Synthesis of Functional Aromatic Multisulfonyl Chlorides and Their Masked Precursors

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The synthesis of functional aromatic bis(sulfonyl chlorides) containing an acetophenone and two sulfonyl chloride groups, i.e., 3,5-bis[4-(chlorosulfonyl)phenyl]-1-acetophenone (**16**), 3,5-bis(chlorosulfonyl)-1-acetophenone (**17**), and 3,5-bis(4-(chlorosulfonyl)phenyloxy)-1-acetophenone (**18**) via a sequence of reactions, involving in the last step the quantitative oxidative chlorination of *S*-(aryl)-*N*,*N*′-diethylthiocarbamate, alkyl- or benzyl thiophenyl groups as masked nonreactive precursors to sulfonyl chlorides is described. A related sequence of reactions was used for the synthesis of the aromatic trisulfonyl chloride 1,1,1-tris(4-chlorosulfonylphenyl)ethane (**24**). 4-(Chlorosulfonyl)-phenoxyacetic acid, 2,2-bis[[[4-(chlorosulfonyl)phenoxyacetyl]oxy]methyl]-1,3-propanediyl ester (**27**), 5,11,17,23-tetrakis(chlorosulfonyl)-25,26,27,28-tetrakis(ethoxycarbonylmethoxy)calix[4]arene (**38**), 5,11,17,23,29,35-hexakis(chlorosulfonyl)-37,38,39,40,41,42-hexakis(ethoxycarbonylmethoxy)calix-[6]arene (**39**), 5,11,17,23,29,35,41,47-octakis(chlorosulfonyl)-49,50,51,52,53,54,55,56-octakis(ethoxy-carbonylmethoxy)calix[8]arene (**40**), 5,11,17,23-tetrakis(*tert*-butyl)-25,26,27,28-tetrakis(chlorosulfonyl phenoxyacetoxy)calix[4]arene (**44**), 5,11,17,23,29,35-hexakis(*tert*-butyl)-37,38,39,40,41,42-hexakis(chlorosulfonylphenoxyacetoxy)calix[6]arene (**45**), and 5,11,17,23,29,35,41,47-octakis(*tert*-butyl)-49,40,51,52,53,54,55,56-octakis(chlorosulfonylphenoxyacetoxy)calix[8]arene (**46**) were synthesized by two different multistep reaction procedures, the last step of both methods consisting of the chlorosulfonation of compounds containing suitable activated aromatic positions. 2,4,6-Tris-(chlorosulfonyl)aniline (**47**) was obtained by the chlorosulfonation of aniline. The conformation of two series of multisulfonyl chlorides i.e., **38**, **39**, **40** and **44**, **45**, **46**, was investigated by ^{1}H NMR spectroscopy. The masked nonreactive precursor states of the functional aromatic multisulfonyl chlorides and the aromatic multisulfonyl chlorides reported here represent the main starting building blocks required in a new synthetic strategy elaborated for the preparation of dendritic and other complex organic molecules.

Introduction

Aromatic sulfonyl chlorides are precursors with extensive uses in organic synthesis.[1] Some of the most notable recent additions to their applications are in the synthesis of ligands for novel catalytic processes[2] and in radical reactions.[3] Functional aromatic multisulfonyl chlorides have been shown to be valuable intermediates for the preparation of molecular receptors with high and unusual selectivity.[4]

We are interested in the design of two classes of aromatic multisulfonyl chlorides. The first one consists of soluble and stable aromatic multisulfonyl chlorides that produce sulfonyl radicals of equal reactivity. These molecules are potential precursors for the construction of the focal point of dendritic molecules. The second class consists of reactive 1,1-disubstituted olefins containing groups that are nonreactive in the presence of radical species and act as precursors to sulfonyl chlorides (i.e., they can be considered masked sulfonyl chlorides). The addition of a sulfonyl or a carbon-centered radical to this 1,1-disubstituted olefin should not propagate a chain

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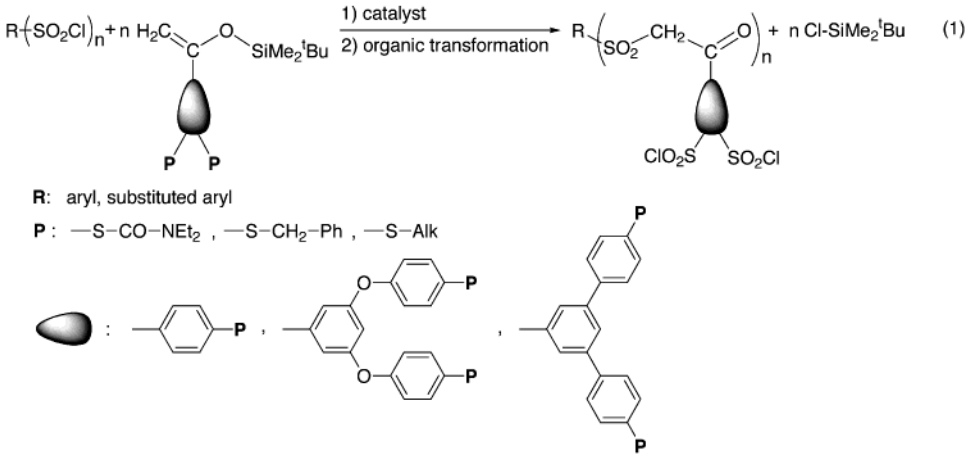
Scheme 1



reaction and the transformation of the nonreactive precursor into the reactive sulfonyl chloride represents the first step toward the generation of a branching point (Scheme 1). A main requirement of both classes of compounds is that the neighboring groups of the sulfonyl chlorides should not affect their reactivity. Aniline, pentaerythritol, 1,1,1-tris(4-hydroxyphenyl)ethane, and *p*-*tert*-butylcalix[*n*]arenes (with $n = 4$, 6, 8) were used as precursors for the synthesis of multisulfonyl chlorides containing three, four, six, and eight sulfonyl chloride groups. The survey of various synthetic options for the second class directed us to acetophenone(s) which in their silyl enol ether form provide access to 1,1-disubstituted olefins[5] of suitable reactivity for our subsequent synthetic endeavor. Therefore, we have considered incorporating in the same compound at least two nonreactive precursor groups to sulfonyl chloride. These precursor groups should tolerate silylation and radical reaction conditions and should be quantitatively transformed into sulfonyl chlorides under mild conditions. After considering various synthetic transformations, we have decided upon *S*-(aryl)-*N*,*N*′-diethylthiocarbamate, thioalkyl, and thiobenzyl groups, as precursor groups to sulfonyl chlorides. They were selected both because they can be transformed into sulfonyl chlorides via oxidative chlorination under mild conditions[6] and because they are accessible as intermediary groups to the thiophenol groups generated from phenols via the Newmann−Kwart rearrangement of the *O*-(aryl)-*N*,*N*′-dialkylthiocarbamates.[7] These precursor groups to sulfonyl chlorides were also of interest to us because they would be accessible in several reaction steps starting directly from phenol groups via a *completely odorless synthesis*. Therefore, the first step of such a synthetic strategy requires the generation of various acetophenones containing at least two phenol groups. These two classes of multifunctional sulfonyl chlorides are the main building blocks required in a new synthetic strategy elaborated in our laboratory for the preparation of dendrimers and of other complex organic molecules.

This manuscript describes the synthesis of three examples of acetophenone derivatives containing two *S*-(aryl)-*N*,*N*′-diethylthiocarbamate, and two alkyl or benzyl thiophenyl, groups as masked, nonreactive precursors to sulfonyl chlorides. It also describes the synthesis of seven novel soluble aromatic multisulfonyl chlorides containing from three to eight sulfonyl chloride groups. The conformational analysis of two series of multisulfonyl chlorides based on various calix[*n*]arenes with $n = 4$, 6 and 8 was investigated by ^{1}H NMR spectroscopy and is also reported.

Results and Discussion

Acetophenone Derivatives Containing *S*-(Aryl)-*N*,*N*′-Diethylthiocarbamate, Benzylthiophenyl, or Alkylthiophenyl as Precursor Groups to Sulfonyl Chlorides. The synthesis of **4** is outlined in Scheme 2. The starting compound **2** was prepared according to a modified literature procedure[8] with an improvement in yield from 69% to 74%. The cross-coupling reaction of **2** and 4-methoxyphenyl boronic acid synthesized from 4-bromomethoxybenzene was performed in toluene under conventional Suzuki reaction conditions,[9a−f] in the presence of $[Pd(PPh_3)_4]$,[10] to produce **3** in 94% yield. The cleavage of the methyl aryl ether group of **3** was accomplished with PhSH/HMPA/K_2CO_3 in 98% yield. A number of reagents routinely used to cleave the primary alkyl aryl ethers,[11a−c] such as BBr_3[12a−d] EtSNa/DMF,[13a−c] TMSI,[14] py-HCl,[15] HBr/AcOH,[16,17] NaCN/DMSO,[18] PhSH/K_2CO_3 (catalytic),[19] etc., were considered for this reaction. Treatment of **3** with BBr_3 or with py-HCl produced **4** in

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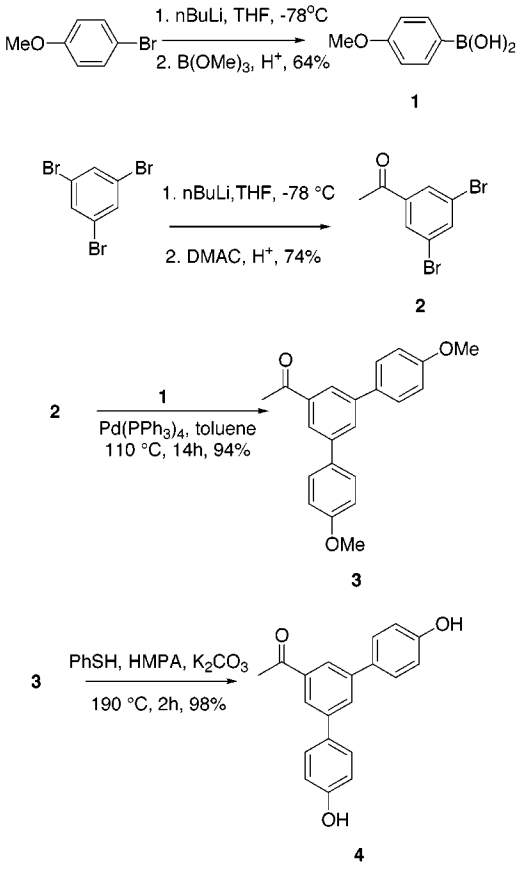
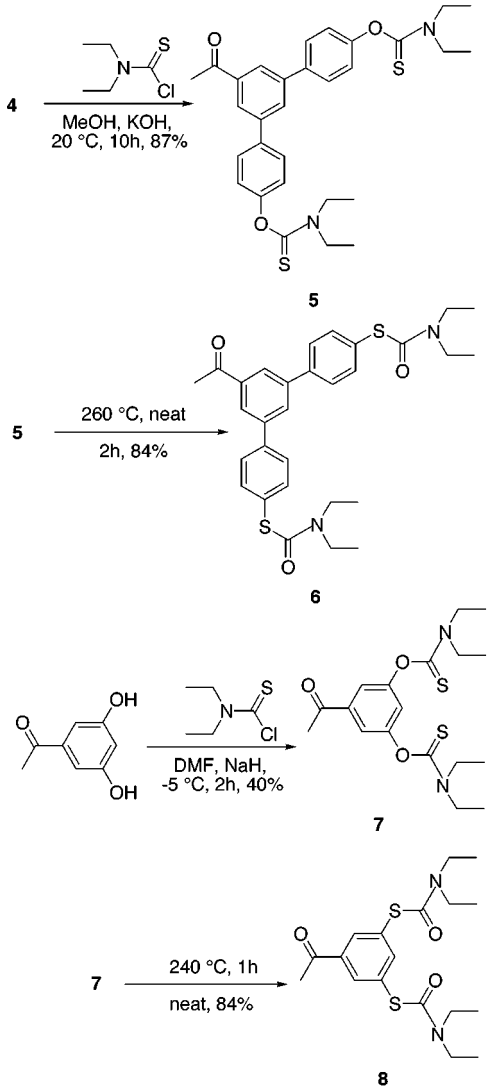
Scheme 2



low yields (40−45%). Treatment of **3** with EtSNa/DMF, TMSI, HBr/AcOH, or NaCN/DMSO did not give the desired product **4**. This is most probably due to the reactivity of the acetophenone group from **3** both under nucleophilic and electrophilic conditions. In our view, the $PhSH/K_2CO_3$ reagent is very mild since it generates only a catalytic amount of the very weak nucleophile potassium phenylthiolate, which is the active reagent for the cleavage of primary alkyl aryl ethers.[19] Therefore, demethylation of **3** was carried out with $PhSH/K_2CO_3$ (5 mol %) in HMPA at 190 °C for 2 h to produce **4** in almost quantitative yield (98%).

