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S-Alkylation of Thiacalixarenes: How the Regio- and Stereoselectivities Depend on the Starting Conformation

Ondrej Kundrat,[†] Hana Dvorakova,[‡] Stanislav Böhm,[†] Vaclav Eigner,[§] and Pavel Lhotak*[,†]

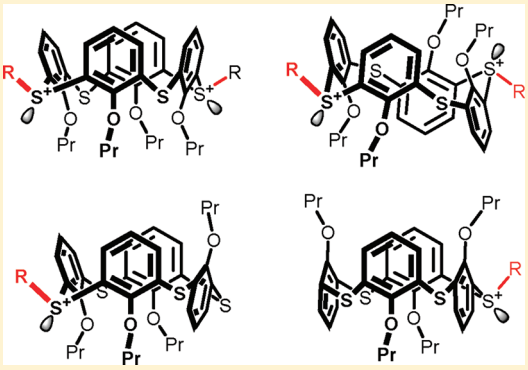
[†]Department of Organic Chemistry, Prague Institute of Chemical Technology, Technicka 5, 166 28 Prague 6, Czech Republic

[‡]Laboratory of NMR Spectroscopy, Prague Institute of Chemical Technology, Technicka 5, 166 28 Prague 6, Czech Republic

[§]Department of Solid State Chemistry, Prague Institute of Chemical Technology, Technicka 5, 166 28 Prague 6, Czech Republic

Supporting Information

ABSTRACT: *S*-alkylation of all four thiacalix[4]arene conformations was accomplished using alkyl triflates. The corresponding sulfonium salts are formed in a highly regio- and stereoselective manner depending on the conformation used. Interestingly, only mono- or disubstituted sulfonium salts can be prepared. Although many regio- and stereoisomers are theoretically possible, only one dialkylated *cone* and *1,2-alternate* derivatives were formed, while only a single isomer of monoalkylated *partial cone* and *1,3-alternate* were isolated. The combination of experimental results with the quantum-chemical approach using the B3LYP/6-311G(d,p) method resulted in the elucidation of the rules governing the regio- and stereochemical outcomes of the alkylation reactions. All *S*-alkylated compounds represent a novel type of substitution pattern in calixarene chemistry showing the wide-ranging possibility of thiacalixarene skeleton modifications.



INTRODUCTION

Since their first appearance[1] in 1997, thiacalix[4]arenes have attracted considerable attention from supramolecular chemists because of their structural similarity with the well-established calix[4]arene family. The main difference, the presence of sulfur atoms instead of common methylene bridges, imparts these macrocycles[2] with many unusual features in comparison to classical calixarenes. Thus, because of additional S···metal interactions,[3] the basic thiacalix[4]arene proved to be a much better complexation agent toward transition metals. As a consequence of longer S−C bonds, the bigger cavity results in substantially altered dynamic conformational behavior[4] or conformational preferences in lower-rim alkylation reactions.[5] The sulfur bridges of thiacalixarene skeletons can be regio- and/or stereoselectively oxidized to sulfoxides or sulfones,[3b,6] to name at least the most obvious differences between thiacalixarenes and calixarenes.

Last but not least, the chemical behavior of thiacalixarenes can be dramatically different in comparison with their classical calixarene analogues. As we have shown in our recent papers, the lower-rim tetraalkylated thiacalix[4]arenes possess an unprecedented regioselectivity in electrophilic substitutions. Thus, nitration or formylation reactions give us the opportunity to introduce substituents directly to the *meta*-positions of the thiacalixarene skeleton.[7] Consequently, the use of alkylated thiacalixarenes can lead to substitution patterns so far inaccessible in classical calixarene chemistry.[8] What is more, the results of these reactions can be strictly dependent on the conformation used for the reaction, another feature proving a remarkable difference in the reactivity of the thiacalix[4]arene and calix[4]arene skeletons.[7b,d]

Very recently, we have described the *S*-alkylation of thiacalix[4]arenes[9] using strong alkylating reagents (alkyl triflates or trialkyloxonium salts). The corresponding sulfonium derivatives were formed highly regio- and stereoselectively starting from the *cone* conformation. In this paper, we report the *S*-alkylation study of the three remaining thiacalix[4]arene conformations: *partial cone*, *1,2-alternate*, and *1,3-alternate*. On the basis of the results obtained, we suggest simple rules that govern the regio- and stereoselective outcomes of these reactions.

RESULTS AND DISCUSSION

Synthesis. As we have shown in our previous paper,[9] compound **1**, immobilized in the *cone* conformation, can be *S*-alkylated using alkyl triflates or trialkyloxonium salts, while the application of other alkylating reagents (iodide, tosylate, brosylate, nosylate, mesylate) showed no conversion of the starting thiacalixarene. Depending on the reaction conditions, either monosubstituted or disubstituted sulfonium salts can be selectively obtained in very high yields. Thus, stirring of **1** with 12 equiv of MeOTf in 1,2-dichloroethane (DCE) for three days gave monoalkylated derivative **2** (R = Me) in 93% yield, while using a larger excess of the same alkylating agent (36 equiv)

