Syntheses of All Possible O-Methylation Products Derivable from 5,11,17,23,29,35-Hexa-*tert*-butylcalix[6]arene-37,38,39,40,41,42-hexol

Hideyuki Otsuka, Koji Araki, and Seiji Shinkai*

Department of Organic Synthesis, Faculty of Engineering, Kyushu University, Hakozaki, Fukuoka 812, Japan

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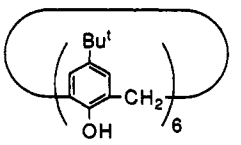
We here report methods for the synthesis of all twelve possible O-methylation products from 5,11,17,23,29,35-hexa-*tert*-butylcalix[6]arene-37,38,39,40,41,42-hexol (1): one mono-, three di-, three tri-, three tetra-, one penta-, and one hexamethylated products. The strategies used are (i) direct O-methylation with different $1/K_2CO_3$ ratios, (ii) selective mono-O-methylation of O-alkylation products, (iii) demethylation with $TiCl_4$ or LiI, and (iv) protection–deprotection with a benzyl group or an *o*- or *m*-xylenyl group. We believe that these O-methylation products are useful as basic skeletons to design functionalized calix[6]arenes with the desired number of substituents and regioselectively-positioned functional groups.

Calix[*n*]arenes are cyclic oligomers that belong to the class of $[1_n]$-metacyclophanes. As calix[*n*]arenes have a cavity-shaped architecture, they are useful as building blocks for host–guest-type receptors and catalysts through appropriate modification of the edges.[1] Functional groups can be introduced either to the upper rim by means of electrophilic substitution reactions[1-5] or to the lower rim by means of Williamson-type OH-modifications,[1,6-12] but there is no doubt that the latter method is much more convenient than the former. Functionalization of OH groups in calix[4]arenes has been thoroughly investigated.[1,6-12] By the skillful use of solvents, bases, molar ratios of reactants, protecting groups, etc., it is now possible to selectively synthesize all possible O-alkylation products (including conformational isomers) derivable from calix[4]arenes.[1,6-12] The reaction routes to each O-alkylation product have also been investigated by HPLC analysis of the time dependence of the product distribution.[9a,13,14]

The selective syntheses of O-alkylation products derivable from calix[6]arenes have been investigated only partially.[5a,6c,7c,15] The difficulty of this investigation arises from the complicated isolation and characterization of starting 5,11,17,23,29,35-hexa-*tert*-butylcalix[6]arene-37,38,39,40,41,42-hexol (1) and from the 12 O-alkylation



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products from mono- to hexa-O-alkylated calix[6]arenes (2–7: see Scheme 1). Kanamathareddy and Gutsche[6c] carried out arylmethylations to determine the effect of para substituents on the structural and/or conformational outcome of the reactions. Casnati et al.[7c] reported that refluxing 1 with K_2CO_3 and MeI in dry acetone gave symmetrically trisubstituted 5,11,17,23,29,35-hexa-*tert*-butyl-37,39,41-trimethoxy-38,40,42-trihydroxycalix[6]-arene ($4_{1,3,5}$) in 30% yield, but the reason for the formation of $4_{1,3,5}$ as the major product was not explained. More recently, Janssen et al.[15] carefully analyzed O-methylation products obtained from the reaction of 1 and MeI and succeeded in isolating several new products. To the best of our knowledge, however, the systematic synthesis of all possible O-alkylation products derivable from 1 has never