Scheme 3 describes the synthesis of **6** and **8** via the Newman−Kwart rearrangement[7] of the corresponding *O*-aryl isomers **5** and **7**. Several methods are available for the esterification involved in the synthesis of *O*-(aryl)-*N*,*N*′-dialkylthiocarbamate by reacting *N*,*N*′-dialkylthiocarbamoyl chloride with the corresponding phenolic precursors in the presence of a base such as DMF/NaH,[20a−c] $DMF/NaOH/K_2CO_3$/PTC (phase transfer catalyst),[21] KOH/MeOH,[22] and quinoline.[23] **5** was synthesized from **4** and *N*,*N*′-diethylthiocarbamoyl chloride using methanolic KOH in MeOH in 87% yield. Although *N*,*N*′-diethylthiocarbamoyl chloride is available commercially, we observed that freshly made *N*,*N*′-diethylthiocarbamoyl chloride produces higher yields than the commercially available reagent. Other reaction conditions, such as DMF/NaH, $DMF/NaOH/K_2CO_3$/PTC, and quinoline, were also investigated but gave low yields. However, when the same reaction conditions, i.e., methanolic KOH, were used to produce **7** from 3,5-dihydroxyacetophenone and *N*,*N*′-diethylthiocarbamoyl chloride, no desired product **7** was obtained. When this reaction was carried out in quinoline at 190 °C[23] or in DMF with $NaOH/K_2CO_3$ under phase transfer-catalyzed reaction conditions, **7** was obtained in less than 10% yield. A modest yield (40%) was obtained when the reaction was carried out in DMF with NaH at −5 °C. The Newman−Kwart rearrangement[7] at 240−260 °C of **5** and **7** in bulk for 2 h (Scheme 3) provided

Scheme 3



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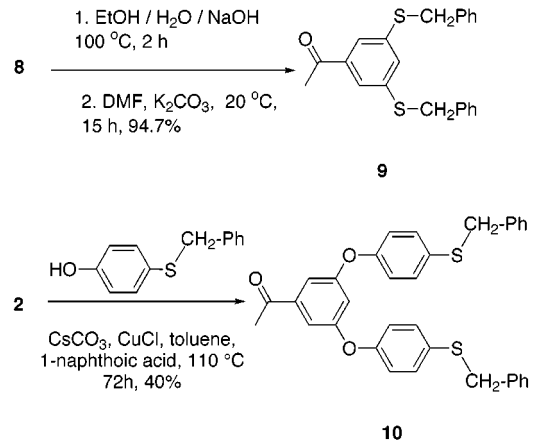
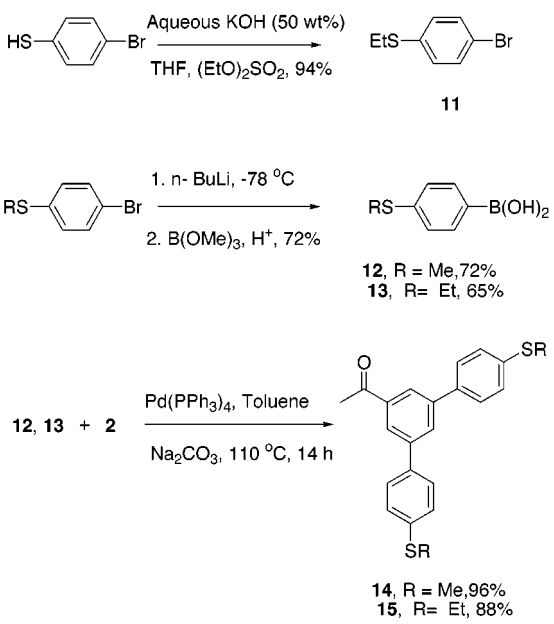
Scheme 4



Scheme 5

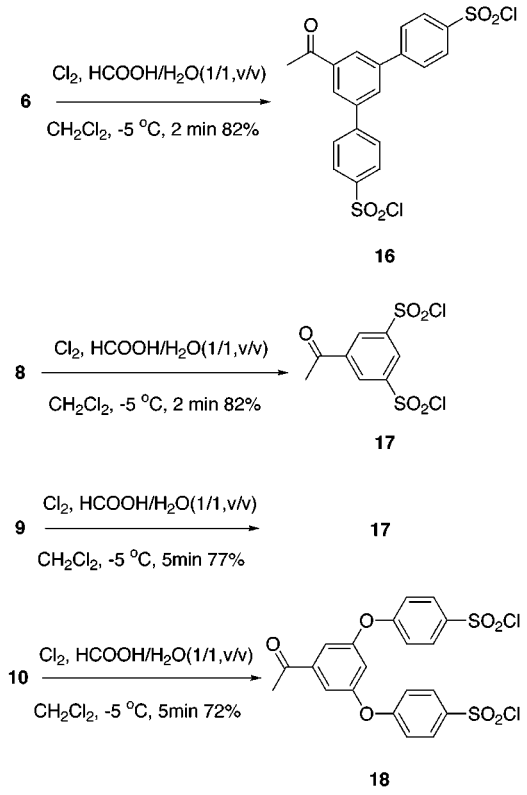


the *S*-(aryl)-thiocarbamates **6** and **8** in 84% to 89% yields.

The synthesis of thiobenzyls **9** and **10** is presented in Scheme 4. These compounds are used for the synthesis of sulfonyl chlorides **17** and **18**. **9** was synthesized in a two-step reaction. In the first step, **8** was hydrolyzed to the corresponding thiol by NaOH in refluxing EtOH in 100% yield. In the second step, the thiol was reacted without any purification with benzyl chloride in DMF at 20 °C using K_2CO_3 to produce **9** in 95% yield. **10** was synthesized by etherification of **2** with 4-thiobenzylphenol using Cs_2CO_3 and CuCl as catalyst in toluene, at 110 °C, for 72 h (40% yield).[24]

14 and **15** were synthesized as shown in Scheme 5. In the first step **11** was synthesized from 4-bromothiophenol in THF using 50 wt % aqueous NaOH and diethyl sulfate as alkylating agent in 94% yield. 4-Bromothioanisole and **11** were then transformed into the corresponding boronic acids by lithiation with n-BuLi followed by reaction with $B(OMe)_3$ in THF to produce **12** and **13** in 65 and 72% yields. In the subsequent step, the boronic acids **12** and **13** were used immediately without any further purification. Suzuki cross-coupling[17a−e] of **2** with **12** and respectively with **13** in toluene at 110 °C produced **14** and **15** in 96−98% yields.

Scheme 6



Scheme 6 summarizes the oxidative chlorination of **6**, **8**, **9**, and **10** to produce the sulfonyl chlorides **16**, **17**, and **18**. Oxidative chlorination with chlorine gas in aqueous CH_3COOH provides sulfonyl chlorides from sulfides[6a−i] and *S*-(aryl)thiocarbamates.[6j] Since the starting compounds **6**, **8**, **9**, and **10** were not soluble in CH_3COOH, all reactions were carried out under heterogeneous conditions in a reaction mixture containing CH_2Cl_2/H_2O/HCOOH. We observed that extremely pure compounds were isolated when the chlorination was carried out in the presence of a 50% HCOOH in H_2O (v/v) instead of a catalytic amount of HCOOH in H_2O. Using these reaction conditions, **6**, **8**, **9**, and **10** were transformed into **16**, **17**, and **18** in 72−82% yields after recrystallization. Reaction of **16**, **17**, and **18** with excess of diethylamine in dry THF produced the desired *N*,*N*′-diethylarenesulfonamides **19**, **20**, and **21** in 77−82% yields (Scheme 7). These compounds were used for analytical purposes when the corresponding sulfonyl chlorides were not sufficiently stable.

Aromatic Multisulfonyl Chlorides. Two different procedures were used for the synthesis of multisulfonyl chlorides. In the first one the sulfonyl chloride group was introduced starting from a phenol group via the sequence of reactions described above. In the second one the sulfonyl chloride group was introduced via direct chlorosulfonation of a suitable activated aromatic group.

The synthesis of trifunctional aromatic sulfonyl chloride **24** is outlined in Scheme 8. **22** was synthesized by the esterification of the commercially available 1,1,1-tris-(4-hydroxyphenyl)ethane with *N*,*N*′-diethylthiocarbamoyl chloride using methanolic KOH in MeOH (72% yield). When this reaction was carried out in quinoline at 190

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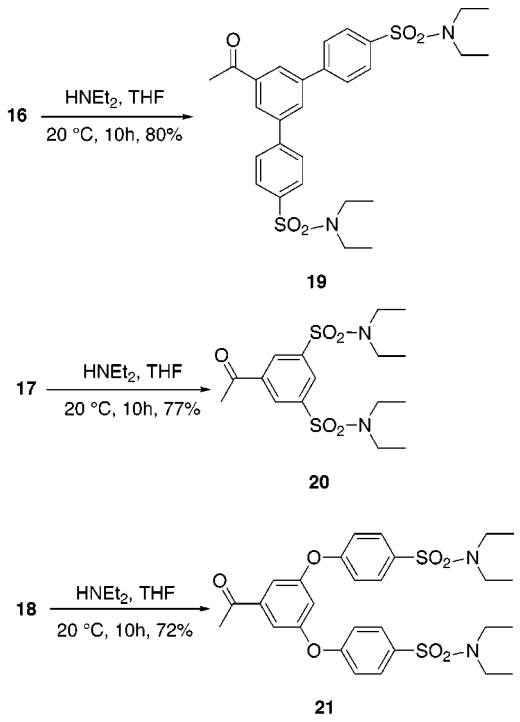
Scheme 7



°C, a lower yield (51%) was obtained. The Newmann−Kwart rearrangement of **22** at 260 °C in bulk for 2 h produced **23** in 89% yield. Oxidative chlorination of **23** in the presence of a catalytic amount of HCOOH produced **24** with a purity of 92−95%. Purification of **24** by recrystallization using different solvents or solvent mixtures was unsuccessful. **24** could not be purified by column chromatography since it reacts with SiO_2 and Al_2O_3. *The only way to obtain pure **24** is to synthesize it without any impurities*. During this investigation, we observed that the chlorination of **24** in the presence of a 50% HCOOH in H_2O (v/v) at −5 °C for 2 min yielded **24** without any impurities (97% yield after recrystallization from benzene). Reaction of **24** with excess of diethylamine produced **25** in 82% yield. Table 1 summarizes the results of oxidative chlorination of different compounds. *S*-(Aryl)-*N*,*N*′-diethylthiocarbamate and thiobenzyl groups are converted into sulfonyl chlorides quantitatively. However, thioalkyl groups are not the best choice as precursors to sulfonyl chlorides since conversion does not exceed 80% even after extended exposure to chlorine gas.

Scheme 9 shows the synthesis of tetrafunctional aromatic sulfonyl chloride **27**. In the first step, pentaerythritol was esterified with 5 equiv of phenoxyacetyl chloride in CH_2Cl_2 at 20 °C for 24 h using Et_3N to produce **26** (89% yield).[25] The use of an equimolecular amount of phenoxyacetyl chloride (i.e., 4 equiv instead of 5) leads to a small amount (1−2%) of incomplete esterification product. Chlorosulfonation of **26** was carried out with $ClSO_3H$ in CH_2Cl_2 at −5 °C to 20 °C for 3 h to produce **27.** It is essential that fresh chlorosulfonic acid of 99% purity is used in this reaction. Being thermally unstable, **27** was purified by fractional precipitation at 20 °C. Reaction of **27** with excess of diethylamine in dry THF yielded the desired **28** (90% yield).

The synthesis of five new calix[*n*]arenes containing 4, 6, and 8 sulfonyl chloride groups, respectively, is summarized in Schemes 10 and 11. These building blocks produced soluble multisulfonyl chlorides with equal reactivity of the resulted sulfonyl chloride groups. Although *p*-*tert*-butyl calix[*n*]arene **29**, **30**, and **31** are commercially available, we synthesized them in our laboratory to obtain samples of higher purity.[26−28] The calix[*n*]arenes **29**, **30**, and **31** were dealkylated by using $AlCl_3$ and phenol in toluene to produce calix[*n*]arenes **32**, **33**, and **34.**[29] The phenolic groups of calix[*n*]arenes **32**, **33**, and **34** were functionalized by etherification or esterification to increase their solubility. The alkylation of **32**, **33**, and **34** with ethyl bromoacetate in the presence of K_2CO_3/KI in refluxing CH_3CN[30] produced calix[*n*]-arenes **35**, **36**, and **37** in 65−70% yields. We have noticed

Scheme 8

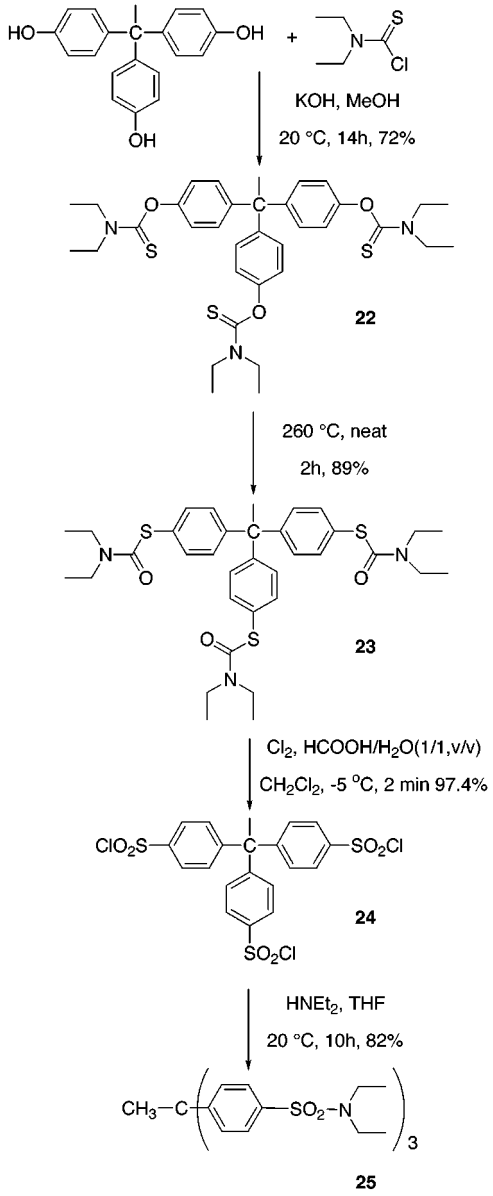


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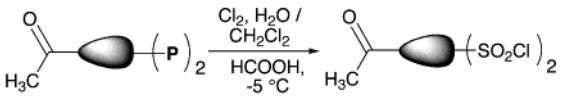
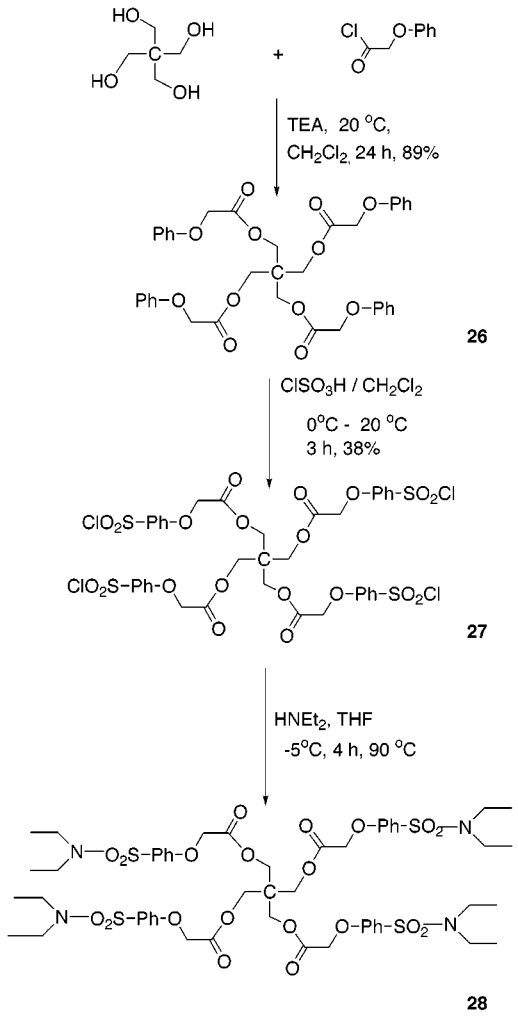
Table 1. Oxidative Chlorination of Various Precursors to Sulfonyl Chloride

