.4, 139.9, 135.6, 135.5, 134.4, 130.9, 127.0, 126.8, 126.7, 123.4, 116.5, 115.4, 111.3, 65.0, 64.8, 45.7, 43.4, 36.4, 35.0, 31.3, 31.2, 31.0, 30.0, 26.5; IR (cm^{-1}): 3854 (w), 3746 (w), 3674 (w), 3387 (m), 3046 (m), 2959 (s), 2823 (m), 2362 (m), 2033 (w), 1699 (w), 1596 (s), 1480 (s), 1362 (m), 1264 (s), 1206 (s), 1119 (m), 1023 (s), 873 (m), 792 (m), 739 (m). HRMS calculated for $C_{58}H_{76}Cl_2NO_4$ [M+H]$^+$: 920.5151, found: 920.5141.

*4.5.15. 2-(5-(2,5-Dichloroanilino)pentyl)tetramethoxy-p-tert-butylcalix[4]arene (**5-N^{Cl}**).* Reagents: **5-Cl·4/3LiBr** (0.925 g, 1.00 mmol); KH (0.120 g, 3.00 mmol); 2,5-dichloroaniline (0.486 g, 3.00 mmol). Yield: 0.683 g (73.0%); ^{1}H NMR: δ 7.33–7.30 (m, 6H), 7.21 (d, 2H, $^4J_{HH}$=2 Hz), 7.14 (d, 1H, 8 Hz), 6.56 (d, 1H, $^4J_{HH}$=2 Hz), 6.51 (dd, 1H, $^3J_{HH}$=8 Hz, $^4J_{HH}$=2 Hz), 4.72 (t, 1H, 7 Hz), 4.54 (t, 1H, 7 Hz), 4.14 (d, 3H, $^2J_{HH}$=12 Hz), 4.01 (s, 6H), 4.00 (s, 6H), 3.49 (d, 3H, $^2J_{HH}$=12 Hz), 3.06 (q, 2H, 7 Hz), 2.10 (q, 2H, 7 Hz), 1.54 (pent, 2H, 7 Hz), 1.39 (pent, 2H, 7 Hz), 1.29 (pent, 2H, 7 Hz), 1.11 (s, 18H), 1.10 (s, 18H); ^{13}C{^{1}H} NMR: δ 151.50, 151.47, 151.4, 149.4, 149.34, 149.32, 139.06, 139.03, 135.6, 135.4, 127.0, 126.6, 126.5, 123.4, 123.3, 111.2, 64.84, 64.80, 45.9, 43.4, 36.3, 35.0, 34.8, 32.7, 31.3, 31.2, 31.15, 31.10, 30.0, 27.4; IR (cm^{-1}): 3847 (w), 3746 (w), 3660 (w), 3422 (w), 3172 (w), 3073 (m), 2958 (s), 2819 (m), 2362 (m), 2034 (w), 1740 (w), 1694 (w), 1596 (s), 1479 (s), 1362 (m), 1260 (s), 1206 (s), 1112 (s), 1022 (s), 872 (m), 803 (m), 738 (m). HRMS calculated for $C_{59}H_{78}Cl_2NO_4$ [M+H]$^+$: 934.5308, found: 934.5269.

4.6. Crystallography

A summary of crystal data and collection parameters for the crystal structure of **4-N^{iPr}** is provided in Table 2. A detailed description of data collection, as well as data solution, is provided below. The ORTEP diagram was generated with the ORTEP-3 software package.[56]

Table 2
Crystal data and collection parameters

Compound	**4-N^{iPr}**
Formula	$C_{64}H_{89}NO_4\cdot 2CH_3CN$
M_r	1018.47
Space group	$P2_1/n$ (#14)
T [K]	140(2)
a [Å]	12.0770(6)
b [Å]	25.390(1)
c [Å]	19.7979(9)
α [°]	90
β [°]	99.752(1)
γ [°]	90
V [Å^3]	5983.0(5)
Z	4
ρ_{calcd} [g cm^{-3}]	1.131
Diffractometer	Siemens SMART
Radiation	Mo Kα (λ=0.71073 Å)
Monochromator	Graphite
Detector	CCD area detector
Scan type, width	ω, 0.3°
Scan speed	30.0 s/frame
No. of reflns measd	Hemisphere
2θ range [°]	2.6–56.7
Crystal size [mm]	0.26×0.14×0.09
No. of reflns measd	68,306
No. of unique reflns	14,929
No. of observations	6282
No. of parameters	706
R, R_w, R_{all}	0.0636, 0.1540, 0.1429
GOF	0.795

X-ray quality crystals were grown from a solution of acetonitrile at −25 °C. A colorless crystalline rod with dimensions 0.26×0.14×0.09 mm was mounted on a pulled glass fiber using Paratone-N hydrocarbon oil. The crystal was transferred to a Siemens SMART[57] diffractometer with a CCD area detector, centered in the X-ray beam, and cooled to 140 K using a nitrogen-flow low-temperature apparatus that had been previously calibrated by a thermocouple placed at the same position as the crystal. An arbitrary hemisphere of data was collected using 0.3° ω-scans that were counted for a total of 30 s per frame. The data was integrated by SAINT[58] to a maximum 2θ of 56.7°, and the final unit cell parameters were determined by a least-squares refinement of 5207 reflections with $I>10\sigma(I)$. Data analysis using Siemens XPREP[59] gave a primitive monoclinic cell and based on the successful solution and refinement of the structure, the space group was determined to be $P2_1/n$ (#14).

Of the 68,306 reflections that comprised the hemisphere, 14,929 were unique (R_{int}=0.3096), and all equivalent reflections were averaged. The structure was solved by direct methods using the SHELXTL[60] software package. The unit cell contained two molecules of acetonitrile. One was located in open space, while the other was localized within the calix[4]arene cone. All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were included in fixed positions. The final cycle of full-matrix least-squares refinement was based on 6282 observed reflections and 706 variable parameters and converged yielding final residuals: R=0.0636, R_{all}=0.1429, and GOF=0.795.

Crystallographic data (excluding structure factors) for the structure in this paper has been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC 734236. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44 (0)1223 336033 or email: deposit@ccdc.cam.ac.uk).

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