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Scheme 1

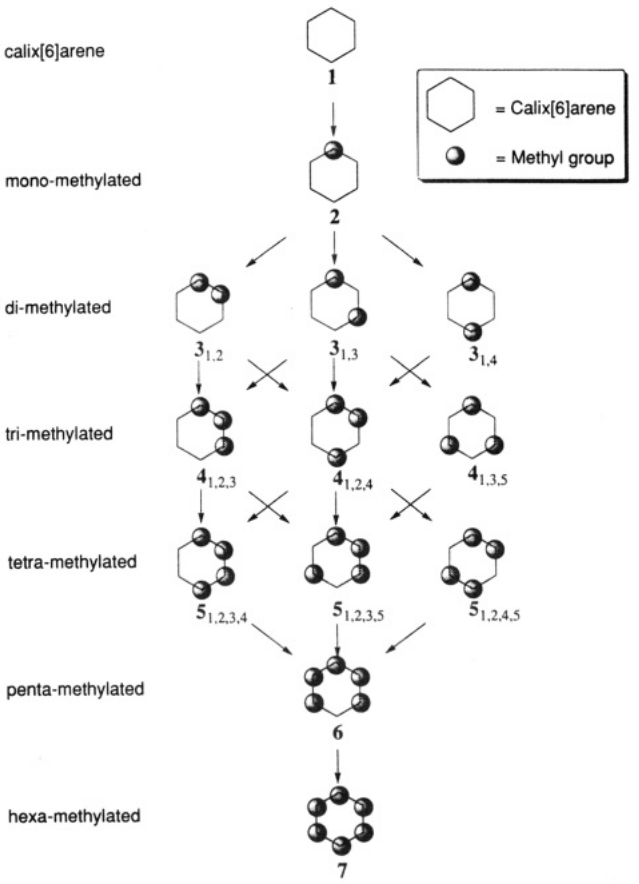


Table 1. Direct Methylation of 1 with MeI

	reactants, mmol			yield (%) of isolated products					
run	1	K_2CO_3	MeI	2	$3_{1,2}$	$3_{1,3}$	$4_{1,3,5}$	6	7
1	1.03	1.03	6.2	35	*a*	10	*a*	*a*	*a*
2	3.08	9.26	24.7	*a*	10	*a*	25	6	*a*
3	1.03	30.9	37.1	*a*	*a*	*a*	*a*	*a*	86

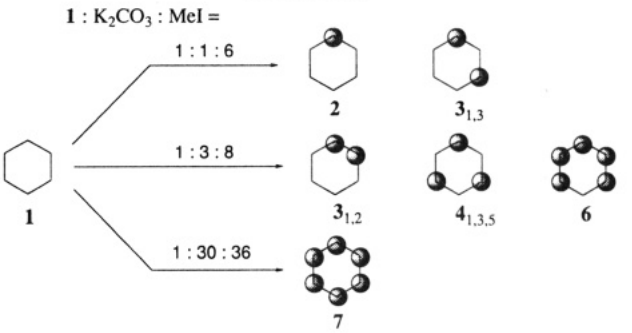
[a] Since the spot on the TLC plate was very small, the yield was estimated to be less than 5%.

been investigated. We here report various methods for the selective synthesis and isolation of the O-methylation products. In O-alkylation of calix[*n*]arenes, the methyl group and the benzyl group are frequently employed. We chose the methyl group because (i) the benzyl group is nonselectively deprotected, (ii) it increases the steric crowding, and (iii) it complicates the NMR spectra because its protons overlap with the calixarene benzene protons. We introduced two novel synthetic strategies in addition to those that have already been exploited for the syntheses of calix[4]arene derivatives:[9] (i) cleavage of proximal MeO groups with $TiCl_4$ and (ii) regioselective protection of two OH groups with an *o*- or *m*-xylenyl group.

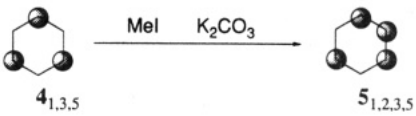
Results and Discussion

Direct Methylation. We first attempted direct methylation of 1 with several $1/K_2CO_3/MeI$ ratios and isolated the products either by preparative TLC or by column chromatography. The major products isolable by these methods are recorded in Table 1. When $1/K_2CO_3/MeI$ = 1:1:6 (run 1), **2**, $3_{1,3}$, and unchanged **1** were isolated. This result implies that the second methyl group predominantly enters into the 3-position rather than the 4-position. When $1/K_2CO_3/MeI$ = 1:3:8 (run 2), the major product was

Scheme 2



Scheme 3



symmetrically trimethylated $4_{1,3,5}$. The result is in accord with that previously reported by Casnati et al.[7c] In addition, we also isolated $3_{1,2}$ and **6**. Isolation of $3_{1,2}$ is curious because $3_{1,3}$, which is a precursor to $4_{1,3,5}$, was scarcely detected, whereas $3_{1,2}$, which is precursor for $4_{1,2,3}$ and $4_{1,2,4}$, was detected. A similar paradox was previously observed for di-O-alkylation of calix[4]arenes: in the presence of excess NaH, proximal isomers were selectively formed in preference to distal isomers.[8c,14,16] It was later confirmed, however, that proximal isomers and distal isomers were formed in the statistically expected 2:1 ratio, but the rate of further tri-O-alkylation for distal isomers was faster than that for proximal isomers; as a result, proximal isomers were selectively recovered.[14] We therefore believe that in run 2 the rate of further tri-O-methylation of $3_{1,3}$ to give $4_{1,3,5}$ is faster than that for $3_{1,2}$. This rate difference means that $3_{1,3}$ is isolable only in the presence of a small amount of K_2CO_3 (as in run 1). The isolation of **6** (but not of **5**) suggests that the reaction **5** → **6** is faster than the reaction **6** → **7**. When $1/K_2CO_3/MeI$ = 1:30:36 (run 3), **1** was fully O-methylated to give only **7**. The foregoing results demonstrate that one can synthesize six O-methylation products by direct methylation of **1** (Scheme 2). The results are roughly in line with those reported by Janssen et al.[15]