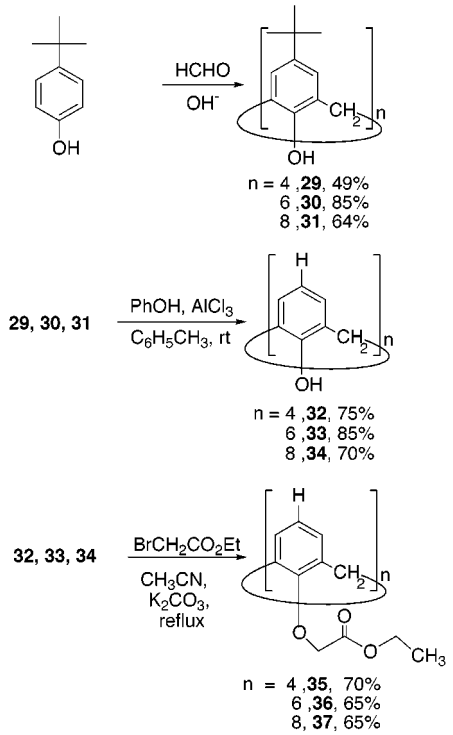


	P	reaction time (min)	conv.(%)	yield (%)
6	—S—CO—NEt_2	2	100	82
8	—S—CO—NEt_2	2	100	82
9	—S—Bn	5	100	77
10	—S—Bn	5	100	72
14	—S—CH_3	15	80	-
15	—S—C_2H_5	15	80	-
23	—S—CO—NEt_2	2	100	97

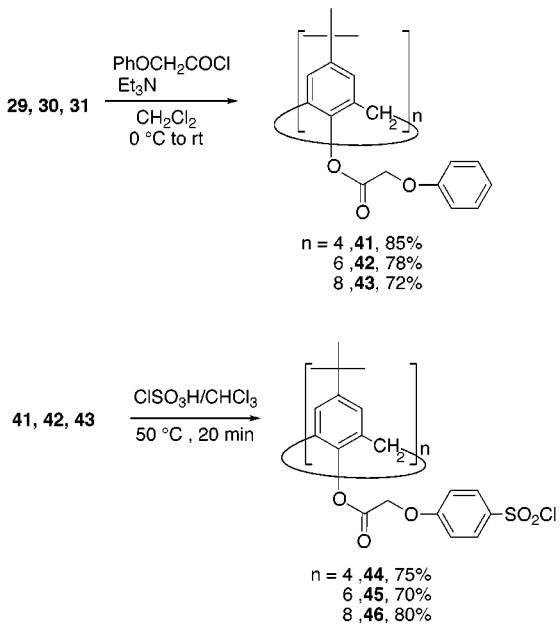
Scheme 9



Scheme 10



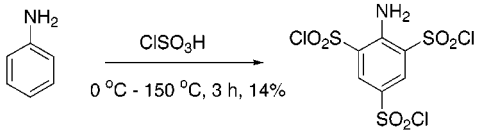
Scheme 11



that the chemical shifts reported for **35** seem to correspond to a single conformer.[30] Our ^{1}H NMR and 2D-NMR COSY analysis shows that **35** consists of a mixture of conformers. Moreover, in our case, product **35** is liquid at 23 °C, while literature reports mp 108−109 °C.[30] Careful analytical investigation and multiple duplication of the synthesis led us to conclude that we indeed obtained the cyclic calix[4]arene **35**.

In an alternate procedure, the phenolic groups of calix[*n*]arenes **29**, **30**, **31** were esterified with phenoxyacetyl

Scheme 12



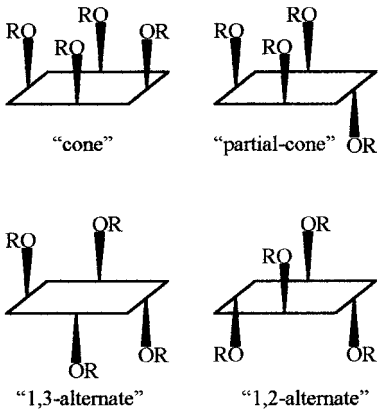
47

chloride using Et_3N in CH_2Cl_2 at 20 °C, to generate the new series of functional calix[*n*]arenes **41**, **42**, and **43** in 80−90% yields (Scheme 11). Reaction of calix[*n*]arenes **35**, **36**, and **37** with chlorosulfonic acid in $CHCl_3$ at −10 °C for 10 min and at 50 °C for 20 min afforded the chlorosulfonyl calix[*n*]arenes **38**, **39** and **40** in 50−62% yields. Although **38** was previously reported,[31] **39** and **40** are new compounds. The melting point of our compound **38** (108−109 °C) agrees with the literature,[31] thus reconfirming that its precursor **35** has the correct structure. Introduction of chlorosulfonyl groups at the lower rim of calix[*n*]arenes was accomplished by the chlorosulfonation of phenoxy groups present in the lower rim of **41**, **42**, **43**. Reaction of **41**, **42**, and **43** with chlorosulfonic acid in $CHCl_3$ at −10 °C for 10 min and at 50 °C for 20 min afforded chlorosulfonyl calix[*n*]arenes **44**, **45**, and **46** in 70−80% yields (Scheme 11). Compounds **44**, **45**, and **46** represent a new series of soluble chlorosulfonated calix[*n*]arenes. We have noticed that the incomplete chlorosulfonation can be *qualitatively* established by the occurrence of foaming when a few drops of the reaction mixture are poured over ice−water. This observation facilitated the elaboration of the reaction conditions for a quantitative chlorosulfonation.

Functional Aromatic Multisulfonyl Chloride. A single example of trifunctional sulfonyl chloride compound containing an amine group i.e., **47** was synthesized (Scheme 12). Although its synthesis was available in the literature,[32a] we improved the reaction conditions to obtain **47** in high purity.[33a−c]

Conformational Analysis of Compounds 35−46 by NMR Spectroscopy. Calixarenes have many conformers due to the rotational modes of individual arene units that are able to undergo clockwise and respectively counterclockwise through-the-annulus rotation.[34] The simplest case is calix[4]arene that can adopt four stable conformations: cone, partial-cone, 1,2-alternate, and 1,3-alternate (Scheme 13). Each of these conformers are fluctuating, and it is accepted that the "cone" conformation is rapidly interconverting between two flattened cone conformations, or "pinched cone".[35] The ratio between the four conformers is highly dependent on the temperature, the size and functionality of the substituent, and the presence of solvent and other guest molecules.[36] Previous publications have shown that the ring-inversion process

Scheme 13



is slowed or even inhibited when the macrocycle has substituents able to increase the rotational barrier,[34] and it was shown that the through-the-annulus exchange is impeded when substituents on the lower rim are bulkyer than ethyl. Moreover, functionalization of the upper rim results in complete immobilization of the calix[4]arene conformation which can be observed by NMR spectroscopy.[37]

The same type of considerations hold for larger cavities, i.e., calix[*n*]arenes with $n = 6, 8$, with the difference that the conformational freedom of the macrocycle increases significantly.[34,35] The number of theoretically possible conformers increases dramatically, and their description is beyond the purposes of this paper. The dynamics of these molecules can be quantified in terms of rate of exchange or coalescence temperature, T_c, and inversion barrier, ΔG. Such parameters can be determined by variable temperature NMR experiments that encompass the coalescence and discrete regimes.

We have employed 1D-NMR (^1H, ^{13}C) and 2D-NMR (COSY, HETCOR, NOESY) techniques for the conformational studies of compounds **35** through **46.** As expected, we generally observed an increase of conformational freedom with the size of the calixarene cavity and an increase in the stability of the conformers with introduction of bulky substituents on the calixarene rim. Nevertheless, each compound displays specific features, as follows. Compound **35** presents a mixture of "cone" with "1,2-alternate" (1:3) as detected in DMSO-d_6 at 21 °C, as opposed to $CDCl_3$, where a majoritary "partial cone" conformation is observed. The corresponding substituted compound, **38**, displays two conformers, "partial cone" and "1,3-alternate" in DMSO-d_6 at 21 °C. An increase in the temperature does not result in conformational exchange; the conformations are locked. Similar findings are provided by 2D-NMR COSY and ^1H NMR spectroscopy in $CDCl_3$ at 21 °C (Figure 1).

An averaged conformation is obtained for compound **36** in DMSO-d_6 between 21 and 90 °C. In $CDCl_3$, the same averaged conformation is observed, due to a very low coalescence temperature. Since the substitution changes the conformational features, compound **39** has the coalescence temperature $T_c = 21$ °C in DMSO-d_6 and an averaged conformation is obtained only at 90 °C. In $CDCl_3$, the ^1H NMR spectrum is similar, despite a lower solubility.

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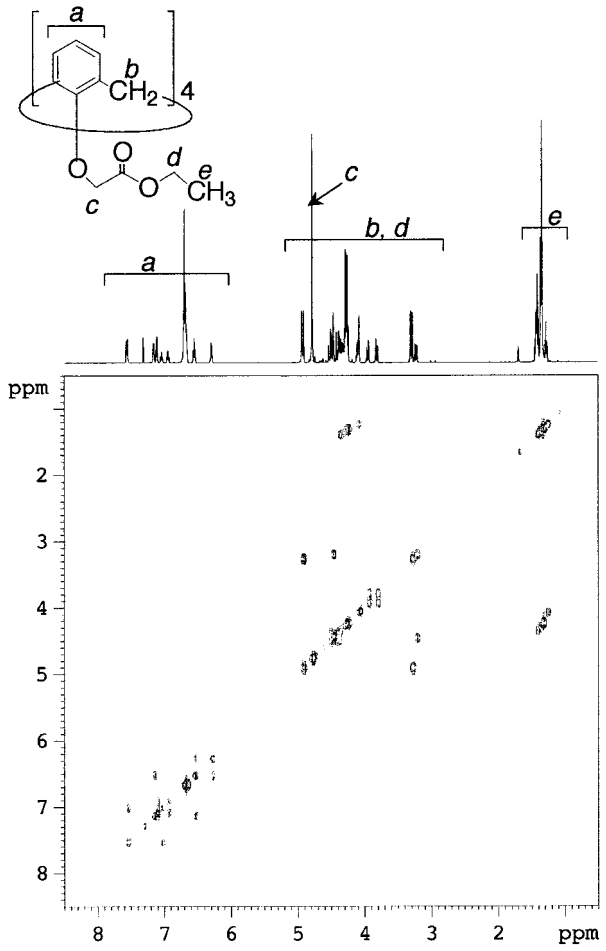

Figure 1. 200 MHz ^{1}H- and COSY-NMR spectra of compound **38** in $CDCl_3$ at 21 °C.

For compound **37**, no discrete conformations are observed in DMSO-d_6 between 21 and 90 °C or in $CDCl_3$ between 21 and 50 °C. Nevertheless, investigations of the substituted compound **40** reveals discrete conformations up to 50 °C in $CDCl_3$ and up to 170 °C in DMSO-d_6. The change of solvent does not have much influence on the features of the spectrum. Prolonged exposure of **40** at 170 °C in DMSO-d_6 leads to decomposition.

Fast conformational exchange is observed with increasing the temperature for compound **41** in DMSO-d_6 between 21 and 160 °C. Nevertheless, several different conformations are still observed at 160 °C. Compound **44** presents discrete conformations in DMSO-d_6 with no exchange between 21 and 170 °C. Extended exposure at 170 °C in DMSO-d_6 leads to decomposition.

Discrete conformations are also detected in DMSO-d_6 between 21 °C and 170 °C for compounds **42** and **45**. A tendency to exchange faster is seen with increasing the temperature, yet several conformations are still observed at 170 °C. As observed for most of these chlosulfonated calixarenes, extended exposure of compound **45** at 170 °C in DMSO-d_6 leads to decomposition.

For compound **43**, ^{1}H NMR spectroscopy in DMSO-d_6 at 21 °C shows broad signals corresponding to a slow conformational exchange. At 90 °C, sharp signals are obtained, corresponding to an averaged conformation. When DMSO-d_6 was replaced with $CDCl_3$, the conformational mobility was drastically reduced (Figure 2). Consequently, the signals are broad up to 55 °C and T_c is 35 °C. When the temperature is lowered to −25 °C, the conformational exchange becomes very slow, and the spectrum displays discrete signals for two conformers, most probable the "1,3,5-alternate" and "1,4-alternate". The exchange barrier $\Delta G = 14.63$ kcal/mol. Further decrease in temperature to −60 °C did not change the features of the spectrum. Compound **46** shows a faster conformational exchange in DMSO-d_6 and sharp signals corresponding to an averaged conformation are observed at 90 °C. In $CDCl_3$, the conformational studies are more difficult than for the precursor **43**, since the functionalization of the upper rim reduces the conformational freedom. Multiple conformations are visible from −60 °C to 21 °C, and conformational exchange does not produce an averaged structure up to 60 °C.