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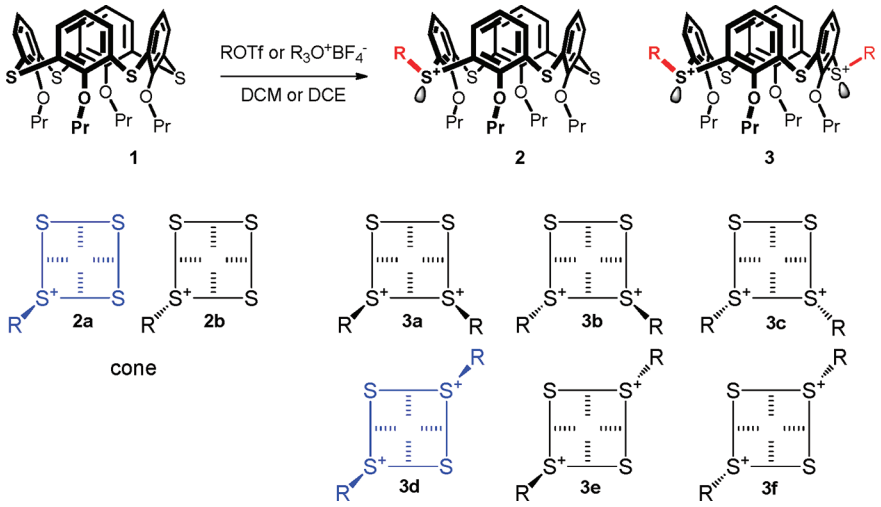
Scheme 1. *S*-Alkylation of Thiacalix[4]arene in the *Cone* Conformation[a]



[a]Blue color denotes isomers isolated from the reaction mixture. Hashed bonds denote the orientation of the alkyl groups on the lower rim.

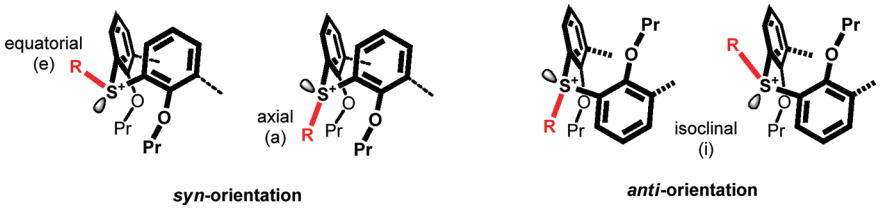
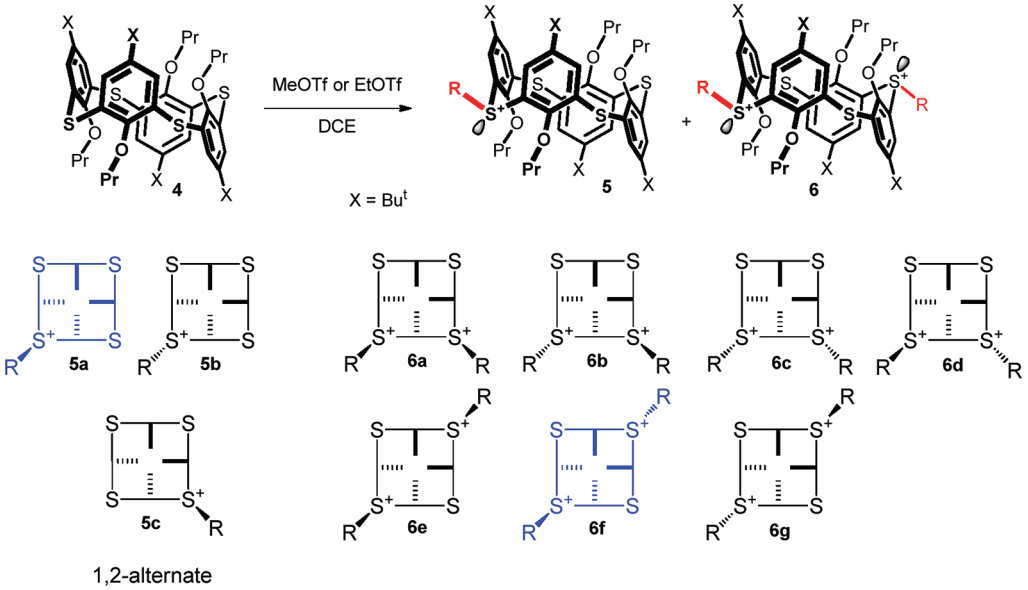


Figure 1. Mutual orientation of the neighboring aromatic rings in *S*-alkylated thiacalix[4]arenes and the assignment of the stereochemistry of *S*-alkyl groups.

Scheme 2. *S*-Alkylation of Thiacalix[4]arene in the *1,2-Alternate* Conformation[a]



[a]Blue color denotes isomers isolated from the reaction mixture. Hashed and bold bonds denote the mutual orientations of the alkyl groups on the lower rim.

and a longer reaction time (5 days) led smoothly to dialkylated compound **3** (R = Me) in 89% yield.

The stereoselectivity of the alkylation reactions was studied by ^{1}H NMR NOE technique with **2** and **3**. These experiments showed that the alkylating agents always attacked *cone* conformer **1** from the upper-rim direction, probably to minimize possible steric or electrostatic repulsions with the lower-rim substituents. As a result, only the stereoisomer **2a**, with alkyl groups pointing to the upper rim direction, was isolated. Interestingly, despite the use of a very high excess of the alkylating agents together with long reaction times (2 weeks), the higher sulfonium salts (tri- or tetrasubstituted) have

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never been observed in the reaction mixtures. What is more, the regioselectivity of *S*-dialkylation reactions is strictly limited to the formation of the distal derivative, obviously to avoid the presence of two positive charges nearby. Consequently, isomers having sulfonium groups in proximal positions (**3a**−**3c**) have never been observed.

If we take into account what has been stated in a previous paragraph, we can now understand the surprising results of the alkylation reaction depicted in Scheme 1, where only one monoalkyl and one dialkyl derivatives were identified in the reaction mixture (blue colored). Although six different dialkylsulfonium isomers are theoretically possible, only isomer **3d** having alkyl substituents in the distal position and oriented toward the upper rim direction is actually formed. As the mutual orientation of all neighboring aromatic rings in the *cone* conformation is *syn*, the preferred stereochemistry of *S*-alkyl groups can be assigned as equatorial (Figure 1).