Compound $5_{1,2,3,5}$ has not been previously synthesized. We expected that $4_{1,3,5}$, which could be synthesized by direct methylation of **1** in reasonable yield, would serve as a useful intermediate; for example, monodemethylation would give $3_{1,3}$ and monomethylation would give $5_{1,2,3,5}$. We thus attempted methylation of $4_{1,3,5}$ with a $4_{1,3,5}/K_2CO_3/MeI$ = 1:1:1 ratio and isolated $5_{1,2,3,5}$ in 39% yield (Scheme 3). This result that $5_{1,2,3,5}$ can be synthesized in two steps.

Demethylation. Previously, Arduini et al.[17] reported the demethylation of 5,11,17,23-tetra-*tert*-butyl-25,26,-27,28-tetramethoxycalix[4]arene with $TiBr_4$. Very interestingly, they recovered 1,2-didemethylated 5,11,17,23-tetra-*tert*-butyl-25,26-dimethoxy-27,28-dihydroxy-

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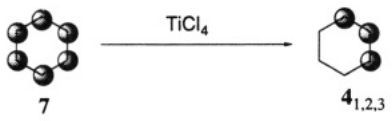
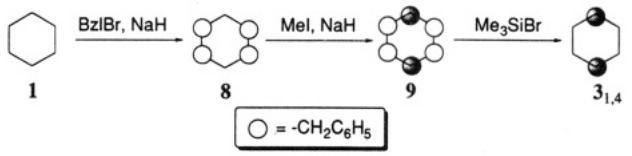
Scheme 4



Scheme 5



calix[4]arene as the major product.[18] We believed that this method would be applicable to our system. Compound **7** was treated with $TiCl_4$ with a **7**/$TiCl_4$ = 1:12 ratio. The major product was $\mathbf{4}_{1,2,3}$ (Scheme 4). This reuslt confirmed that Ti(IV) cleaves vicinal methyl groups in **7** as it does in the tetramethoxycalix[4]arenes.[17] We believed that the synthesis of $\mathbf{3}_{1,2}$ and $\mathbf{5}_{1,2,3,4}$ from **7** would be also possible by changing the mole ratio of **7** and $TiCl_4$. We also found that $\mathbf{3}_{1,3}$ could be synthesized from $\mathbf{4}_{1,3,5}$ by demethylation with LiI in 2,4,6-trimethylpyridine (see Experimental Section);[19] however, direct methylation of **1** was more practical.

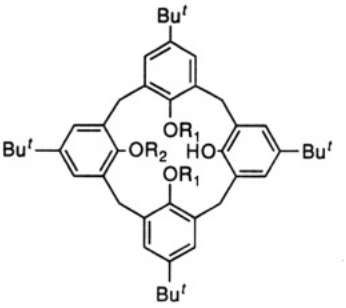
Protection–Deprotection Methods. Of the 12 O-methylation products in Scheme 1, so far we have discussed eight. The remaining derivatives are $\mathbf{3}_{1,4}$, $\mathbf{4}_{1,2,4}$, $\mathbf{5}_{1,2,3,4}$, and $\mathbf{5}_{1,2,4,5}$. Among these four products, $\mathbf{5}_{1,2,4,5}$ can be isolated from the prouct mixture obtained from direct methylation of **1**,[15] but the methods for the syntheses of other three derivatives are unknown. In O-alkylation of calix[4]-arenes, it was demonstrated that the products, which are difficult to synthesize by direct alkylation, could be synthesized via protection–deprotection with a benzyl group.[8a,9] We expected this strategy to be also useful for our system. Kanamathareddy and Gutsche[6c] have shown that tetra-O-benzylation occurs at the 1,2,4,5-positions. It thus occurred to us that di-O-methylation of tetra-O-benzylated calix[6]arene **8** followed by debenzylation would afford $\mathbf{3}_{1,4}$ (Scheme 5).

Compound **9** was synthesized from **8** in 81% yield. The four benzyl groups in **9** were removed by treatment with Me_3SiBr at room temperature. As expected, the product was identified to be $\mathbf{3}_{1,4}$ from spectral evidence and elemental analysis (see Experimental Section).