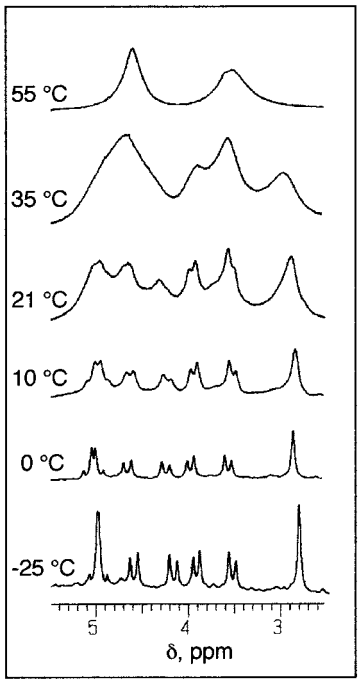

Figure 2. ^{1}H NMR spectra of compound **43** in $CDCl_3$ at various temperatures.

Experimental Section

Materials. Formaldehyde (solution 37%, Fisher Scientific) was used as received. Acetone (ACS reagent, Fisher Scientific) was dried over K_2CO_3 and distilled. THF (ACS reagent, Fisher Scientific) was dried over sodium/benzophenone ketyl and distilled. NEt_3 and $NHEt_2$ were dried over KOH, distilled, and stored over KOH. CH_2Cl_2 was distilled from CaH_2. CuCl (Fisher, 96%) was purified by grinding and stirring with H_2SO_4 (1 N), followed by filtration and successive washing with glacial HOAc (four times), EtOH, and Et_2O.[38] The white CuCl powder was dried at 100 °C for 30 min and stored in an airtight bottle. Hexamethylphosphoramide (HMPA) and *N*,*N*′-dimethylacetamide (DMAC) were distilled over CaH_2 at reduced pressure. 4-Bromothioanisole, 4-bromoanisole, chlorine pentaerythritol, 1,1,1-tris(4-hydroxyphenyl)ethane, and chlorosulfonic acid (all of the highest purity available from Aldrich) were used as received. Thiophenol (Aldrich, 97%) was dried over Na and distilled. Aniline (Aldrich, 99.5%) was distilled over KOH and stored in the dark under N_2. 4-Thiobenzylphenol,[39] *N*,*N*′-diethylthiocarbamoyl chloride,[40] and $Pd(PPh_3)_4$[10] were prepared according to literature procedures.

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General Methods. ^{1}H NMR (200, 250, 300, and 500 MHz) and ^{13}C NMR (50, 90 and 106 MHz) spectra were recorded on Bruker spectrometers at 20 °C in $CDCl_3$ with tetramethylsilane (TMS) internal standard. Melting points were determined by using a Thomas-Hoover capillary melting point apparatus and are uncorrected. Chromatographic purification was conducted using 200−400 mesh silica gel obtained from Natland International Corporation, Morrisville, NC. The purity was determined by a combination of thin-layer chromatography (TLC) on silica gel plates (Kodak) with fluorescent indicator, high-pressure liquid chromatography (HPLC), ^{1}H and ^{13}C NMR, mass spectrometry, and elemental analysis. HPLC experiments were carried out by using a Perkin-Elmer Series 10 high-pressure liquid chromatograph equipped with an LC-100 column oven (40 °C), a Nelson Analytical 900 Series integrator data station, a Perkin-Elmer 785A UV/Vis Detector (254 nm), and a Varian STAR 9040 RI Detector. The HPLC column was PL gel (5 μm, 100 Å). THF (Fisher, HPLC-grade) was used as eluent at a flow rate of 1 mL/min. The elemental analysis (C, H, N) were performed on Perkin-Elmer (Model 2400) elemental analyzer. The elemental analysis (C, H, S, Cl) for compounds **38**, **39**, **40**, and **47** were performed by M−H−W Laboratories, Phoenix, AZ. Mass spectra were run by direct sample introduction on a LCMS (Micromass) platform (electron spray ionizer, electron energy 70 eV).

(4-Methoxyphenyl)boronic Acid (1).[41] A three-necked 1 L flask fitted with two dropping funnels, magnetic stirring bar, and low-temperature thermometer was charged with 4-bromoanisole (50.0 g, 0.267 mol) under N_2. Dry THF (500 mL) was added, and the solution was cooled with a dry ice−acetone bath. To this solution was added *n*-butyllithium (166.8 mL of a 1.6 M solution, 0.267 mol) dropwise through the first dropping funnel. The solution was stirred at −78 °C for 2 h whereupon trimethyl borate (41.61 g, 0.40 mol) dissolved in 50 mL of dry THF was added dropwise through the second dropping funnel. The solution was allowed to warm to room temperature overnight. The reaction was quenched with dilute HCl (20%, 400 mL), and the reaction mixture was concentrated at 30 °C to 50% of its original volume by rotary evaporation and poured into H_2O. The resulted biphasic solution was extracted with Et_2O (2 × 200 mL). The ethereal solution was washed twice with H_2O and concentrated by rotary evaporation. The crude product (viscous liquid) was dissolved in 10% aqueous NaOH (500 mL) and extracted with Et_2O to remove liquid byproducts. The clear basic aqueous phase was collected and acidified by 10% HCl at 0 °C. **1** was collected as a white solid powder by filtration and washed with H_2O several times to remove HCl. **1** was dried at 20 °C under vacuum and used without further purification (25.96 g, 64%). mp 209−210 °C (lit.[4] 206−207 °C). ^{1}H NMR (200 MHz, CD_3COCD_3): δ 7.8−7.6 (d, 2H, J = 8.59), 7.0−6.8 (m, 4H), 3.8 (s, 3H). ^{13}C NMR (90 MHz, CD_3COCD_3): δ 137.2, 135.6, 135.84, 124.35, 112.97, 54.81.

3,5-Dibromoacetophenone (2)[8]**.** A three-necked 1 L flask fitted with two dropping funnels, magnetic stirring bar, and low-temperature thermometer was charged with 1,3,5-tribromobenzene (20.0 g, 63.4 mmol) under N_2. Dry Et_2O (500 mL) was added, and the solution was cooled with a dry ice−acetone bath. To this solution was added *n*-butyllithium (39.6 mL of a 1.6 M solution, 63.4 mmol) dropwise through the first dropping funnel. The solution was stirred at −78 °C for 2 h whereupon DMAC (6.06 g, 69.6 mmol) dissolved in 50 mL of dry Et_2O was added dropwise through the second dropping funnel. The solution was allowed to warm to room temperature overnight. The reaction was quenched with dilute HCl (10%, 350 mL). The organic layer was separated, washed with H_2O (two times) and brine, and dried over $MgSO_4$. The solvent was removed at reduced pressure, and the residue was recrystallized from 95% EtOH to yield 13 g (74%) of 3,5-dibromoacetophenone. mp 61−63 °C (lit.[5] 61−63 °C). ^{1}H NMR (200 MHz, $CDCl_3$): δ 8.00 (s, 2H), 7.85 (s, 1H), 2.59 (s, 3H); ^{13}C NMR (90 MHz, $CDCl_3$): δ 195.1, 139.4, 138, 130.2, 123.6, 26.5. R_f : 0.52 (hexanes/EtOAc = 9/1).

3,5-Bis(4-methoxyphenyl)-1-acetophenone (3). A three-necked 500 mL flask fitted with a magnetic stirring bar, condenser, and N_2 inlet was charged with 3,5-dibromoacetophenone (17.0 g, 61.2 mmol) and freshly prepared Pd-$(PPh_3)_4$[10] (6.93 g, 6.0 mmol) under N_2. Solutions of **1** (20.44 g, 134.5 mmol) in EtOH (100 mL) and of Na_2CO_3 (2 M, 100 mL) in H_2O were prepared and deoxygenated with a stream of N_2. These two solutions and 300 mL of deoxygenated toluene were added to the reaction vessel, and the mixture was refluxed under N_2 for 14 h. The reaction mixture was poured into a mixture of 300 mL of H_2O and 500 mL of ether, and the two phases were separated. The aqueous phase was washed with Et_2O, and the organic phases were combined and washed with 1 M NaOH followed by brine. The ethereal solution was dried over $MgSO_4$ and concentrated by rotary evaporation. The crude product was passed through 500 g of silica gel using Et_2O as eluent, and the resulting solid was recrystallized from CH_2Cl_2/MeOH to produce 22 g of 3,5-bis(4-methoxyphenyl)-1-acetophenone as white crystals (93.93%). Purity: 99.99% (HPLC). mp 103−105 °C. ^{1}H NMR (200 MHz, $CDCl_3$): δ 8.10 (s, 2H), 7.85 (s, 1H), 7.7−7.5 (d, 4H, J = 10 Hz), 7.1−6.9 (d, 4H, J = 10 Hz), 3.87 (s, 6H), 2.69 (s, 3H); ^{13}C NMR (90 MHz, $CDCl_3$): δ 198.38, 159.71, 141.91, 138.2, 132.84, 129.78, 128.52, 128.41, 125.02, 114.56, 114.43, 55.49, 27.03. R_f: 0.12 (hexanes/EtOAc = 9/1).

3,5-Bis(4-hydroxyphenyl)-1-acetophenone (4). A two-necked 250 mL flask fitted with a magnetic stirring bar and N_2 inlet was charged with **3** (19.8 g, 59.6 mmol), thiophenol (13.4 mL, 131 mmol), K_2CO_3 (0.86 g, 6.25 mmol), and 45 mL of HMPA under N_2. The reaction mixture was heated at 190 °C for 2 h whereupon reaction was completed (TLC). The reaction mixture was cooled to 20 °C and poured into a 10% aqueous KOH (300 mL) solution. This aqueous phase was extracted with Et_2O (2 × 200 mL) to remove thioanisole from the reaction mixture. The clear basic aqueous phase was collected and acidified at 0 °C and then washed with EtOAc (2 × 300 mL). The combined organic phase was washed several times with H_2O and finally with brine. The EtOAc solution was dried over $MgSO_4$ and concentrated by rotary evaporation. The crude product was recrystallized from EtOAc/hexanes to yield 17.76 g of 3,5-bis (4-hydroxyphenyl)-1-acetophenone as light yellow crystals (98%). mp 208−210 °C. Purity: 99.99% (HPLC). ^{1}H NMR (200 MHz, $CDCl_3$ containing one drop of DMSO-d_6): δ 7.8 (d, 2H, J = 1.65 Hz), 7.65 (t, 1H, J = 1.62 Hz), 7.32−7.2 (d, 4H, J = 6.12 Hz), 6.6−6.7 (d, 4H, J = 6.8 Hz), 4.5 (s, 2H) 2.49 (s, 3H). ^{13}C NMR (90 MHz, $CDCl_3$ containing one drop of DMSO-d_6): δ 198.58, 157.2, 141.86, 137.77, 131.32, 129.28, 128.22, 128.08, 124.31, 115.97, 115.88, 26.81. R_f: 0.58 (hexanes/EtOAc = 5/5).

3,5-Bis(*O*-phenyl 4-*N*,*N*′-diethylthiocarbamate)acetophenone (5). A two-necked 100 mL flask fitted with N_2 inlet and magnetic stirring bar was charged with KOH (0.944 g, 16.9 mmol) and 10 mL of MeOH. When all KOH dissolved in MeOH, **4** (1.72 g, 5.64 mmol) was added portionwise under N_2. The reaction was continued for 3 h at 20 °C with stirring whereupon 50 mL of additional MeOH was added to the reaction mixture, and then solid *N*,*N*′-diethylthiocarbamoyl chloride (2.56 g, 16.9 mmol) was added in one portion. After the reaction was stirred for 10 h, the precipitate was collected by filtration and washed with MeOH/H_2O (2 × 100 mL). A white solid (2.6 g, 87%) was obtained after recrystallization from CH_2Cl_2/MeOH. mp 169−171 °C. Purity: 99.99% (HPLC). ^{1}H NMR (200 MHz, $CDCl_3$): δ 8.13 (s, 2H), 7.9 (s, 1H), 7.8−7.6 (d, 4H, J = 8.0 Hz), 7.2−7.1 (d, 4H, J = 8.0 Hz) 4.0−3.8 (q, 4H, J = 6.0 Hz), 3.8−3.6 (q, 4H, J = 6.0 Hz), 2.7 (s, 3H), 1.4−1.2 (t, 12H, J = 8.0 Hz). ^{13}C NMR (90 MHz, $CDCl_3$): δ 198.07, 186.7, 153.95, 141.58, 138.18, 137.82, 130.63, 128.21, 128.13, 126.04, 126.0, 123.53, 123.38, 48.55, 44.45, 27.04, 13.67, 11.93. R_f: 0.20 (hexane/EtOAc = 8/2).

3,5-Bis(*S*-phenyl 4-*N*,*N*′-diethylthiocarbamate)acetophenone (6). A two-necked 50 mL flask fitted with N_2 inlet

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(43) Wong, M. S.; Nicound, J. F. *Tetrahedron Lett.* **1993**, 8237.

and magnetic stirring bar was charged with **5** (2.0 g, 3.7 mmol) and was heated in bulk at 260 °C for 2 h under N_2. After cooling to room temperature, the crude solid was passed through 50 g of silica gel using 30% EtOAc in hexanes as eluent. The resulting solid was recrystallized from MeOH to yield 1.68 g (84%) of **6**. mp 128−130 °C. Purity: 99.99% (HPLC). ^{1}H NMR (200 MHz, $CDCl_3$): δ 8.09 (d, 2H, J = 1.8 Hz), 7.91 (t, 1H, J = 1.6 Hz), 7.7−7.5 (d, 8H, J = 8.0 Hz), 3.5−3.3 (q, 8H, J = 8.0 Hz), 2.63 (s, 3H), 1.4−1.1 (br, 12H). ^{13}C NMR (90 MHz, $CDCl_3$): δ 197.9, 165.53, 141.73, 140.84, 138.30, 137.34, 136.40, 136.34, 130.62, 128.85, 127.81, 126.38, 126.32, 42.53, 27.03, 26.99, 13.97, 13.27. R_f: 0.54 (hexanes/EtOAc = 5/5).