To check the general applicability of the above-mentioned preferences in the *S*-alkylation reactions, we carried out the alkylation study of the three remaining conformers: *1,2-alternate*, *1,3-alternate*, and *partial cone*. The *1,2-alternate* conformer **4** bearing *tert*-butyl groups on the upper rim was stirred with 12 equiv of ethyl triflate in dry DCE for 3 days at room temperature. The resulting reaction mixture was purified by column chromatography on silica gel to give monoalkylated compound **5** (R = Et) and dialkylated derivative **6** in 74 and 22% yields, respectively (Scheme 2). The structures of both alkylated products were assigned by MS and NMR experiments. Thus, the HRMS ESI$^+$ analysis of **5** showed a signal at m/z = 917.4692, which corresponded to the molecular weight of monocation formed (theory = 917.4705). Similarly, the signal at m/z = 473.2548 for bis-*S*-ethyl derivative **6** agreed with the value predicted for the dication (473.2545). Similarly, the reaction of starting **4** with MeOTf gave the corresponding bis-methylated sulfonium salt **6** (R = Me) as the only isolable product in 59% yield (m/z = 459.2389).

The regio- and stereoselectivity of the alkylation in the *1,2-alternate* series was studied by ^{1}H NMR NOE experiments (see the Supporting Information.). The *1,2-alternate* molecule could theoretically be considered as two opposite halves that can possess either a *syn* or an *anti* orientation (Figure 1), depending on the position of the bisecting plane. As revealed by NOE interactions of the *S*-alkyl group with aromatic protons, the alkyl group enters the bridge with *syn*-oriented aromatic rings, and again it prefers the direction from the upper rim of the thiacalixarene, the equatorial position. As a result, a monoalkylsulfonium salt adopts structure **5a**, which perfectly corresponds with the preferences found for the *cone* conformation.[9] If bis-alkylated compounds **6** followed the same rules, one should obtain an isomer with distally disubstituted sulfur atoms possessing the equatorial orientation. Indeed, although there are seven theoretically possible regio- and stereoisomers (**6a**−**6g**), only compound **6f** with opposing equatorial arrangements allows the correct regio- and stereochemistry, and it was isolated as the only bis-alkylated product. The structure of bis-methyl derivative **6** (R = Me) was also confirmed by X-ray crystallography, which showed clearly the expected regiochemistry and stereochemistry (methyl at the sulfur with *syn*-oriented aromatic rings located in the equatorial position of the *1,2-alternate* conformation) on both alkylated sulfur atoms (Figure 2a). Interestingly, the regio- and stereochemistry of **6f** is the same as the bridge-disubstituted

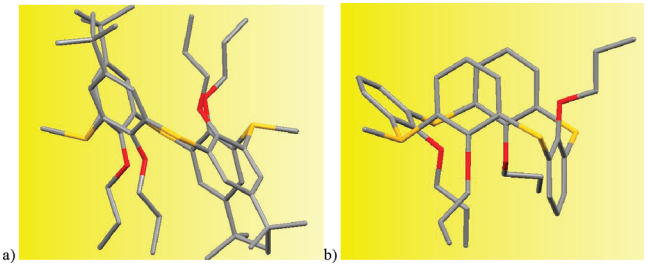

Figure 2. Crystallographic structures: (a) compound **6** (R = Me), (b) compound **8** (only one enantiomer shown). All hydrogen atoms and counteranions (triflates) were omitted for better clarity.

calix[4]arene derivatives recently obtained via lithiation/alkylation treatment of the methylene bridges.[10]

The *S*-alkylation of *partial cone* conformer **7** was carried out under standard conditions (12 equiv of ROTf, DCM, rt, 2 days), and the corresponding methyl and ethyl derivatives were isolated in 57 and 67% yields, respectively. Mass spectrometry confirmed in both cases the formation of monosubstituted derivatives **8** (m/z = 679.28, R = Me and 693.27, R = Et), which were isolated as the only alkylation products. The *partial cone* molecule can again be bisected into two halves: the first one having the *cone*-like arrangement with the *syn* orientation of the aromatic units and the second one possessing the *1,3-alternate*-like features (*anti*-oriented phenolic rings). Theoretically, monosulfonium salts **8** could adopt four different structures **8a**−**8d** (Scheme 3). Obviously, only isomer **8a** fulfills the requirements of *S*-alkylation reactions (*syn* position with the equatorial orientation of alkyl group), and indeed, both methyl and ethyl derivatives were proven to possess this preferred stereo- and regiochemistry. The final evidence of this structure was obtained by X-ray crystallography and can be seen in Figure 2b (as compound **8a** is inherently chiral, the basic cell contains both enantiomers; only one of them is shown for better clarity).

Interestingly, although 14 different regio- and stereoisomers could be theoretically formed by dialkylation of *partial cone* conformer **7**, none of them were isolated from the reaction mixture. Even the use of higher excess of the alkylation agents together with longer reaction times did not lead to any isolable amount of dialkylated derivatives. A thorough inspection of Scheme 3 gave us the clue: there is no other isomer that would enable the introduction of the second alkyl group into the preferred distal *syn* position with equatorial orientation.

The last conformer (*1,3-alternate*) represents a very special case, as there is no *syn* position that is obviously strongly preferred by the alkyl group. All neighboring aromatic units of the *1,3-alternate* conformer possess the *anti* stereochemistry, which does not allow the preferred equatorial orientation of the alkyl groups. Despite this fact, tetrapropoxy derivative **9** was alkylated with MeOTf (DCM, rt, 4 days) to give monoalkylated product **10** in 65% yield (Scheme 4). As shown in Figure 1, in this case the stereochemistry is meaningless, as the same product is formed by the attack of the alkylating agents from both sides of the molecule; this arrangement can be designated as isoclinal as suggested by Biali.[11] Not surprisingly, no dialkylsulfonium derivatives were isolated from the reaction mixture, otherwise both alkyl groups would have to adopt the less preferred isoclinal arrangement.