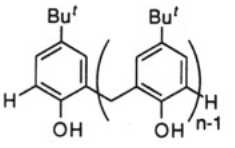
As demonstrated above, $\mathbf{4}_{1,2,4}$ and $\mathbf{5}_{1,2,3,4}$ could be also synthesized if the benzyl group could be regioselectively introduced into calix[6]arenes. In fact, however, this process is not as easy as it is for calix[4]arenes.[9] Recently, Saiki et al.[20] reported that the reaction of **1** with α,α'-dibromo-*m*-xylene derivatives affords 1,4-bridged calix-[6]arenes. This finding suggests that *o*- and *m*-xylene units may be useful for regioselective protection of two OH groups (Scheme 6). Compound **10** and **11** were synthesized in moderate yields (47 and 71%, respectively). As described in the Experimental Section, acetone and K_2CO_3 were used for the synthesis of **10**, whereas DMF and NaH were used for the synthesis of **11**. The different reaction conditions were used because the reaction of **1** and α,α'-dibromo-*m*-xylene is much slower than that of **1** and α,α'-dibromo-*o*-xylene. The reaction of **1** with α,α'-dibromo-*o*-xylene resulted in 1,2-bridged calix[6]arene **10**, whereas that of **1** with α,α'-dibromo-*m*-xylene resulted in 1,4-bridged calix[6]arene **11**. The regioselectivity is exactly in line with what we expected from the building of CPK molecular models. After methylation of the residual OH groups, we deprotected the xylenyl units with Me_3SiBr. Deprotection of the benzyl group with Me_3-SiBr proceeds at room temperature.[8a,9] In contrast, deprotection of the xylenyl units did not take place to an appreciable extent at room temperature. The low reactivity is probably associated with the stabilization arising from the ring structure. Deprotection occurred slowly at the reflux temperature in the presence of excess Me_3SiBr, but these drastic reaction conditions made it difficult to selectively remove the xylenyl units. For example, when we treated **12** with Me_3SiBr at the reflux temperature, we could isolate $\mathbf{5}_{1,2,3,4}$ in 17% yield by preparative TLC. We detected several additional spots on the TLC plate. The low yield and the complex product distribution suggest that this reaction occurs less selectively. We believed that the selectivity would be improved if we used more-activated xylenyl groups for protection. However, the nonselectivity was good for the isolation of $\mathbf{4}_{1,2,4}$. Deprotection of **13** resulted in $\mathbf{4}_{1,2,4}$ (9% yield) in addition to $\mathbf{5}_{1,2,4,5}$ (28% yield), indicating that treatment with Me_3SiBr cleaves not only the *m*-xylenyl group but also the methyl group. Although the yield of $\mathbf{4}_{1,2,4}$ is not high, it is reproducible.

On the δ_{OH} of O-Alkylation Products. It is known that the δ_{OH} of calix[*n*]arenes appears at low field because of the strong intramolecular hydrogen-bonding interaction.[1,21–23] When the OH groups are partially alkylated, the intramolecular hydrogen-bonding interaction is weakened, and the δ_{OH} moves to higher field.[23]

In Figure 1, we summarize the δ_{OH} values for **1**–**6**, calix-[4]arene derivatives **14**–**17**,and acyclic analogs **18** and **19**.[23]



14 : $R_1 = R_2 = H$
15 : R_1 = H, R_2 = Me
16 : R_1 = Me, R_2 = H
17 : $R_1 = R_2$ = Me



18 : n = 3
19 : n = 4

All of the measurements were carried out at 25 °C in $CDCl_3$. The δ_{OH} for **1** appeared at 10.53 ppm, which is comparable with that for 5,11,17,23-tetra-*tert*-butylcalix[4]arene-25,-26,27,28-tetrol (**14**: 10.34 ppm) but much lower than the δ_{OH} values for **18** and **19** (9.46–8.32 ppm). The OH groups in partially O-methylated calix[*n*]arenes are classified into

(18) We recently found that treatment of 25,26,27,28-tetramethoxycalix-[4]arene with $TiBr_4$ under the same reaction conditions gives 1,3-didemethylated 25,27-dimethoxy-26,28-dihydroxycalix[4]arene in 80% yield. This result indicates that the selectivity is profoundly influenced by the Bu^t groups.