***O*-Acetophenone 3,5-Bis(*N*,*N*′-diethylthiocarbamate) (7).** A three-necked flask fitted with dropping funnel, N_2 inlet, and magnetic stirring bar was charged with 3,5-dihydroxyacetophenone (10.0 g, 65.7 mmol) and 100 mL of dry DMF under N_2. After cooling to −5 °C (ice and NaCl), NaH (3.15 g, 131 mmol) in 25 mL of DMF (slurry) was added to the reaction mixture with such a rate that the temperature of the reaction mixture remained below 0 °C. After the addition was complete, stirring was continued for 3 h at −5 °C whereupon *N*,*N*′-diethylthiocarbamoyl chloride (19.93 g, 131.4 mmol) was added portionwise as solid. The solution was allowed to warm to 20 °C, and stirring was continued for another 2 h. The reaction mixture was poured into a mixture of 300 mL of H_2O and 300 mL of EtOAc, and the two phases were separated. The aqueous phase was washed with EtOAc, and the organic phase was washed with 1 M NaOH followed by brine. The EtOAc solution was dried over $MgSO_4$ and concentrated by rotary evaporation. The crude product was purified by column chromatography (silica gel and 10% EtOAc in hexanes as eluent), and the resulting material was recrystallized from MeOH to yield 10 g (40%) of **7**. mp 124−126 °C. Purity: 99.99% (HPLC). ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.6−7.5 (d, 2H, J = 2.17 Hz), 7.0−7.1 (t, 1H, J = 2.21 Hz), 3.95−3.8 (q, 4H, J = 7.17 Hz), 3.8−3.6 (q, 4H, J = 7.17 Hz), 2.59 (s, 3H), 1.4−1.1 (t, 12H, J = 7.09 Hz). ^{13}C NMR (90 MHz, $CDCl_3$): δ 196.08, 185.94, 154.08, 138.14, 123.09, 122.95, 120.50, 120.36, 48.52, 44.46, 26.8, 13.6, 11.77. R_f: 0.78 (hexanes/EtOAc = 5/5).

***S*-Acetophenone 3,5-Bis(*N*,*N*′-diethylthiocarbamate) (8).** A two-necked 50 mL flask fitted with N_2 inlet and magnetic stirring bar was charged with **7** (2.0 g, 3.7 mmol) and heated at 240 °C for 1 h under N_2. After cooling, the crude solid was passed through 50 g of silica gel using 30% EtOAc in hexanes as eluent. The resulting product was recrystallized from MeOH to yield 1.68 g (84%) of **8** as white crystals. mp 73−75 °C. Purity: 99.99% (HPLC). ^{1}H NMR (200 MHz, $CDCl_3$): δ 8.6 (s, 2H,), 8.4(s,), 3.4−3.1 (q, 4H, J = 7.15 Hz), 2.7 (s, 3H), 1.3−1.1 (t, 12H, J = 7.09 Hz). ^{13}C NMR (90 MHz, $CDCl_3$): δ 196.61, 164.64, 146.66, 137.93, 136.02, 130.49, 42.54, 26.82, 13.92, 13.22 R_f: 0.50 (hexanes/EtOAc = 5/5).

3,5-Bis(thiobenzyl)-1-acetophenone (9). To a mixture of 3.0 g (9.2 mmol) of **8** and 40 mL of ethanol was added 2.0 g (50 mmol) of NaOH dissolved in 5 mL of H_2O and heated at 100 °C for 2 h. The reaction mixture was cooled to 20 °C and poured into H_2O. The aqueous phase was acidified by 10% HCl at 0 °C and extracted with Et_2O (2 × 100 mL). The ethereal phase was washed several times with water and finally with brine. Drying ($MgSO_4$) and complete evaporation of Et_2O gave an oily residue. To this were added DMF (50 mL) and K_2CO_3 (8.37 g, 60.6 mmol). The reaction mixture was deoxygenated with a stream of N_2 with gentle stirring for 20 min, and benzyl chloride (2.55 g, 20.2 mmol) was added through a syringe under N_2. The reaction was continued for 15 h at 20 °C. The reaction mixture was poured into a mixture of cold 10% HCl (200 mL) and 200 mL of Et_2O, and the two phases were separated. The aqueous phase was washed with Et_2O (100 mL), and the organic phases were combined and washed with H_2O (2 × 200 mL) followed by brine. Drying ($MgSO_4$) and evaporation gave an oily residue. Purification by column chromatography (silica gel, 10% EtOAc in hexanes) gave **9** as a light yellow oil (3.8 g, 94.7%). Purity: 99.99% (HPLC). ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.6 (s, 2H), 7.1−7.4 (m, 11H), 4.1 (s, 4H), 2.4(s, 3H), 2.59 (s, 3H). ^{13}C NMR (90 MHz, $CDCl_3$): δ 197.2, 138.11, 137.78, 136.85, 134.29, 129.04, 128.77, 127.6, 127.18, 38.77, 26.78. R_f: 0.96 (hexanes/EtOAc = 5:5).

3,5-Bis(4-thiobenzylphenyloxy)-1-acetophenone (10). A two-necked 250 mL flask equipped with a N_2 inlet and a magnetic stirring bar was charged with 4-thiobenzylphenol (11.0 g, 50.9 mmol), **2** (4.71 g, 16.9 mmol), Cs_2CO_3 (16.6 g, 50.9 mmol), CuCl (0.1 g, 1.0 mmol), 1-naphthoic acid (8.75 g, 50.9 mmol), EtOAc (0.176 g, 2.01 mmol), 8 g of activated 4 Å dust, and 20 mL of dry toluene successively under N_2. The reaction mixture was heated for 72 h at 110 °C with gentle stirring. After cooling to 20 °C, the reaction mixture was poured into a mixture of 300 mL of H_2O and 300 mL of EtOAc, and the two phases were separated. The aqueous phase was washed with EtOAc, and the organic phases were combined and washed with 1 M NaOH followed by brine. The EtOAc solution was dried over $MgSO_4$ and concentrated by rotary evaporation. The crude product was purified by column chromatography using silica gel and 10% EtOAc in hexanes as eluent to produce light yellow crystals (3.34 g, 40%) after recrystallization from CH_2Cl_2/MeOH. mp 101−102 °C. Purity: 99.99% (HPLC). ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.4−7.1 (m, 16H,), 6.85−7.1 (d, 4H, J = 8.25 Hz), 6.6−6.7 (t, 1H, J = 1.49 Hz) 4.1 (s, 4H) 2.5 (s, 3H). ^{13}C NMR (90 MHz, $CDCl_3$): δ 196.82, 158.93, 155.36, 139.92, 137.63, 133.20, 129.03, 128.64, 127.60, 127.37, 119.92, 113.38, 112.87, 40.33, 26.95. R_f: 0.78 (hexanes/EtOAc = 5/5)

4-Bromo-1-thioethoxy-benzene (11).[38] To a mixture of 15.0 g (79.33 mmol) of 4-bromothiophenol and 100 mL of THF was added 25 mL (50 wt %) of aqueous NaOH under N_2. Diethyl sulfate (12.23 g, 79.33 mmol) was added dropwise through a syringe with vigorous stirring, and the reaction was heated at 100 °C for 1 h. The reaction mixture was cooled to 20 °C and poured into 500 mL of ice/H_2O. The aqueous phase was acidified by 10% HCl at 0 °C and extracted with Et_2O (2 × 200 mL). The ethereal phase was washed several times with water and finally with brine. Drying ($MgSO_4$) and complete evaporation of Et_2O gave an oily residue. Vacuum distillation (62−65 °C, 0.5 Torr) gave 16.2 g (94%) of **11** as a colorless liquid. Purity: 99.99% (HPLC). ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.5−7.4 (d, 2H, J = 9.25 Hz), 7.2−7.1 (d, 2H, J = 8.69 Hz) 3.0−2.8 (q, 2H, J = 7.31 Hz), 1.3−1.1 (t, 3H, J = 7.30 Hz). ^{13}C NMR (90 MHz, $CDCl_3$): δ 136.05, 132.25, 130.52, 119.58, 27.78, 14.38.

(4-Thiomethoxyphenyl)boronic Acid (12).[39] This compound was synthesized from (4-bromophenyl)thioanisole using a similar procedure as the one used for **1.** Starting from 10.0 g (49.2 mmol) of (4-bromophenyl)thioanisole, 5.95 g (72%) of **12** was obtained. mp 211−213 °C. ^{1}H NMR (200 MHz, CD_3COCD_3): δ 7.8−7.9 (d, 2H, J = 8.27 Hz), 7.2−7.1 (d, 2H, J = 7.46 Hz) 7.0 (s, 2H), 2.9 (s, 3H).^{13}C NMR (90 MHz, CD_3COCD_3): δ 142.39, 136.04, 135.5, 125.56, 14.82.

(4-Thioethoxyphenyl)boronic Acid (13). This compound was synthesized from **11** using a similar procedure as the one used for **1**. Starting from 15.28 g (70.37 mmol) of **11**, 8.4 g (66%) of **13** was obtained. mp 132−134 °C. ^{1}H NMR (200 MHz, CD_3COCD_3): δ 7.8−7.9 (d, 2H, J = 8.77 Hz), 7.2−7.1 (d, 2H, J = 7.96 Hz) 6.6 (s, 2H),) 3.1−2.9 (q, 2H, J = 7.81 Hz), 1.5−1.2 (t, 3H, J = 7.70 Hz). ^{13}C NMR (90 MHz, CD_3COCD_3): δ 143.44, 137.01, 136.2, 126.89, 31.57, 16.82.

3,5-Bis(4-thiomethoxyphenyl)-1-acetophenone (14). This compound was synthesized from **12** and **2** using a similar procedure as the one used for **3**. Starting from 2.34 g (8.43 mmol) of **2** and 3.40 g (20.2 mmol) of **12**, 3.0 g (96%) of **14** was obtained. mp 107−109 °C. Purity: 98% (HPLC). ^{1}H NMR (200 MHz, $CDCl_3$): δ 8.1−8.2 (d, 2H, J = 1.71 Hz), 8.0−7.9 (t, 1H, J = 1.7 Hz), 7.7−7.5 (d, 4H, J = 9.52 Hz), 7.4−7.2 (d, 4H, J = 7.5 Hz), 2.8 (s, 6H), 2.5 (s, 3H). ^{13}C NMR (90 MHz, $CDCl_3$): δ 198.21, 141.87, 138.86, 138.42, 136.98, 132.13, 129.98, 128.63, 127.77, 127.04, 125.65, 27.11, 15.93. R_f: 0.52 (hexanes/EtOAc = 4:1).

3,5-Bis(4-thioethoxyphenyl)-1-acetophenone (15). This compound was synthesized from **13** and **2** using a similar procedure as the one used for **3** except that **15** was recrystallized from methanol. Starting from 5.20 g (18.7 mmol) of **2** and 6.91 g (38.0 mmol) of **13**, 6.45 g (88%) of **15** was obtained. mp 66−68 °C. Purity: 99% (HPLC). ^{1}H NMR (200 MHz,

$CDCl_3$): δ 8.2−8.1 (d, 2H, J = 1.77 Hz), 8.0−7.9 (t, 1H, J = 1.81 Hz), 7.6−7.4 (d, 4H, J = 10.45 Hz), 7.4−7.3 (d, 4H, J = 8.5 Hz), 3.0−2.8 (q, 2H, J = 8.71 Hz), 2.6 (s, 3H), 1.4−1.2 (t, 3H, J = 7.30 Hz). ^{13}C NMR (90 MHz, $CDCl_3$): δ 197.12, 140.77, 139.66, 137.49, 135.91, 131.95, 130.10, 127.95, 128.97, 126.94, 125.15, 31.55, 26.91, 16.80. R_f: 0.63 (hexanes/EtOAc = 4/1).

3,5-Bis[4-(chlorosulfonyl)phenyl]-1-acetophenone (16). A 100 mL Schlenk tube equipped with magnetic stirring bar was charged with **6** (0.5 g, 0.93 mmol) and 50 mL of CH_2Cl_2. To this flask was added 25 mL of HCOOH and 25 mL of H_2O. After cooling to 0 °C, Cl_2 gas was bubbled through the heterogeneous reaction mixture with vigorous stirring. The reaction mixture turned yellowish-green and then became colorless, indicating complete conversion after 1.5 min of bubbling Cl_2 gas. Cl_2 gas bubbling was continued for another 10 s to ensure complete conversion. The organic phase was separated and diluted with 100 mL of CH_2Cl_2. The aqueous phase was washed with 50 mL of CH_2Cl_2, and the organic phases were combined and washed with 0.5 M NaOH followed by brine (three times). The CH_2Cl_2 solution was dried over Na_2SO_4 and concentrated by rotary evaporation. The resulting material was recrystallized from CH_2Cl_2/hexane to yield 0.35 g (82%) of **16** as white crystals. mp 167−170 °C. ^{1}H NMR (200 MHz, $CDCl_3$): δ 8.1 (d, 2 H, J = 2 Hz), 8.0 (d, 4H, J = 6.0 Hz), 7.9 (t, 1H, J = 0.8 Hz), 7.8 (d, 4H, J = 12.0 Hz), 2.65 (s, 3H). ^{13}C NMR (90 MHz, $CDCl_3$): δ 197.01, 146.73, 143.98, 140.57, 139.07, 130.94, 128.75, 128.05, 127.93, 27.08.