To gain deeper insight into the regioselectivity and stereoselectivity of the *S*-alkylations, we have attempted to

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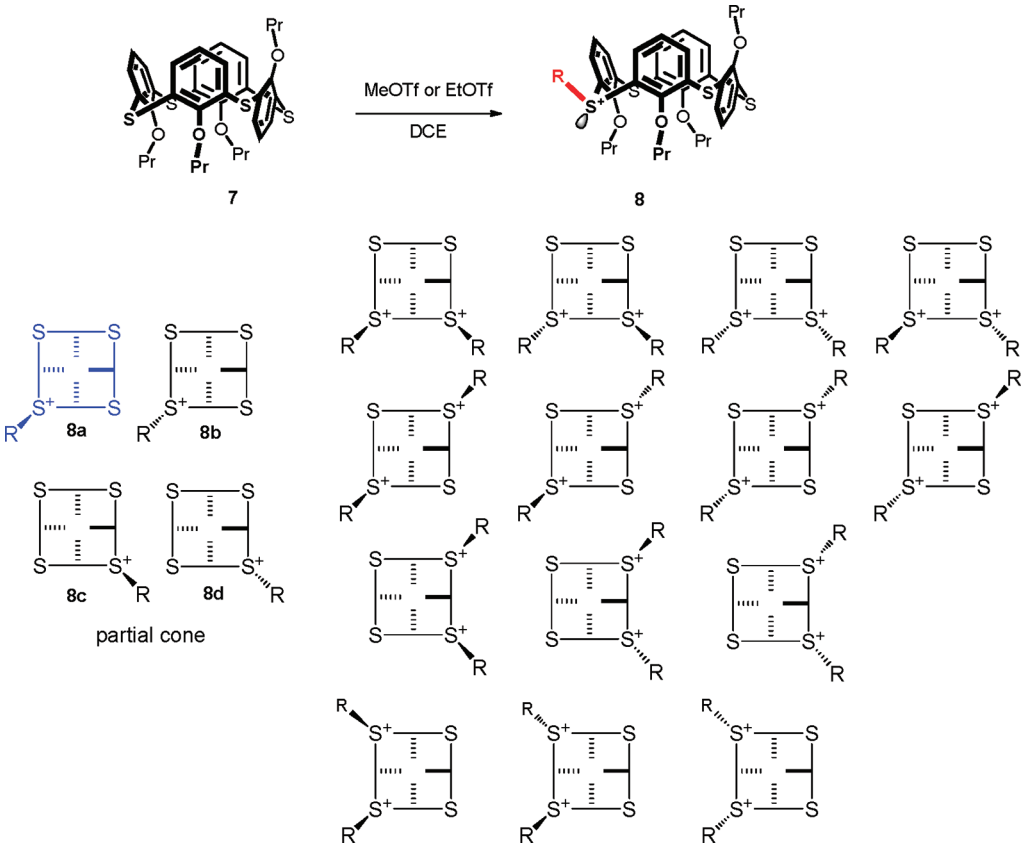
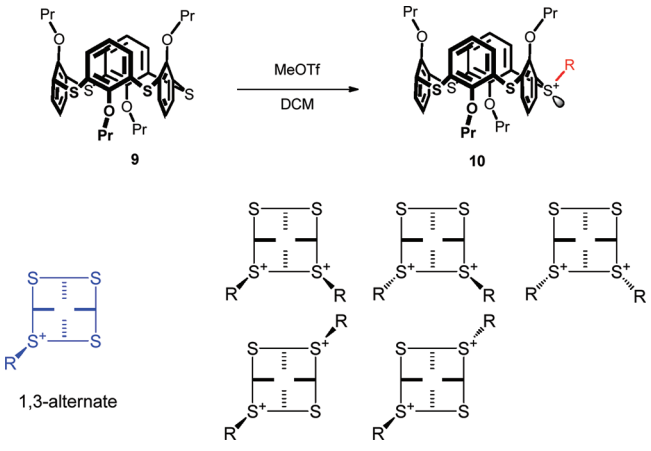
Scheme 3. *S*-Alkylation of Thiacalix[4]arene in the *Partial Cone* Conformation[a]



[a]Blue color denotes isomers isolated from the reaction mixture. Hashed and bold bonds denote the mutual orientations of the alkyl groups on the lower rim.

Scheme 4. *S*-Alkylation of Thiacalix[4]arene in the *1,3-Alternate* Conformation[a]



[a]Blue color denotes isomer isolated from the reaction mixture. Hashed and bold bonds denote the mutual orientations of the alkyl groups on the lower rim.

analyze reaction products in terms of thermodynamic stability. The free energies of all possible mono- and bis-*S*-methylated isomers for the *cone* conformations were evaluated using the B3LYP/6-311G(d,p) method, and the results are collected in Table 1. Obviously, the attack of the methyl group from the lower rim direction leads to isomer **2b**, which is destabilized by 5 kcal/mol compared to isomer **2a**. This result indicates that

Table 1. Comparison of Total and Relative Energies of the Corresponding Cone Mono- and Bis-sulfonium Salts, B3LYP/6-311G(d,p) Method Used

isomer	total energy[a]	relative energy[b]
2a	−3329.7296411	**0.0**
2b	−3329.7219146	4.8
3a	−3369.3179779	12.8
3b	−3369.3072916	19.5
3c	−3369.2966271	26.2
3d	−3369.3383717	**0.0**
3e	−3369.3279030	6.6
3f	−3369.3180901	12.7

[a]In [a.u.]. [b]In [kcal·mol^{-1}].

the alkylation is governed by a thermodynamic stability of products formed. The comparison of bis-methylated isomers **3a**−**3f** clearly confirms the experimental finding that proximally dialkylated isomers were never detected in the reaction mixtures. The quantum-chemical calculations showed that all proximal isomers **3a**−**3c** possess much higher relative energy compared with distally disubstituted isomers **3d**−**3f**. Obviously, the presence of two positively charged sulfur atoms in proximal positions destabilizes the system if compared with a distal arrangement. This effect is maximal in the case of **3c** (26.2 kcal/mol) where, moreover, both alkyl groups have a disfavored axial orientation. The most stable isomer **3d** corresponds to the structure of product isolated from the reaction mixture. As shown in Table 1, other distally disubstituted isomers are

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destabilized by 6.6 kcal/mol (isomer **3e**) and 12.7 kcal/mol (isomer **3f**) showing the influence of a wrong stereochemistry (one or two alkyl groups, respectively) to the overall thermodynamic stability of **3**.