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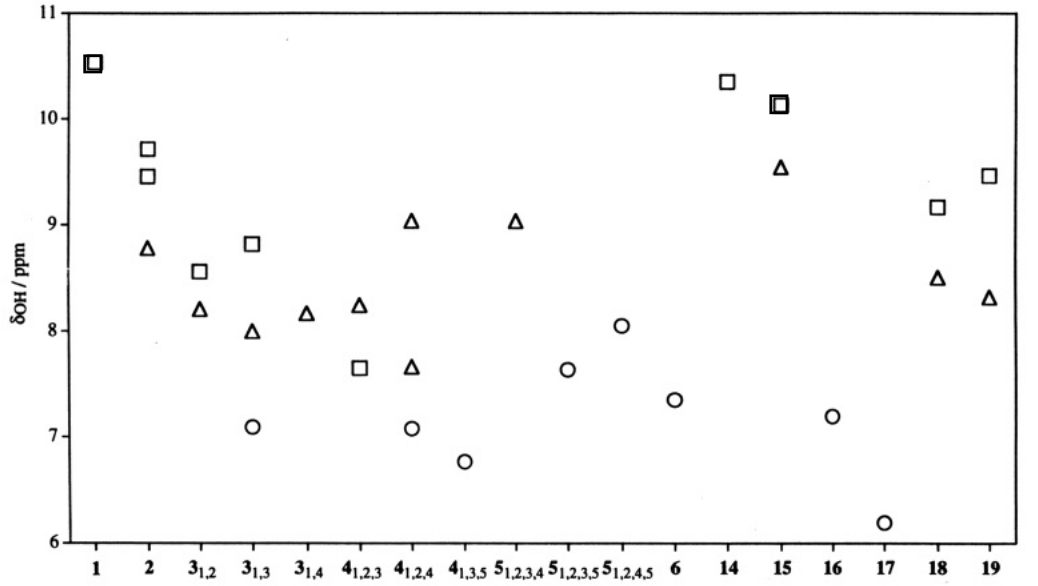
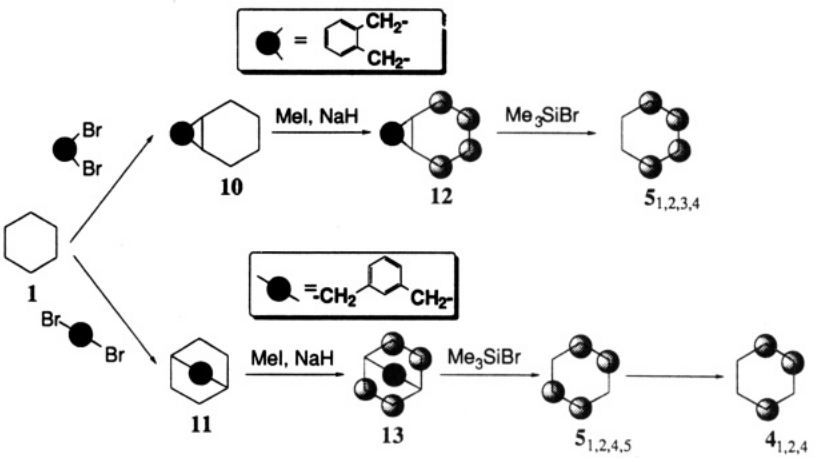


Figure 1. δ_{OH} at 25 °C in $CDCl_3$: (□) OH sandwiched between two OH groups, (△) OH sandwiched between one OH group and one OMe group, and (○) OH sandwiched between two OMe groups. (Compounds 14–17 have been reported in ref 23).

Scheme 6



three categories: (i) OH groups sandwiched between two OH groups, (ii) OH groups sandwiched between one OH group and one OMe group, and (iii) OH groups sandwiched between two OMe groups. For example, $3_{1,3}$ contains one type i OH, two type ii OH groups, and one type iii OH, which appear at 8.81, 8.00, and 7.09 ppm, respectively. These chemical shifts imply that the interaction in the type OH···OH···OH is strongest and the interaction in the type OMe···OH···OMe is weakest. This rule is applicable to most O-methylation products, but the difference among the three types in the calix[6]arene series is not as drastic as that in the calix[4]arene series.[1,21–23] There exists one exception, however: in $4_{1,2,3}$ the δ_{OH} for type ii OH groups (8.25 ppm) appeared at lower magnetic field than the δ_{OH} for type i OH (7.65 ppm). Although the reason is not clear yet, we believe that unsymmetrical tri-O-methylation induces "flattening" of three OH groups, which weakens the type i hydrogen bond. It is also interesting to note that the weakest, type iii hydrogen bond is observed for symmetrically tri-O-methylated $4_{1,3,5}$ but not for $5_{1,2,4,5}$ or **6**.