3,5-Bis(chlorosulfonyl)-1-acetophenone (17). This compound was synthesized from **8** using a similar procedure as the one used for **16**. Starting from 0.5 g of **8** (1.3 mmol), 0.3 g (77%) of **17** was obtained. mp 100−101 °C. ^{1}H NMR (200 MHz, $CDCl_3$): δ 8.9 (s, 2H), 8.8 (s, 1H), 2.8 (s, 3H). ^{13}C NMR (90 MHz, $CDCl_3$): δ 192.94, 146.59, 140.27, 132.12, 128.8, 26.98.

3,5-Bis(4-chlorosulfonylphenyloxy)-1-acetophenone (18). This compound was synthesized from **10** using a similar procedure as the one used for **16** except that Cl_2 was bubbled for 5 min. The yellowish green color of the reaction mixture did not disappear during chlorination. Starting from 0.5 g (1.0 mmol) of **10**, 0.36 g (72%) of **18** was obtained. mp 128−130 °C. ^{1}H NMR (200 MHz, $CDCl_3$): δ 8.1−8.0 (d, 4H, J = 9.06 Hz), 7.58 (d, 2H, J = 2.11 Hz), 7.22−7.12 (d, 4H, J = 10.0 Hz), 7.1 (t, 1H, J = 2.2 Hz), 2.59 (s, 3H). ^{13}C NMR (90 MHz, $CDCl_3$): δ 193.73, 162.33, 156.66, 139.18, 130.112, 118.49, 116.92, 116.74, 27.00.

3,5-Bis(4-*N*,*N*′-diethylsulfonamidephenyl)-1-acetophenone (19). A two-necked flask fitted with magnetic stirring bar, septum, and a nitrogen inlet was charged with **16** (100 mg, 0.021 mmol) and 10 mL of dry THF. After cooling to 0 °C, diethylamine (124 mg, 0.17 mmol) was added dropwise through a syringe under N_2. The solution was allowed to warm to 20 °C, and stirring was continued for 6 h. The reaction mixture was poured into H_2O (100 mL), and the aqueous phase was extracted with EtOAc (3 × 50 mL). The combined organic phase was washed with 10% HCl, two times with H_2O, and finally with brine. The EtOAc solution was dried over $MgSO_4$ and concentrated by rotary evaporation. The crude solid was recrystallized from CH_2Cl_2/MeOH to yield 90 mg (80%) of **19** as white crystals. mp 191−193 °C. Purity: 99.99% (HPLC). ^{1}H NMR (200 MHz, $CDCl_3$): δ 8.2 (d,2H, J = 1.68 Hz), 8.0−7.9 (m, 5H), 7.7−7.8 (d, 4H, J = 6.83 Hz), 3.4−3.2 (q, 8H, J = 7.2 Hz), 2.8 (s, 3H), 1.3−1.1 (t, 12H, J = 7.11 Hz). ^{13}C NMR (90 MHz, $CDCl_3$): δ 197.55, 143.81, 141.1, 140.19, 138.71, 130.76, 128.05, 127.9, 127.1, 42.26, 27.07,24.36. R_f: 0.78 (hexanes/EtOAc = 5/5). Anal. Calcd for $C_{28}H_{34}O_5S_2N_2$: C, 61.97; H, 6.3; N, 5.16. Found: C, 61.65; H, 6.46; N, 5.01.

3,5-Bis(*N*,*N*′-diethylsulfonamide)-1-acetophenone (20). This compound was synthesized from **17** using a similar procedure as the one used for **19**. Starting from 100 mg of **17** (0.33 mmol), 110 mg (77.5%) of **20** was obtained. mp 83−85 °C. Purity: 99.99% (HPLC). ^{1}H NMR (200 MHz, $CDCl_3$): δ 8.6 (s, 2H), 8.4 (s, 1H), 3.4−3.3 (q, 4H, J = 7.17 Hz), 2.7 (s, 3H), 1.4−1.1 (t, 12H, J = 7.14 Hz). ^{13}C NMR (90 MHz, $CDCl_3$): 195.01, 143.23, 138.82, 129.59, 128.93, 42.43, 26.98, 14.33. R_f: 0.76 (hexanes/EtOAc = 5/5). Anal. Calcd for $C_{16}H_{26}O_5S_2N_2$: C, 49.21; H, 6.76; N, 7.17. Found: C, 49.42; H, 6.81; N, 7.08.

3,5-Bis(4-*N*,*N*′-diethylsulfonamidephenyloxy)-1-acetophenone (21). This compound was synthesized from **18** using a similar procedure as the one used for **19**. Starting from 100 mg (0.33 mmol) of **18**, 110 mg (82%) of **21** was obtained. mp 83−85 °C. Purity: 99% (HPLC). ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.9−7.8 (d, 4H, J = 9.7 Hz), 7.4 (d, 2H, J = 2.2 Hz), 7.1−7.0 (d, 4H, J = 8.82 Hz),6.9 (t, 1H, J = 2.24 Hz), 3.4−3.2 (q, 8H, J = 7.2 Hz), 2.6 (s, 3H), 1.3−1.1 (t, 12H, J = 7.11 Hz); ^{13}C NMR (90 MHz, $CDCl_3$): δ 196.3, 159.77, 157.73, 140.45, 135.64, 129.52, 118.57, 115.23, 115.04, 42.23, 26.92, 14.34. R_f: 0.78 (hexanes/EtOAc = 5/5). Anal. Calcd for $C_{28}H_{34}O_7S_2N_2$: C, 58.52; H, 5.95; N, 4.87. Found: C, 58.43; H, 6.18; N, 4.67.

1,1,1-Tris(*O*-phenyl 4-*N*,*N*′-diethylthiocarbamate)ethane (22). A two-necked 100 mL flask fitted with N_2 inlet and magnetic stirring bar was charged with KOH (1.09 g, 19.6 mmol) and 10 mL of MeOH. When all KOH dissolved in MeOH, 1,1,1-tris(4-hydroxyphenyl)ethane (1.0 g, 3.3 mmol) was added portionwise under N_2. The reaction was continued for 4 h at 20 °C with stirring whereupon 50 mL of additional MeOH was added to the reaction mixture. Solid *N*,*N*′-diethylthiocarbamoyl chloride (3.01 g, 19.9 mmol) was added in one portion. After the reaction was stirred for 10 h, the precipitate was collected by filtration and washed with MeOH−H_2O (2 × 100 mL) to produce white crystals (1.53 g, 72%) after recrystallization from CH_2Cl_2/MeOH. mp 209−211 °C. Purity: 99.99% (HPLC). ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.1−7.0 (d, 6H, J = 8.0 Hz), 7.0−6.9 (d, 6H, J = 10.0 Hz), 3.9−3.8 (q, 6H, J = 8.0 Hz), 3.8−3.5 (q, 6H, J = 6.0 Hz), 2.1 (s, 3H), 1.3−1.2 (t, 18H, J = 6.0 Hz). ^{13}C NMR (90 MHz, $CDCl_3$): δ 186.66, 152.15, 146.09, 129.62, 129.47, 122.08, 122.0, 51.75, 48.42, 44.33, 30.89, 13.62, 11.91. R_f: 0.21 (hexanes/EtOAc = 8/2)

1,1,1-Tris(*S*-phenyl 4-*N*,*N*′-diethylthiocarbamate)ethane (23). This compound was synthesized from **22** using a similar procedure as the one used for **6**. Starting from 1.0 g (1.5 mmol) of **22,** 0.89 g (89%) of **23** was obtained. mp 157−159 °C. Purity: 99.99% (HPLC). ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.5−7.3 (d, 6H, J = 8.32 Hz), 7.2−7.08 (d, 8H, J = 8.23 Hz), 3.5−3.4 (q, 12H, J = 7.17 Hz), 2.2 (s, 3H), 1.4−1.1 (br,18H). ^{13}C NMR (90 MHz, $CDCl_3$): δ 165.79, 149.2, 135.38, 135.23, 129.45, 129.31, 126.6, 52.49, 42.43, 30.52, 13.91, 13.30. R_f: 0.24 (hexanes/EtOAc = 7/3).

1,1,1-Tris(4-chlorosulfonylphenyl)ethane (24). This compound was synthesized from **23** using a similar procedure as the one used for **16** except that the product was recrystallized from benzene. Starting from 0.5 g (0.77 mmol) of **23**, 0.41 g (97%) of **24** was obtained. mp 270 °C (decomp), ^{1}H NMR (200 MHz, $CDCl_3$): δ 8.1−7.9 (d, 6H, J = 11.0 Hz), 7.4−7.3 (d, 6H, J = 10.6 Hz) 2.3 (s, 3H). ^{13}C NMR (90 MHz, CD_3COCD_3): δ 155.67, 143.65, 131.46, 128.28, 61.44, 55.03.

1,1,1-Tris(4-*N*,*N*′-diethylsulfonamidephenyl)ethane (25). This compound was synthesized from **24** using a similar procedure as the one used for **19**. Starting from 0.15 g (0.27 mmol) of **24**, 0.147 g (82%) of **25** was obtained. mp 193−195 °C. Purity: 99.99% (HPLC). ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.8−7.7 (d, 6H, J = 8.46 Hz), 7.2−7.0 (d, 6H, J = 9.51 Hz), 3.5−3.2 (q, 12H, J = 7.23 Hz), 2.2 (s, 3H), 1.2−1.0 (t, 18H, J = 7.12 Hz). ^{13}C NMR (90 MHz, $CDCl_3$): δ 151.65, 139.29, 129.25, 127.25, 53.10, 42.35, 30.36, 14.46. R_f: 0.72 (hexanes/EtOAc = 5/5). Anal. Calcd for $C_{32}H_{45}O_6S_3N_3$: C, 57.88; H, 6.82; N, 6.32. Found: C, 57.76; H, 6.9; N, 6.29.

Phenoxyacetic Acid, 2,2-bis[(phenoxyacetyl)oxy]methyl]-1,3-propanediyl Ester (26).[25] To a mixture of NEt_3 (12.64 g, 125 mmol) and pentaerythritol (3.4 g, 25 mmol) in CH_2Cl_2 (100 mmol) was added phenoxyacetyl chloride (21.32 g, 125 mmol) at 0 °C under N_2. The mixture was stirred for 24 h at 20 °C. The reaction mixture was poured into a mixture of H_2O, and the organic layer was separated, washed with H_2O (2 × 200 mL), and dried over $MgSO_4$. Evaporation of the organic solvent and crystallization of the solid product from EtOAc two times yielded white crystals of **26** (14.9 g, 89%). mp 126−128 °C (lit.[9] 127−128 °C). Purity: 99.99% (HPLC). ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.32−7.24 (m, 8H), 7.0−6.8 (m, 12H), 4.6 (s, 8H), 3.9 (s, 8H). ^{13}C NMR (50 MHz,$CDCl_3$): δ 168.26, 157.43, 129.63, 121.86, 114.34, 64.78, 62. 42.

4-(Chlorosulfonyl)phenoxyacetic Acid, 2,2-Bis[[[4-(chlorosulfonyl)phenoxyacetyl]oxy]methyl]-1,3-propanediyl Ester (27). To a solution of **26** (1.0 g, 1.48 mmol) in CH_2Cl_2 (20 mL) was added dropwise chlorosulfonic acid (5.0 mL, purity: 99%, Aldrich) at −5.0 °C under N_2. The reaction mixture was stirred at 20 °C for 3 h and then was poured onto a mixture of crushed ice and H_2O with vigorous stirring. Upon addition of 300 mL of hexanes to the stirring mixture, a white solid separated from the solution. The white product was filtered and washed several times with H_2O and hexanes. The white product was first dried under vacuum (0.5 Torr) at 20 °C for 24 h and then dissolved in 50 mL of acetone and 50 mL of $CHCl_3$. To this clear solution was added 40 mL of hexane to produce a first fraction. After separating the first fraction by filtration, 100 mL of additional hexane was added to precipitate the remaining compound from an acetone/$CHCl_3$ solution mixture and the white precipitate was collected by filtration and dried in a vacuum to produce 0.6 g (38%) of **27**. mp 133−135 °C. ^{1}H NMR (200 MHz, CD_3COCD_3): δ 8.1−8.0 (d, 8H, J = 9.07 Hz), 7.4−7.2 (d, 8H, J = 9.08 Hz), 5.1 (s, 8H,), 4.3 (s, 8H). ^{13}C NMR (125 MHz,CD_3COCD_3): δ 168.39, 164.47, 137.51, 130.56, 116.78, 65.94, 63.99, 63.45, 43.45. Anal. Calcd for: $C_{37}H_{32}O_{20}S_4Cl_4$: C, 41.66; H, 3.02; S, 12.02; Cl, 13.29. Found: C, 41.80; H, 3.12; S, 11.89; Cl, 13.20. FAB-MS m/z (relative intensity), 289 (60), 307 (100), 1031(82), 1065.91 (M^+) (9).

4-(*N*,*N*′-Diethylsulfonamide)phenoxyacetic Acid, 2,2-Bis[[[4-(*N*,*N*′-diethylsulfonamide)phenoxyacetyl]oxy]-methyl]-1,3-propanediyl Ester (28). A two necked flask fitted with magnetic stirring bar, septum, and N_2 inlet was charged with **27** (200 mg, 0.021 mmol) and 10 mL of dry THF. After cooling to −5 °C, diethylamine (0.76 g, 10.5 mmol) was added dropwise through a syringe under N_2. The solution was stirred for 4 h, and the reaction mixture was poured into H_2O (100 mL). The aqueous phase was extracted with EtOAc (3 × 50 mL). The combined organic phase was washed with 10% HCl two times, with H_2O, and finally with brine. The EtOAc solution was dried over $MgSO_4$ and concentrated by rotary evaporation. The crude product was recrystallized from CH_2Cl_2/MeOH to yield 0.226 g (90%) of **28**. mp 166−168 °C. Purity: 99.99% (HPLC). ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.6−7.5 (d, 8H, J = 9.04 Hz), 6.9−6.7 (d, 8H, J = 9.01 Hz), 4.5 (s, 8H), 3.7 (s, 8H) 3.0−2.8 (q, 16H, J = 6.18 Hz), 0.95−0.8 (t, 24H, J = 7.18 Hz); ^{13}C NMR (90 MHz, $CDCl_3$): δ 167.73, 160.52, 133.78, 129.4, 114.95, 65.07, 62.22, 42.67, 42.19, 14.34. R_f: 0.25 (hexanes/EtOAc = 5/5). MS (ES$^+$, m/z): 1235.2 (M^+ + 23 − 1), 1236.3 (M^+ + 23), 1237.2 (M^+ + 23 + 1), 1238.3 (M^+ + 23 + 2), 1239.2 (M^+ + 23 + 3). Anal. Calcd for $C_{53}H_{72}O_{20}S_4N_4$: C, 52.46; H, 5.97; N, 4.61. Found: C, 52.15; H, 6.04; N, 4.44.