Similar calculations were carried out for mono- and bis-*S*-methylation of the *1,2-alternate* conformer. As can be seen from Table 2, the comparison of relative energies of the corresponding monomethylated isomers **5a**–**5c** obtained by the B3LYP/6-311G(d,p) method showed that the most stable is isomer **5a**. The equatorial disposition of the alkyl group of **5a** is favored by 1.6 kcal/mol over the corresponding isoclinal arrangement in **5c**. Again, the wrong orientation (axial) of alkyl group in **5b** is strongly disfavored by 6.6 kcal/mol. The same features can be seen in the stability of dimethylsulfonium salts **6a**–**6g**. The most stable isomer **6f** (diequatorial arrangement) is reasonably stabilized (15.8 kcal/mol) if compared with **6g** having the same arrangement with a wrong (axial) stereochemistry of alkyl groups. As it is already obvious from the analysis of the *cone* conformation, all proximally bis-substitued isomers **6a**–**6d** are strongly disfavored (10–20 kcal/mol) if compared with **6f**.

Table 2. Comparison of Total and Relative Energies of the Corresponding *1,2-Alternate* Isomers, B3LYP/6-311G(d,p) Method Used

isomer	total energy[a]	relative energy[b]
5a	−3329.7322911	**0.0**
5b	−3329.7217142	6.6
5c	−3329.7298117	1.6
6a	−3369.3219800	10.1
6b	−3369.3105849	17.3
6c	−3369.3061239	20.1
6d	−3369.3182036	12.5
6e	−3369.3236306	9.1
6f	−3369.3381463	**0.0**
6g	−3369.3130286	15.8

[a]In [a.u.]. [b]In [kcal·mol^{-1}].

On the basis of the above experimental results and the theoretical calculations, we could formulate the rules governing the *S*-alkylation of thiacalix[4]arenes:

(i) Equatorial orientation of the *S*-alkyl group is strongly preferred over the axial one.
(ii) Proximal sulfur bridges cannot be alkylated; only distally dialkylated compounds can be formed.
(iii) *syn* position is preferred over *anti* position.
(iv) *anti* position is alkylated only if the molecule does not contain any bridge possessing the *syn* stereochemistry.

In conclusion, the *S*-alkylations of all four conformers of thiacalix[4]arene were carried out using alkyl triflates as the alkylating agents. Although many regio- and stereoisomers are theoretically possible, it was found that the corresponding sulfonium salts are formed in a highly regio- and stereoselective manner depending on the starting conformation used. The combination of experimental results with the quantum-chemical approach using the B3LYP/6-311G(d,p) method resulted in the elucidation of the rules governing the regio- and stereochemical outcomes of the alkylation reactions. The *S*-alkylation of thiacalixarenes is another spectacular example of a remarkable different reactivity of the thiacalix[4]arene and calix[4]arene systems.

EXPERIMENTAL SECTION

General Experimental Methods. All chemicals were purchased from commercial sources and used without further purification. Solvents were dried and distilled using conventional methods. Melting points are uncorrected. NMR spectra for all compounds were accomplished at 298 K on NMR spectrometers operating at 300 or 500 MHz for ^{1}H and 75 or 125 MHz for ^{13}C. Acetone-d_6 (99.90%) was used as a deuterated solvent. Chemical shifts (δ) are expressed in ppm and are referred to the residual peak of the solvent or TMS as an internal standard; coupling constants (J) are in Hz. The signal assignment was supported by ^{1}H–^{1}H COSY, ^{1}H–^{13}C HMQC, or ^{1}H–^{13}C HMBC 2D NMR and 1D ^{1}H–DPFGSE NOE experiments using the standard pulse sequences provided by NMR producer. All samples for elemental analyses were dried in the desiccator over P_2O_5 under a vacuum (1 Torr) at 80 °C for 8 h. The IR spectra were measured on an FT-IR spectrometer in KBr tablets. Usually, the 100 scans for one spectrum were accumulated at a spectral resolution of 4 cm^{-1}. The courses of the reactions were monitored by TLC using TLC aluminum sheets with Silica gel 60_{254}. The column chromatography was performed using Silica gel 60. Starting compounds **4**, **7**, and **9** were prepared according to known procedures.[12,4a,5] For the numbering of protons in ^{1}H NMR spectra, see the Supporting Information.

***S*-Alkylation of *1,2-Alternate* 4 with Ethyl Triflate.** A mixture of thiacalixarene **4** (89 mg, 0.10 mmol) and 12 equiv of ethyl triflate (160 μL, 1.20 mmol) was stirred under nitrogen in dry 1,2-dichloroethane (25 mL) at room temperature for 3 days. The reaction mixture was then evaporated to dryness, and products **5a** (**R** = **Et**) and **6f** (**R** = **Et**) were separated by column chromatography (silica gel, eluent = CH_2Cl_2/MeOH 14:1 v/v) as a colorless solid.