Conclusions

In this paper we demonstrate the synthetic methods for 12 O-methylation products derivable from **1**. Although eight of them have been reported previously,[6c,7c,9,15] the yields are much improved in some cases, and four of the products are new compounds. These O-methylation products are useful as basic skeletons for the design of tailor-made functionalized calix[6]arenes. Of particular interest are (i) the correlation between regioisomers and metal selectivities in ionophoric calix[6]arene derivatives, (ii) the uranyl affinities and selectivities in the regioisomers of tri-O-substituted calix[6]aryl acetic acid derivatives,[24,25] (iii) the influence of regioselectively-introduced substituents on the rate of ring inversion,[6c,7c,26,27] (iv) the suppression of ring inversion by the cross-link, and (v) the molecular design of new calix[6]arene-based receptors for metal cations and organic molecules.

Experimental Section

5,11,17,23,29,35-Hexa-*tert*-butyl-37-methoxy-38,39,40,41,-42-pentahydroxycalix[6]arene (2) and 5,11,17,23,29,35-hexa-*tert*-butyl-37,39-dimethoxy-38,40,41,42-tetrahydroxycalix-

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[6]arene ($3_{1,3}$). Compound 1 (1.0 g, 1.03 mmol) and MeI (0.4 mL, 6.2 mmol) were dissolved in anhyd acetone, and the solution was stirred at the reflux temperature for 20 h in the presence of K_2CO_3 (142 mg, 1.03 mmol). The mixture was filtered, and the filtrate was concentrated in vacuo to dryness. The residue was shaken with aqueous 1 M HCl and chloroform, and the organic layer was separated and washed with water three times. The solution was dried over $MgSO_4$ and then concentrated to dryness. The residue was subjected to preparative TLC (silica gel (60 GF_{254}, Merck 7730, 0.75 mm), dichloromethane). There were six spots on the TLC plate. The three larger spots were recovered. 1: R_f = 0.91, recovered percentage 20%. 2: R_f = 0.86, mp > 270 °C dec (lit.[15] > 320 °C), yield 36%; ^{1}H NMR ($CDCl_3$, 24 °C, 250 MHz) δ 1.15, 1.20, 1.23, and 1.25 (*t*-Bu, s each, 9H, 9H, 18H, and 18H), 3.74, 3.90, and 3.93 ($ArCH_2$, s each, 4H each), 4.00 (OCH_3, s, 3H), 6.99, 7.08, 7.10, 7.13, and 7.14 (ArH, s, d, s, s, and d, J = 2.3 Hz for 7.08 and 7.14, 2H, 2H, 2H, 4H, and 2H), 8.77, 9.45, and 9.71 (OH, s each, 2H, 1H and 2H). $3_{1,3}$: R_f = 0.51, mp 253–255 °C dec (lit.[15] > 257 °C), yield 10%; ^{1}H NMR ($CDCl_3$, 24 °C) δ 1.07, 1.25, 1.27, and 1.29 (*t*-Bu, s each, 18H, 9H, 18H, and 9H), 3.78 (OCH_3, s, 6H), 3.78, 3.90, and 3.92 ($ArCH_2$, s each, 4H each), 6.86, 6.90, 7.05, 7.09, 7.10, and 7.11 (ArH, d, d, s, d, s, and d, J = 2.3 Hz for 7.09 and 7.11, 2H each), 7.09, 8.00, and 8.81 (OH, s each, 1H, 2H and 1H).

Demethylation of $4_{1,3,5}$ (100 mg, 0.20 mmol) with LiI (19.8 mg, 0.30 mmol) in 2,4,6-trimethylpyridine at the reflux temperature for 24 h also gave $3_{1,3}$ in 60% yield. The result supports the assumption that in the above-mentioned reaction the 1,3-OH groups are methylated.