***p*-*tert*-Butylcalix[4]arene or 5,11,17,23-Tetrakis(*tert*-butyl)-25,26,27,28-tetrakis(hydroxy)calix[4]arene (29).**[26] A mixture of 31 mL (1.2 mol) of 37% formaldehyde was added to 50 g (0.3 mol) *p*-*tert*-butyl phenol in a 1 L three-necked round-bottom flask. NaOH (1.2 mL, 0.09 mmol) (40% solution in H_2O) was added to the mixture. The flask was stirred uncovered at 20 °C for 15 min and then was heated to 120 °C for 2 h under a steady flow of N_2. As H_2O was removed, the clear solution turned from yellow to dark yellow. After 2.5 h, some frothing occurred, and the solution became more viscous. Stirring was continued until the yellow to amber viscous material did not stick to the side of the flask. The cooled very viscous solid was dissolved in 500 mL of diphenyl ether in 30 min. The dissolved solution was heated to 120 °C while N_2 was bubbled into the reaction mixture to facilitate the removal of H_2O. After about 1 h, the solution was brought to reflux (ca. 350 °C), and the flask was fitted with a condenser. After 3 h the color of the solution changed from yellow to clear dark brown. A crude white precipitation (33.0 g, 61%) was obtained upon addition of EtOAc to the cooled reaction mixture and was filtered and washed, successively, with EtOAc (2 × 50 mL), acetic acid (100 mL), H_2O (2 × 50 mL), and acetone (2 × 25 mL). Recrystallization from toluene yielded 30.0 g (49%) of **29** as gleaming white crystals. mp 342.5 °C (lit.[26] 342−344 °C). Purity: 99.9% (HPLC). ^{1}H NMR (200 MHz, $CDCl_3$): δ 10.35 (s, 4H), 7.06 (s, 8H), 4.26 (d, 4H, J = 0.1 Hz), 3.52 (d, 4H, J = 0.1 Hz), 1.19 (s, 36H). R_f: 0.55 ($CHCl_3$ / hexane = 3/4).

***p*-*tert*-Butylcalix[6]arene or 5,11,17,23,29,35-Hexakis-(*tert*-butyl)-37,38,39,40,41,42-hexakis(hydroxy)calix[6]-arene (30).**[27] Formaldehyde (solution, 37%) (62.5 mL, 2.1 mol) was added to *p*-*tert*-butylphenol (50 g, 0.332 mol) in a 1 L three-necked round-bottom flask. KOH (7.5 g, 0.133 mol) was added to the mixture. The flask was heated to 120 °C for 2 h under a rapid flow of N_2. As H_2O was removed, the clear solution turned bright lemon yellow. After 2.5 h, some frothing occurred and the solution turned golden yellow and viscous. Stirring was continued until the yellow to amber viscous material did not stick to the side of the flask. The cooled viscous solid was dissolved in 500 mL of xylene. The dissolved solution was quickly brought to reflux (ca. 190 °C). After 3 h at reflux, a white opaque solution remained. The cooled reaction mixture was filtered and washed with xylene to yield 45−50 g of crude, colorless crystals. The solid was dissolved in 1.25 L of chloroform (not completely soluble) and treated with 400 mL 1 N HCl. After stirring for 10 min, the organic layer was drawn off, and the aqueous layer was extracted with an additional amount of chloroform. The chloroform extracts were combined and washed again with H_2O and dried over $MgSO_4$. The filtrate was concentrated to ca. 800 mL by boiling, and 500 mL of hot acetone was added to the boiling $CHCl_3$ solution. On cooling, 35.0 g (85% yield) of white crystals were obtained. mp 373 °C (lit.[27] 372−374 °C). Purity: 100% (HPLC). ^{1}H NMR (200 MHz, $CDCl_3$): δ 10.4 (s, 6H), 7.9 (s, 12H), 3.9 (s, 12H), 1.27 (s, 54H). R_f: 0.4 (CH_2Cl_2/hexane = 1/2).

***p*-*tert*-Butylcalix[8]arene or 5,11,17,23,29,35,41,47-Octakis(*tert*-butyl)-49,50,51,52,53,54,55,56-octakis(hydroxy)-calix[8]arene (31).**[28] A mixture of 35 g (1.1 mol) of paraformaldehyde and 100 g (0.67 mol) of *p*-*tert*-butylphenol was added to 600 mL of xylene into a 2 L three-necked round-bottom flask. NaOH (2.0 mL 10 N, 0.02 mol) was added to the mixture. The flask was heated to reflux under a rapid flow of N_2. After about 30 min a homogeneous solution formed. A white precipitate formed 30 min later. After 4 h the mixture was cooled to 20 °C, and the precipitate was filtered. The crude product was washed successively with toluene, diethyl ether, and acetone and dried under vacuum. Recrystallization from chloroform yielded colorless crystals (28.0 g, 62−65%). mp 418 °C (decomp) (lit.[28] 418−420 °C). Purity: 99.9% (HPLC). ^{1}H NMR (200 MHz, $CDCl_3$): δ 9.63 (s, 8H), 7.18 (s, 16H), 4.38 (d, 8H, J = 0.1 Hz), 3.49 (d, 8H, J = 0.1 Hz), 1.23 (s, 72H). R_f: 0.3 (CH_2Cl_2/hexane = 1/2).

25,26,27,28-Tetrakis(hydroxy)calix[4]arene (32).[29] A slurry of 15.0 g (22.5 mmol) of *p*-*tert*-butylcalix[4]arene **29**, 10.2 g (108 mmol) of phenol, and 15.8 g (118 mmol) of $AlCl_3$ was stirred in 125 mL of toluene at 20 °C for 1 h under N_2. The mixture was poured into 250 mL of 0.2 N HCl, the organic phase was separated, and the solvent was evaporated. Upon addition of MeOH the precipitate formed was filtered to give 8.7 g of a solid. The crude product was recrystallized from MeOH/$CHCl_3$ to afford colorless crystals (7.6 g, 75%). mp 313 °C (lit.[29] 313−315 °C). Purity: 100% (HPLC). ^{1}H NMR (200 MHz, $CDCl_3$): δ 10.2 (s, 4H), 7.09 (d, 8H, J = 0.1 Hz), 6.77 (t, 4H, J = 0.1 Hz), 4.28 (s, 4H), 3.61 (s, 4H).

37,38,39,40,41,42-Hexakis(hydroxy)calix[6]arene (33).[29] A slurry of 10.5 g (11 mmol) of *p*-*tert*-butylcalix[6]arene **30**, 6.20 g (66 mmol) of phenol and 11.8 g (88 mmol) of $AlCl_3$ was stirred in 100 mL of toluene at 20 °C for 1 h under N_2. The reaction was quenched by the addition of 150 mL of ice−H_2O, and the organic phase was separated. The solvent was evaporated, and the residue was triturated with 80 mL of MeOH to leave 6.9 g of a crude, colorless product. Recrystallization from MeOH/$CHCl_3$ afforded white crystals (6.0 g, 85%). mp 420 °C (lit.[29] 417−418 °C). ^{1}H NMR (200 MHz, $CDCl_3$): δ 10.4 (s, 6H), 7.4−6.7 (m, 18H), 4.0 (s, 6H).

49,50,51,52,53,54,55,56-Octakis(hydroxy)calix[8]-arene (34).[29] A slurry of 15.0 g (11.5 mmol) of *p*-*tert*-butylcalix-[8]arene **31**, 8.7 g (93 mmol) of phenol, and 18.5 g (140 mmol) of $AlCl_3$ was stirred in 200 mL of toluene at 20 °C for 1 h under N_2. The mixture was poured into 250 mL of 0.2 N HCl, the organic phase was separated, and the solvent was evaporated.

Upon addition of acidic MeOH (500 mL of MeOH containing a few drops of concentrated HCl), the precipitate formed was collected by filtration to give 12.0 g of an orange solid. The crude insoluble solid was extracted with 200 mL of $CHCl_3$ for 12 h, cooled, and filtered, and the process was repeated successively with acetone, MeOH, and diethyl ether to yield 6.88 g (70%) of **34** as light gray crystals. ^{1}H NMR (200 MHz, C_5D_5N): δ 6.0−7.0 (m, 24H), 3.5 (br, s, 16H).

25,26,27,28-Terakis(ethoxycarbonylmethoxy)calix[4]-arene or Tetraethyl calix[4]arenetetraacetate (35).[30] 25,-26,27,28-Tetrakis(hydroxy)calix[4]arene **32** (2.0 g, 4.8 mmol) was suspended in 100 mL of acetonitrile containing 27.0 g (195.8 mmol) of anhydrous K_2CO_3 and 6.5 g of KI, and the mixture was warmed to 70 °C while purging with N_2 to eliminate dissolved air for 15 min. Finally, 32.71 g (195.8 mmol) of ethyl bromoacetate were added dropwise to the solution via an addition funnel. The mixture was refluxed for 24 h and cooled. The reaction mixture was poured into 500 mL of H_2O. The aqueous phase was extracted with Et_2O (2 × 200 mL), and the ethereal phases were combined and washed with 0.1 N HCl and then washed with H_2O twice followed by brine. The ethereal solution was dried over $MgSO_4$ and concentrated by rotary evaporation. Purification by column chromatography (silica gel, 10% CH_2Cl_2) gave **35** (2.53, 70%) as a colorless viscous oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.56−6.29 (m, 12H), 4.8−3.3 (m, 24H), 1.2 (m, 12H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.9, 170.44, 169.7, 156.6, 156.1, 155.5, 136.4, 135.8, 133.8, 133.0, 132.4, 131.1, 129.6, 129.3, 128.9, 128.8, 123.1, 122.6, 71.5, 70.9, 68.4, 68.1, 61.2, 60.7, 60.2, 34.8, 32.0, 31.7, 14.4. MS (ES^+, *m*/*z*): 791.30 ($M^+ + 23$).

37,38,39,40,41,42-Hexakis(ethoxycarbonyl methoxy)-calix[6]arene or Hexaethyl calix[6]arenehexaacetate (36).[30] 37,38,39,40,41,42-Hexakis(hydroxy)calix[6]arene **33** (1.0 g, 1.63 mmol) was suspended in 50 mL of acetonitrile containing 9.01 g (65.2 mmol) of anhydrous K_2CO_3 and 3.25 g of KI, and the mixture was warmed to 70 °C while purging with N_2 to eliminate dissolved air for 15 min. Finally, 10.9 g (65.2 mmol) of ethyl bromoacetate were added dropwise to the solution via an addition funnel. The mixture was refluxed for 24 h and cooled. The reaction mixture was poured into 250 mL of H_2O. The aqueous phase was extracted with Et_2O (2 × 100 mL), and the ethereal phases were combined and washed with 0.1 N HCl and then washed with H_2O twice followed by brine. The ethereal solution was dried over $MgSO_4$ and concentrated by rotary evaporation. Purification by column chromatography (silica gel, 10% CH_2Cl_2) gave **36** as a colorless solid. Recrystallization from EtOH afforded 1.34 g (65%) of pure compound. mp 156−157 °C (lit.[30] 154−155 °C). Purity: 99% (HPLC). ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.8 (d, 12H), 6.7 (t, 6H), 4.1−4.3 (m, 36H), 1.28 (t, 18H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 169.3, 155.1, 133.7, 129.6, 124.8, 61.2, 31.7, 14.4

49,50,51,52,53,54,55,56-Octakis(ethoxycarbonylmethoxy)-calix[8]arene or Octaethyl calix[8]areneoctaacetate (37).[30] 49,50,51,52,53,54,56-Octakis(hydroxy)calix[8]arene **34** (2.0 g, 2.44 mmol) was suspended in 100 mL of acetonitrile containing 16.8 g (122.4 mmol) of anhydrous K_2CO_3 and 6.5 g of KI, and the mixture was warmed to 70 °C while purging with N_2 for 15 min to eliminate dissolved air. Finally, 20.44 g (122.4 mmol) of ethyl bromoacetate was added dropwise to the solution via an addition funnel. The mixture was refluxed for 24 h and cooled. The reaction mixture was poured into 500 mL of H_2O. The aqueous phase was extracted with Et_2O (2 × 200 mL), and the ethereal phases were combined and washed with 0.1 N HCl and then washed with H_2O twice followed by brine. The ethereal solution was dried over $MgSO_4$ and concentrated by rotary evaporation. Purification by column chromatography (silica gel, 10% CH_2Cl_2) gave **37** as a colorless viscous oil. Recrystallization from Et_2O/hexane afforded 2.1 g (65%) of pure compound. Purity: 99% (HPLC). ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.9 (bs, 24H), 4.36 (s, 16H), 4.16 (m, 32H), 1.24 (t, 24H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 169.1, 155.2, 134.4, 129.4, 125.0, 70.4, 61.6, 30.8, 14.3.