2-Ethyl-5,11,17,23-tetra-*tert*-butyl-25,26,27,28-tetrapropoxythiacalix[4]arene-2-onium triflate (*1,2-Alternate*) 5a (R = Et). Yield 74% (79 mg): mp 251–252 °C; ^{1}H NMR (CD_3COCD_3, 500 MHz, 298 K) δ 8.06 (d, 2H, J = 2.0 Hz, H-3–*A*), 7.98 (d, 2H, J = 2.0 Hz, H-5–*A*), 7.83 (d, 2H, J = 2.3 Hz, H-3–*B*), 7.63 (d, 2H, J = 2.3 Hz, H-5–*B*), 4.48 (q, 2H, J = 7.2 Hz, SCH_2CH_3), 4.30–4.40 (m, 2H, OCH_2-*A*), 3.70–3.80 (m, 4H, 2 × OCH_2-*B*), 3.62–3.72 (m, 2H, OCH_2-*A*), 1.50 (t, 3H, J = 7.2 Hz, SCH_2CH_3), 1.43 (s, 18H, 2 × *t*-Bu–*A*), 1.36 (s, 18H, 2 × *t*-Bu–*B*), 1.00–1.45 (m, 8H, $CH_2CH_2CH_3$), 0.72 and 0.68 (2 × t, 2 × 6H, J = 7.5 Hz, $CH_2CH_2CH_3$–*A* and $CH_2CH_2CH_3$–*B*) ppm; ^{13}C NMR (CD_3COCD_3, 125 MHz, 298 K) δ 158.7, 157.6, 150.4, 147.4, 136.6, 135.8, 131.3, 130.8, 130.8, 126.9, 125.6, 121.0, 76.2, 75.7, 38.4, 36.0, 35.0, 31.6, 31.3, 23.5, 23.0, 10.4, 10.2, 10.1 ppm; HRMS (ES+) calcd for $C_{54}H_{77}O_4S_4^+$ 917.4705 [M_{cat}^+], found m/z 917.4692 [M_{cat}^+]; IR (KBr) ν 2964, 2876, 1583, 1477, 1446, 1383, 1268, 1159, 1091, 1032, 984 cm^{-1}. Elemental Anal. Calcd for $C_{55}H_{77}F_3O_7S_5$: C, 61.88; H, 7.27; S, 15.02. Found: C, 61.52; H, 7.12; S, 14.88.

2,14-Diethyl-5,11,17,23-tetra-*tert*-butyl-25,26,27,28-tetrapropoxythiacalix[4]arene-2,14-dionium Ditriflate (*1,2-Alternate*) 6f (R = Et). Yield 22% (28 mg): mp 257–258 °C; ^{1}H NMR (CD_3COCD_3, 500 MHz, 298 K) δ 8.19 (d, 4H, J = 2.4 Hz, H-3), 8.13 (d, 4H, J = 2.4 Hz, H-5), 4.57 (q, 4H, J = 7.1 Hz, 2 × SCH_2CH_3), 4.25–4.38 (m, 4H, OCH_2-*B*), 3.70–4.85 (m, 4H, OCH_2-*A*), 1.54 (t, 6H, J = 7.1 Hz, 2 × SCH_2CH_3), 1.40–1.50 (m,4H, $CH_2CH_2CH_3$), 1.45 (s, 36H, 4 × *t*-Bu), 1.03–1.13 (m, 4H, $CH_2CH_2CH_3$), 0.70 (t, 12H, J = 7.5 Hz, 4 × $CH_2CH_2CH_3$) ppm; ^{13}C NMR (CD_3COCD_3, 125 MHz, 298 K) δ 157.6, 151.4, 136.6, 129.4, 126.8, 121.4, 76.3, 38.8, 36.2, 31.3, 23.2, 10.2, 10.0 ppm; HRMS (ES+) calcd for $C_{56}H_{82}O_4S_4^{2+}$ 473.2548 [$(M_{dicat})^{2+}$], found m/z 473.2545 [$(M_{dicat})^{2+}$]; IR (KBr) ν 2965, 2879, 1479, 1457, 1388, 1367, 1259, 1158, 1092, 1031 cm^{-1}. Elemental Anal. calcd for $C_{58}H_{82}F_6O_{10}S_6$: C, 55.92; H, 6.64; S, 15.44. Found: C, 55.69; H, 6.41; S, 15.18.

***S*-Alkylation of *1,2-Alternate* 4 with Methyl Triflate.** A mixture of thiacalixarene **4** (89 mg, 0.10 mmol) and 12 equiv of methyl triflate (140 μL, 1.20 mmol) was stirred under nitrogen in dry 1,2-dichloroethane (20 mL) at room temperature. After 3 days stirring, the reaction mixture was evaporated to dryness and purified by column chromatography on silica gel with DCM/MeOH 12:1 (v/v) mixture to yield 70 mg (57%) of compound **6f** (**R** = **Me**) as a colorless solid.

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2,14-Dimethyl-5,11,17,23-tetra-*tert*-butyl-25,26,27,28-tetrapropoxythiacalix[4]arene-2-dionium Ditriflate (*1,2-Alternate*) 6f (R = Me). Yield 57% (70 mg): mp 286−287 °C; ^{1}H NMR (CD_3COCD_3, 600 MHz, 298 K) δ 8.21 (d, 4H, J = 2.2 Hz, H-3), 8.12 (d, 4H, J = 2.2 Hz, H-5), 4.15−4.30 (m, 4H, OC$\underline{H}_2$- *B*), 3.97 (s, 6H, 2 × SC$\underline{H}_3$), 3.85−3.95 (m, 4H, OC$\underline{H}_2$-*A*), 1.40−1.50 (m, 4H, $CH_2C\underline{H}_2CH_3$), 1.45 (s, 36H, 4 × *t*-Bu), 1.03−1.13 (m, 4H, $CH_2C\underline{H}_2CH_3$), 0.73 (t, 12H, J = 7.5 Hz, 4 × $CH_2CH_2C\underline{H}_3$) ppm; ^{13}C NMR (CD_3COCD_3, 150 MHz, 298 K) δ 155.9, 150.3, 135.6, 128.3, 125.6, 122.4, 75.5, 35.3, 30.5, 26.3, 22.3, 9.1 ppm; HRMS (ES+) calcd for $C_{54}H_{78}O_4S_4^{2+}$ 459.2392 [$(M_{dicat})^{2+}$], found m/z 459.2389 [$(M_{dicat})^{+2}$]; IR (KBr) ν: 2966, 2879, 1479, 1458, 1387, 1366, 1258, 1161, 1092, 1031, 978, 944 cm^{-1}. Elemental Anal. Calcd for $C_{56}H_{78}F_6O_{10}S_6$: C, 55.24; H, 6.46; S, 15.80. Found: C, 55.01; H, 6.29; S, 15.48.