5,11,17,23,29,35-Hexa-*tert*-butyl-37,38-dimethoxy-39,40,41,-42-tetrahydroxycalix[6]arene ($3_{1,2}$), 5,11,17,23,29,35-hexa-*tert*-butyl-37,39,41-trimethoxy-38,40,42-trihydroxycalix[6]-arene ($4_{1,3,5}$) and 5,11,17,23,29,35-hexa-*tert*-butyl-37,38,39,40,41-pentamethoxy-42-hydroxycalix[6]arene (6). Compound 1 (3.0 g, 3.08 mmol) and MeI (1.53 mL, 24.7 mmol) were dissolved in anhyd acetone, and the solution was stirred at the reflux temperature for 12 h in the presence of K_2CO_3 (1.28 mg, 9.26 mmol). The workup was similar to that described above. We subjected the residue to column chromatography and isolated three compounds. $3_{1,2}$: mp 270–272 °C dec (lit.[15] > 270 °C), yield 10%; ^{1}H NMR ($CDCl_3$, 24 °C) δ 1.14, 1.24 and 1.26 (*t*-Bu, s each, 18H each), 3.73, 3.90, and 4.07 ($ArCH_2$, s each, 6H, 4H, and 2H), 3.82 (OCH_3, s, 6H), 6.96, 7.04, and 7.10 (ArH, m each, 4H, 2H, and 6H), 8.20 and 8.55 (OH, s each, 2H each). $4_{1,3,5}$: mp 272–274 °C (lit.[7c] > 273–274 °C), yield 25%; ^{1}H NMR ($CDCl_3$, 24 °C) δ 1.02, 1.21 (*t*-Bu, s each, 27H each), 3.48 (OCH_3, s, 9H), 3.89 ($ArCH_2$, s, 12H), 6.77 (OH, s, 3H), 6.91 and 7.02 (ArH, s each, 6H each). 6: mp 254–256 °C dec (lit.[15] > 274 °C dec), yield 6%; ^{1}H NMR ($CDCl_3$, 24 °C) δ 0.90, 1.12, 1.16, and 1.18 (*t*-Bu, s each, 9H, 9H, 18H, and 18H), 3.05, 3.07 and 3.50 (OCH_3, s each, 6H, 6H, and 3H), 3.81, 3.93 and 3.96 ($ArCH_2$, s each, 4H each), 6.80, 6.88, 7.00, 7.03, and 7.10 (ArH, s, s, d, s, and d, J = 2.5 Hz for 7.00 and 7.10, 2H, 2H, 2H, 4H, and 2H), 7.35 (OH, s, 1H).

5,11,17,23,29,35-Hexa-*tert*-butyl-37,38,39,40,41,42-hexamethoxycalix[6]arene (7). Compound 1 (1.0 g, 1.03 mmol) and MeI (2.31 mL, 37.1 mmol) were dissolved in anhyd acetone, and the solution was stirred at the reflux temperature for 48 h in the presence of K_2CO_3 (4.29 g, 30.9 mmol). The workup was similar to that described above. The residue was recrystallized from chloroform–methanol: mp 315–317 °C dec (lit.[9] 210–213 °C), yield 86%; IR (Nujol) no ν_{OH}; ^{1}H NMR ($CDCl_3$, 24 °C) δ 1.15 (*t*-Bu, s, 54H), 2.99 (OCH_3, s 18H), 3.96 ($ArCH_2$, s, 12H), 7.02 (ArH, s, 12H).

5,11,17,23,29,35-Hexa-*tert*-butyl-37,38,39,41-tetramethoxy-40,42-dihydroxycalix[6]arene ($5_{1,2,3,5}$). Compound $5_{1,2,3,5}$ was synthesized by monomethylation of $4_{1,3,5}$. Compound $4_{1,3,5}$ (100 mg, 0.099 mmol) and MeI (6 mL, 0.099 mmol) were dissolved in anhyd acetone, and the solution was stirred at the reflux temperature for 48 h in the presence of K_2CO_3 (13.6 mg, 0.099 mmol). The workup was similar to that described above. The residue was subjected to preparative TLC (silica gel (60 GF_{254}, Merck 7730, 0.75 mm), dichloromethane:ethyl acetate = 19:1 v/v), and the spot at R_f = 0.73 was recovered: mp 229–231 °C, yield 39%; IR (Nujol) ν_{OH} 3260 cm^{-1}; ^{1}H NMR ($CDCl_3$, 24 °C) δ 0.91, 1.08, 1.21, and 1.34 (*t*-Bu, s each, 18H, 18H, 9H, and 9H), 2.23, 2.58, and 3.97 (OCH_3, s each, 3H, 3H, and 6H), 3.85, 3.86, and 4.02 ($ArCH_2$, s each, 4H each), 6.65, 6.73, 6.98, 7.02, 7.02, and 7.21 (ArH, d, d, d, d, s, and s, J = 2.3 Hz for 6.65, 6.73, and 6.98, 2H each), 7.63 (OH, s, 2H). Anal. Calcd for $C_{70}H_{92}O_6$: C, 81.67; H, 9.01. Found: C, 81.35: H, 9.05.