5,11,17,23-Tetrakis(chlorosulfonyl)-25,26,27,28-tetrakis-(ethoxycarbonylmethoxy)calix[4]arene (38).[31] To a solution of 1.0 g (1.3 mmol) of tetraethyl calix[4]arenetetraacetate **35** in 40 mL of $CHCl_3$ at −10 °C was added chlorosulfonic acid (10.0 mL, 150 mmol) dropwise under N_2. The reaction mixture was warmed to room temperature and heated at 50 °C for 20 min. Finally, the reaction mixture was cooled to 20 °C and was added dropwise onto 500 mL of ice−H_2O with vigorous stirring. Upon addition of hexanes (500 mL) to the stirring mixture, a white solid separated from the solution. The white compound was filtered and washed several times with H_2O and hexanes. The white solid was dissolved in CH_2Cl_2 and dried over anhydrous Na_2SO_4. The organic phase was concentrated under vacuum at 20 °C. The residue was recrystallized from a mixture of CH_2Cl_2/hexanes to afford white crystals of **38**. Yield: 0.75 g (50%). mp 108−109 °C (lit.[31] 108−109 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.4−7.2 (m, 8H), 5.2−4.1 (m, 20H), 3.6 (m, 4H), 1.3 (m, 12H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 169.3, 169.0, 168.1, 162.3, 161.2, 161.2, 160.6, 139.9, 139.5, 139.4, 139.0, 136.8, 135.7, 134.9, 134.6, 133.7, 133.5, 131.0, 129.0, 128.5, 128.0, 72.3, 72.1, 71.1, 69.4, 62.6, 62.2, 62.1, 61.7, 61.5, 35.0, 32.1, 31.9, 31.7, 14.4, 14.3. FAB-MS *m*/*z* (relative intensity): 154.1 (100), 341.3 (22), 1127.2 (93), 1163.1 (MH^+) (24).

5,11,17,23,29,35-Hexakis(chlorosulfonyl)-37,38,39,40,-41,42-hexakis(ethoxycarbonylmethoxy)calix[6]arene (39). To a solution of 1.0 g (0.85 mmol) of hexaethyl calix[6]-arenehexaacetate **36** in 40 mL of $CHCl_3$ at −10 °C was added chlorosulfonic acid (10.0 mL, 150 mmol) dropwise under N_2. The reaction mixture was warmed to room temperature and heated at 50 °C for 20 min. The reaction mixture was cooled to 20 °C and was added dropwise onto 500 mL of ice−H_2O with vigorous stirring. Upon addition of hexanes (500 mL) to the stirring mixture, a white solid separated from the solution. The white product was filtered and washed several times with H_2O and hexanes. The white solid was dissolved in CH_2Cl_2 and dried over anhydrous Na_2SO_4. The organic phase was concentrated under vacuum at 20 °C. The residue was recrystallized from a mixture of CH_2Cl_2/hexanes to afford white crystals of **39**. Yield: 0.90 g (60%). mp 273−274 °C. Purity: 99% (HPLC). ^{1}H NMR (500 MHz, DMSO-d_6): δ 7.3 (s, 12H), 4.5 (s, 12H), 4.0 (m, 24H), 1.1 (t, 18H). ^{13}C NMR (125 MHz, DMSO-d_6): δ 169.8, 168.9, 164.0, 163.7.0, 163.2, 162.0, 141.5, 141.1, 140.8, 140.2, 135.7, 135.3, 129.1, 128.6, 127.5, 127.2, 70.4, 69.7, 61.5, 60.9, 32.0, 29.7, 28.4, 14.2, 14.1. FAB-MS *m*/*z* (relative intensity): 154.1 (100), 341.4 (15), 1693.4 (26), 1745.1 (MH^+).

5,11,17,23,29,35,41,47-Octakis(chlorosulfonyl)-49,50,-51,52,53,54,55,56-octakis(ethoxycarbonylmethoxy)calix-[8]arene (40). To a solution of 1.0 g (0.65 mmol) of octaethyl calix[8]areneoctaacetate **37** in 40 mL of $CHCl_3$ at −10 °C was added chlorosulfonic acid (10.0 mL, 150 mmol) dropwise under N_2. The reaction mixture was warmed to room temperature, heated at 50 °C for 20 min, cooled to 20 °C and added dropwise onto 500 mL of ice−H_2O. Upon addition of hexanes (500 mL) to the stirring mixture, a white solid precipitated. The white precipitate was filtered and washed several times with H_2O and hexanes. The solid product was dissolved in CH_2Cl_2 and dried over anhydrous Na_2SO_4. The organic phase was concentrated under vacuum at 20 °C. The residue was recrystallized from a mixture of CH_2Cl_2/hexanes to afford white crystals of **40**. Yield: 0.93 g (62%). mp 265−266 °C. Purity: 99% (HPLC). ^{1}H NMR (500 MHz, $CDCl_3$, 50 °C): δ 7.6 (m, 16H), 4.6 (s, 16H), 4.7−4.2 (m, 32H), 1.3 (m, 24H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 169.1, 168.6, 168.2, 161.2, 165.9, 165.6, 165.0, 140.5, 139.8, 134.9, 134.6,, 129.3, 128.9, 128.3, 70.6, 69.9, 62.0, 61.8, 61.5, 31.9, 31.6, 31.4, 14.3, 14.2. FAB-MS *m*/*z* (relative intensity) 2273 (78), 2310 (74), 2327 (MH^+) (100).

General Procedure for Esterification of Calix[*n*]arenes 32, 33, 34. To a solution containing calix[4]arene (1.0 g, 1.54 mmol) and phenoxyacetyl chloride (2.1 g, 12.32 mmol) in CH_2Cl_2 (50 mL) at 0 °C, Et_3N (1.24 g, 121.32 mmol) was added dropwise under N_2. The reaction mixture was stirred at 20 °C for 12 h, poured onto cold H_2O, and extracted with CH_2Cl_2 (4 × 50 mL). The organic layer was washed successively with H_2O, 10% HCl, H_2O, saturated solution of $NaHCO_3$, and brine and finally dried over $MgSO_4$. After removal of solvent under

vacuum, the residue was recrystallized from EtOH/$CHCl_3$ to afford white crystals.

5,11,17,23-Tetrakis(*tert*-butyl)-25,26,27,28-tetrakis-(phenoxyacetoxy)calix[4]arene (41). Starting from calix-[4]arene **32** (1.0 g, 1.54 mmol) and phenoxyacetyl chloride (2.1 g, 12.32 mmol), 1.54 g of **41** (85%) was obtained. mp 231−232 °C. Purity: 99% (HPLC). ^{1}H NMR (200 MHz, CD_3SOCD_3): δ 7.42−6.75 (m, 32H), 5.1 (m, 8H), 4.05−3.32 (m, 8H), 1.5−0.9 (m, 36H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 167.5, 157.7, 151.2(t), 148.9, 130.7 (t), 125.5, 122.9, 115.5 (t), 65.3 (t), 35.3, 31.9, 31.8. R_f: 0.75 (hexanes/EtOAc = 7/3).

5,11,17,23,29,35-Hexakis(*tert*-butyl)-37,38,39,40,41,42-hexakis(phenoxyacetoxy)calix[6]arene (42). Starting from calix[6]arene **33** (4.9 g, 5 mmol) and phenoxyacetyl chloride (10.2 g, 60 mmol), 6.9 g of **42** (78%) was obtained. mp 323 °C. Purity: 99% (HPLC). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.8−6.2 (m, 42H), 4.9 (d), 4.3 (t), 4.2 (d), 3.8 (q), 3.5 (q), 2.8 (d, all 12H), 1.6 (s), 1.2 (s), 0.9 (s, all 48H) ^{13}C NMR (125 MHz, $CDCl_3$): δ 166.7, 166.2, 157.5, 157.1, 150.6, 149.6, 145.6, 145.3, 145.0, 132.9, 132.7, 131.1, 130.5, 129.6, 127.5, 125.6, 122.0, 115.4, 114.9, 114.4, 64.0, 63.7, 37.8, 34.9, 34.6, 31.8, 31.4, 31.0. R_f: 0.75 (hexanes/EtOAc = 7/3).

5,11,17,23,29,35,41,47-Octakis(*tert*-butyl)-49,40,51,52,-53,54,55,56-octakis(phenoxyacetoxy)calix[8]arene (43). Starting from calix[8]arene **34** (6.5 g, 5 mmol) and phenoxy-acetyl chloride (13.64 g, 80 mmol), 8.56 g of **43** (72%) was obtained. mp 176−177 °C. Purity: 99% (HPLC). ^{1}H NMR (200 MHz, CD_3SOCD_3): δ 7.04 (m, 32H), 6.75 (m, 24H), 4.75 (s, 16H), 3.68 (s, 16H), 1.1(s, 72H). ^{13}C NMR (50 MHz,$CDCl_3$): δ 167.8, 157.9, 150.9 (t), 149.9, 130.2 (t), 125.9, 122.4, 115.3 (t), 64.3 (t), 35.1, 31.9, 31.6. R_f: 0.65 (hexanes/EtOAc = 7/3.

General Procedure for Chlorosulfonation of Calix[*n*]-arenes 41, 42, 43.[31] To a solution of calix[*n*]arene in $CHCl_3$ (40 mL) at −10 °C was added chlorosulfonic acid dropwise under N_2. The reaction mixture was warmed to room temperature and heated at 50 °C cooled to room temperature and added dropwise onto ice−H_2O (400 mL) with vigorous stirring. Upon addition of 400 mL of hexanes to the vigorous stirring reaction mixture, the white precipitate was collected by filtration and washed several times with water followed by hexane. The white compound was dissolved in CH_2Cl_2 and dried over Na_2SO_4. The organic phase was concentrated under vacuum at 20 °C. The residue was recrystallized from a mixture of CH_2Cl_2/hexanes to afford white crystals.

5,11,17,23-Tetrakis(*tert*-butyl)-25,26,27,28-tetrakis-(chlorosulfonylphenoxyacetoxy)calix[4]arene (44).[31] Starting from 1.0 g (0.85 mmol) of 5,11,17,23-tetrakis(*tert*-butyl)-25,26,27,28-tetrakis(phenoxyacetoxy)calix[4]arene **41**, 40 mL of $CHCl_3$, and chlorosulfonic acid (6.0 mL, 90 mmol), 1.0 g of **44** (75%) was obtained. Purity: 99% (HPLC). ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.8−6.5 (m, 24H), 5.3−4.8 (m, 4H), 4.22−3.25 (m, 12H), 1.52−0.98 (m, 36H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 176.1, 162.5, 150.2, 147.8, 136.1, 131.7, 129.6, 126.5, 115.7, 64.9, 34.9, 30.9.

5,11,17,23,29,35-Hexakis(*tert*-butyl)-37,38,39,40,41,42-hexakis(chlorosulfonylphenoxyacetoxy)calix[6]arene (45). Starting from 1.0 g (0.55 mmol) of 5,11,17,23,29,35-hexakis-(*tert*-butyl)-37,38,39,40,41,42-hexakis(phenoxyacetoxy)calix[6]-arene **42**, 40 mL of $CHCl_3$, and chlorosulfonic acid (7.0 mL, 105 mmol), 0.93 g of **45** (70%) was obtained. Purity: 99% (HPLC). ^{1}H NMR (500 MHz, DMSO-d_6, 80 °C): δ 8.3−6.5 (br, 36H), 5.6−3.4 (br, 24H), 1.5−0.8 (m, 54H). ^{13}C NMR (125 MHz, DMSO-d_6): δ 172.2, 171,8, 171.6, 158.8, 150.7, 150.0, 145.8,-144.9, 140.1, 139.7, 139.4, 136.8, 132.3, 132.0, 128.1, 127.1, 114.8, 65.3, 40.5 (m), 39.9, 31.7.

5,11,17,23,29,35,41,47-Octakis(*tert*-butyl)-49,40,51,52,-53,54,55,56-octakis(chlorosulfonylphenoxyacetoxy)calix-[8]arene (46). Starting from 1.0 g (0.4 mmol) 5,11,17,23,29,-35,41,47-octakis(*tert*-butyl)-49,40,51,52,53,54,55,56-octakis(phenoxyacetoxy)calix[8]arene **43**, 40 mL of $CHCl_3$, and chlorosulfonic acid (8.0 mL, 120 mmol), 1.06 g of **46** (80%) was obtained. Purity: 99% (HPLC). ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.62 (d, 16H, J = 9.1 Hz), 7.01 (s, 16H), 6.83 (d, 16H, J = 9.1 Hz), 4.9 (s, 16H), 3.72 (s, 16H), 1.08 (s, 72H). ^{13}C NMR (50 MHz, CD_3COCD_3): 166.5, 162.9, 149.4, 147.8, 136.9, 131.6, 129.8, 126.6, 115.7, 64.9 (t), 34.3, 30.8, 29.2.

2,4,6-Tris(chlorosulfonyl)aniline (47).[32] To chlorosulfonic acid (40 mL, 0.6 mol) stirred at 0 °C under N_2, aniline (4.6 g, 5 mmol) was carefully added with vigorous evolution of HCl. NaCl (35.1 g, 0.6 mol) was added in small batches over several hours. The reaction mixture was allowed to warm to 20 °C, heated to 150 °C for 3 h, cooled to 0 °C, and carefully quenched by the cautious addition of cold H_2O (100 mL). The mixture was extracted with Et_2O (100 mL portions) until only a faint color was evident in the ether layer. The combined organic fractions were washed with brine and dried ($MgSO_4$), and **47** was recrystallized from warm $CHCl_3$. Several batches of crystals were isolated from the mother liquor. Combined yield: 2.64 g (14%). mp 175−177 °C (lit.[16] 173−175 °C). Purity: 99% (HPLC). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.73 (s, 2H), 7.42-(s, 2H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 146.4, 135.7, 131.3, 128.9. FT-IR (cm^{-1}): 3459, 3368, 3077, 1637, 1589, 1540, 1485, 1370, 1171. MS (EI) *m*/*z* (relative intensity): 393 (3), 391 (11), 389 (26), 387 [$M^+ + 23$], 352 [$M^+ - Cl$] (100).

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Supporting Information Available: ^{1}H NMR and ^{13}C NMR of **16**, **17**, **18**, **24**, **27**, **38**, **39**, **40**, **44**, **45**, and **46**.This material is available free of charge via the Internet at http://pubs.acs.org.

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