2-Methyl-25,26,27,28-tetrapropoxythiacalix[4]arene-2-onium Triflate (*Partial Cone*) 8a (R = Me). A mixture of thiacalixarene **7** (300 mg, 0.450 mmol) and 12 equiv of methyl triflate (0.61 mL, 5.40 mmol) was stirred under nitrogen in dry dichloromethane (20 mL) at room temperature. The reaction mixture was stopped by the evaporation of the solvent after 2 days stirring. Product **8a** (**R = Me**) was obtained by column chromatography (silica gel, eluent = CH_2Cl_2/MeOH 12:1 v/v) as a colorless solid. Yield 57% (212 mg): mp 114−117 °C; ^{1}H NMR (CD_3COCD_3, 500 MHz, 298 K) δ 8.12 (dd, 1H, J = 1.2, 8.0 Hz, H-3−*B*), 8.06 (dd, 1H, J = 1.3, 7.8 Hz, H-5−*B*), 8.02 (dd, 1H, J = 1.5, 7.7 Hz, H-5−*A*), 7.78−7.85 (m, 2H, H-3−*D*, H-5−*D*), 7.60 (dd, 1H, J = 1.9, 7.3 Hz, H-5−*C*), 7.55 (dd, 1H, J = 8.0, 8.0 Hz, H-4−*B*), 7.26 (dd, 1H, J = 1.5, 8.2 Hz, H-3−*A*), 7.20−7.10 (m, 2H, H-4−*A*, H-4−*D*), 6.75−6.65 (m, 2H, H-3−*C*, H-4−*C*), 4.80−4.70 (m, 1H, OCH_2−*A*), 4.25−4.05 (m, 4H, OCH_2−*D, C, D, B*), 4.05−3.95 (m, 1H, OCH_2−*A*), 3.90−3.80 (m, 1H, OCH_2−*B*), 3.75−3.65 (m, 5H, S−CH_3, OCH_2−*C*), 2.12−2.00 (m, 4H, CH_3CH_2−*A, D*), 2.00−1.90 (m, 2H, CH_3CH_2-*C*), 1.35−1.20 (m, 2H, CH_3CH_2-*B*), 1.20−1.08 (m, 9H, 3 × CH_3CH_2−*A, C, D*), 0.78 (t, 3H, CH_3CH_2− *B*) ppm; ^{13}C NMR (CD_3COCD_3, 125 MHz, 298 K) δ 164.3, 162.2, 161.9, 159.1, 145.8, 143.4, 140.0, 139.9, 139.0, 137.4, 133.7, 132.5, 131.9, 130.2, 131.0, 129.3, 130.9, 129.9, 127.2, 127.0, 125.5, 125.1, 125.0, 124.8, 80.2, 79.4, 77.6, 77.1, 26.6, 25.3, 25.0, 24.9, 23.1, 11.8, 11.5, 11.5, 10.0 ppm; MS (ES+) calcd for $C_{37}H_{43}O_4S_4^+$ 679.20 [$(M_{cat})^+$], found m/z 679.28 [$(M_{cat})^+$]; IR (KBr) ν 3499, 2965, 2937, 2876, 1438, 1382, 1261, 1157, 1032 cm^{-1}. Elemetal Anal. Calcd for $C_{38}H_{43}F_3O_7S_5$: C, 55.05; H, 5.23; S, 19.39. Found: C, 54.88; H, 5.10; S, 19.26.

2-Ethyl-25,26,27,28-tetrapropoxythiacalix[4]arene-2-onium Triflate (*Partial Cone*) 8a (R = Et). A mixture of thiacalixarene **7** (300 mg, 0.450 mmol) and 24 equiv of ethyl triflate (1.40 mL, 10.8 mmol) was stirred under nitrogen in dry dichloromethane (20 mL) under reflux. The reaction mixture was stopped by the evaporation of the solvent after 4 days. Product **8a** (**R = Et**) (235 mg, 67%) was obtained by column chromatography (silica gel, eluent = CH_2Cl_2/MeOH 12:1 v/v) as a colorless solid: mp 116−119 °C; ^{1}H NMR (CD_3COCD_3, 500 MHz, 298 K) δ 8.11 (dd, 1H, J = 1.2, 8.0 Hz, H-3−*B*), 8.06 (dd, 1H, J = 1.3, 8.0 Hz, H-5−*B*), 8.04 (dd, 1H, J = 1.5, 7.9 Hz, H-5−*A*), 7.81 (d, 2H, J = 8.3 Hz, H-3−*D*, H-5−*D*), 7.59 (dd, 1H, J = 2.1, 7.9 Hz, H-5−*C*), 7.54 (dd, 1H, J = 8.0, 8.0 Hz, H-4−*B*), 7.24 (dd, 1H, J = 1.5, 8.2 Hz, H-3−*A*), 7.17 (dd, 1H, J = 7.9, 7.9 Hz, H-4−*A*), 7.15 (dd, 1H, J = 8.3, 8.3 Hz, H-4−*D*), 6.70 (dd, 1H, J = 2.1, 7.9 Hz, H-3−*C*), 6.68 (dd, 1H, J = 7.9, 7.9 Hz, H-4−*C*), 5.03−4.96 (m, 1H, OCH_2−*A*), 4.35−4.25 (m, 1H, SCH_2CH$_3$), 4.25−4.05 (m, 5H, OCH_2−*D, C, D, B,* SCH_2CH$_3$), 3.90−3.80 (m, 2H, OCH_2−*A, B*), 3.72−3.65 (m, 1H, OCH_2−*C*), 2.12−2.00 (m, 4H, CH_3CH_2−*A, D*), 2.00−1.89 (m, 2H, CH_3CH_2-*C*), 1.51 (t, 3H, J = 7.3 Hz, SCH_2CH$_3$), 1.35−1.20 (m, 2H, CH_3CH_2-*B*), 1.18 and 1.11 (2 × t, 3H, CH_3CH_2−*A, D*), 1.14 (t, 3H, J = 7.4 Hz, CH_3CH_2−*C*), 0.77 (t, 3H, J = 7.5 Hz, CH_3CH_2−*B*) ppm; ^{13}C NMR (CD_3COCD_3, 125 MHz, 298 K) δ 164.3, 163.4, 161.8, 159.3, 146.1, 143.6, 139.8, 140.0, 138.8, 137.2, 133.7, 132.4,131.9, 129.9, 130.9, 130.9, 129.2, 130.1, 127.3, 127.2, 125.3, 125.0, 124.8, 122.4, 79.5, 79.3, 77.6, 77.0, 38.3, 25.2, 25.0, 24.9, 23.1, 11.8, 11.7, 11.5, 10.5, 10.0 ppm; MS (ES+) calcd for $C_{38}H_{45}O_4S_4^+$ 693.22 [$(M_{cat})^+$]; found m/z 693.27 [$(M_{cat})^+$]; IR (KBr) ν 3432, 2964, 2875, 1630, 1435, 1427, 1382, 1232, 1124, 1084 cm^{-1}. Elemental Anal. Calcd for $C_{39}H_{47}F_3O_7S_4$: C, 55.43; H, 5.61; S, 18.97. Found: C, 55.11; H, 5.40; S, 18.88.

2-Methyl-25,26,27,28-tetrapropoxythiacalix[4]arene-2-onium Triflate (*1,3-Alternate*) 10 (R = Me). A mixture of derivative **9** (100 mg, 0.150 mmol) and 12 equiv of methyl triflate (0.20 mL, 1.80 mmol) was stirred under nitrogen in dry DCM (20 mL) at room temperature. The reaction mixture was evaporated to dryness after 4 days and purified by column chromatography (silica gel, eluent = CH_2Cl_2/MeOH 12:1 v/v) to yield compound **10** (**R = Me**) (81 mg, 65%) as a colorless solid: mp 251−253 °C; ^{1}H NMR (CD_3COCD_3, 500 MHz, 298 K) δ 8.02−8.09 (m, 3H, H-3−*B*, H-5−*B*, H-3−*A*), 7.98 (dd, 1H, J = 1.4 Hz, J = 7.8 Hz, H-5−*A*), 7.60 and 5.54 (2 × dd, 2 × 1H, J = 1.6 Hz, J = 7.9 Hz, H-3−*C* and H-5−*C*), 7.54 and 7.48 (2 × dd, 2 × 1H, J = 1.6 Hz, J = 7.9 Hz, H-3−*D* and H-5−*D*), 7.46 (dd, 1H, J = 7.9 Hz, J = 7.9 Hz, H-4−*A*), 7.34 (dd, 1H, J = 7.9 Hz, 7.9 Hz, H-4−*B*), 7.05 (dd, 1H, J = 7.8 Hz, 7.8 Hz, H-4−*D*), 7.04 (dd, 1H, J = 7.8 Hz, 7.8 Hz, H-4−*C*), 4.71 (m, 1H, OCH_2−*A*), 4.65 (m, 1H, OCH_2−*B*), 3.98, 3.96, 3.89, 3.89, 3.80, and 3.70 (m, 6H, OCH_2−*C*, OCH_2−*C*, OCH_2−*A*, OCH_2−*D*, OCH_2−*D*, OCH_2−*B*), 3.73 (s, 3H, S−CH_3), 1.75−1.05 (5*m*, 8H, 4 × CH_3CH_2-), 0.85 (t, 3H, J = 7.5 Hz, CH_3-*A*), 0.78 (t, 3H, J = 7.5 Hz, CH_3-*C*), 0.70 (t, 3H, J = 7.5 Hz, CH_3-*B*), 0.78 (t, 3H, J = 7.5 Hz, CH_3-*D*) ppm; ^{13}C NMR (CD_3COCD_3, 125 MHz, 298 K) δ 161.3, 160.7, 160.0, 159.0, 143.3, 135.6, 140.1, 134.6, 134.4, 134.0, 132.5, 129.0, 130.3, 130.1, 128.2, 129.8, 127.9, 129.6, 126.0, 126.0, 124.8, 125.7, 121.6, 120.6, 74.9, 73.7, 72.4, 71.6, 25.7, 23.8, 23.3, 22.83, 22.81, 10.3, 10.2, 9.9, 9.7 ppm; MS ES+ calcd for $C_{37}H_{43}O_4S_4^+$ 679.20 [$(M_{cat})^+$]; found m/z 679.41 [$(M_{cat})^+$]; IR (KBr) ν: 2959, 2918, 2650, 1741, 1730, 1640, 1469, 1438, 1361, 1266, 1180 cm^{-1}. Elemental Anal. Calcd for $C_{38}H_{43}F_3O_7S_5$: C, 55.05; H, 5.23; S, 19.39. Found: C, 54.96; H, 5.17; S, 19.22.

X-ray Crystallography. The structures of compound **6** and **8** were deposited into Cambridge Structural Database under CCDC numbers 856289 and 856288, respectively. For details, see the Supporting Information.

■ ASSOCIATED CONTENT

Supporting Information

Synthesis and characterization of all new compounds, the copies of ^{1}H NMR, ^{13}C NMR, HMBC, HMQC, NOE, and MS spectra, quantum-chemical calculations, and crystallographic measurements. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*Tel.: +420-220 445 055, Fax: +420-220 444 288. E-mail: lhotakp@vscht.cz.

Notes

The authors declare no competing financial interest.

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