5,11,17,23,29,35-Hexa-*tert*-butyl-37,38,39-trimethoxy-40,-41,42-trihydroxycalix[6]arene ($4_{1,2,3}$). Compound 7 (300 mg, 0.28 mmol) was treated with $TiCl_4$ (0.37 mL, 3.4 mmol) in anhyd chloroform (50 mL). The reaction was continued for 24 h at rt. The reaction was stopped by the addition of water, and the organic layer was separated and washed with water three times. The solution was dried over $MgSO_4$ and concentrated in vacuo to dryness. The residue was subjected to preparative TLC (silica gel (60 GF_{254}, Merck 7730, 0.75 mm), dichloromethane–ethyl acetate = 97:3 v/v): R_f = 0.74, mp 300–302 °C dec (lit.[15] > 300 °C), yield 20%; ^{1}H NMR ($CDCl_3$, 24 °C) δ 1.10, 1.18, 1.25, and 1.28 (*t*-Bu, s each, 18H, 18H, 9H, and 9H), 2.97 and 3.88 (OCH_3, s each, 3H and 6H), 3.78, 3.84, and 4.06 ($ArCH_2$, s each, 4H each), 6.94, 7.00, 7.06, 7.09, and 7.12 (ArH, dd, d, d, s, and s, J = 2.3 Hz for 6.94 and 7.00 and J = 2.4 Hz for 6.94 and 7.06, 4H, 2H, 2H, 2H, and 2H), 7.65 and 8.25 (OH, s each, 1H and 2H).

5,11,17,23,29,35-Hexa-*tert*-butyl-37,40-dimethoxy-38,39,41,-42-tetrakis(benzyloxy)calix[6]arene (9). 5,11,17,23,29,35-Hexa-*tert*-butyl-37,38,40,41-tetrakis(benzyloxy)-39,42-dihydroxycalix[6]arene (8) was synthesized by means of Gutsche's method.[6c] Compound 8 (1.00 g, 0.75 mmol) was treated with oil-dispersed NaH (150 mg, 3.76 mmol) in THF (40 mL)–DMF (4 mL), and then MeI (0.34 ml, 3.76 mmol) was added. The reaction mixture was refluxed for 24 h. Excess NaH was decomposed with methanol. The mixture was diluted with 0.1 M HCl and extracted with chloroform. The organic layer was washed with water and dried over $MgSO_4$. The solution was concentrated in vacuo to dryness, and the residue was recrystallized from chloroform–methanol: mp > 300 °C dec, yield 81%; IR (Nujol) no ν_{OH}; ^{1}H NMR ($CDCl_3$, 24 °C) δ 0.89 and 1.35 (*t*-Bu, s each, 36H and 18H), 1.49 (OCH_3, s, 6H), 3.43, 3.89, and 4.47 ($ArCH_2$, d, s and d, J = 15.5 Hz for 3.43 and 4.47, 4H each), 4.86 and 4.99 ($ArCH_2O$, d each, J = 10.9 Hz for all peaks, 4H each), 6.56, 7.18, 7.3–7.5, and 7.62 (ArH, d, s, m, and d, J = 2.0 Hz for 6.56 and J = 6.9 Hz for 7.62, 4H, 4H, 16H, and 8H). Anal. Calcd for $C_{96}H_{112}O_6$: C, 84.66; H, 8.29. Found: C, 84.34; H, 8.21.

5,11,17,23,29,35-Hexa-*tert*-butyl-37,40-dimethoxy-38,39,41,-42-tetrahydroxycalix[6]arene ($3_{1,4}$). Compound 9 (800 mg, 0.59 mmol) was treated with Me_3SiBr (0.93 mL, 7.08 mmol) in anhyd chloroform (70 mL). The reaction was continued at the reflux temperature for 72 h. After cooling, the precipitate was recovered by filtration and washed with chloroform. This product turned out to be pure $3_{1,4}$. It was found that $3_{1,4}$ selectively precipitates because of its poor solubility in most solvents: mp > 340 °C dec, yield 38%; IR (Nujol) ν_{OH} 3120, 3390 cm^{-1}; MS (EI) M$^+$ (m/e) 1000; ^{1}H NMR ($CDCl_3$, 24 °C) δ 1.14 and 1.22 (*t*-Bu, s each, 18H and 36H), 3.68 (OCH_3, s, 6H), 3.86 and 3.88 ($ArCH_2$, s each, 4H and 8H), 6.98, 6.99, and 7.11 (ArH, d, s and d, J = 2.5 Hz for 6.98 and 7.11, 4H each), 8.16 (OH, s, 4H). Anal. Calcd for $C_{88}H_{88}O_6 \cdot 0.1\ CHCl_3$: C, 80.71; H, 8.76. Found: C, 80.70; H, 8.70.

5,11,17,23,29,35-Hexa-*tert*-butyl-37,38,39,40-tetrahydroxy-41,42-(*o*-xylylenedioxy)calix[6]arene (1,2-bridged calix[6]-arene, 10). Compound 1 (1.0 g, 1.03 mmol) and α,α'-dibromo-*o*-xylene (272 mg, 1.24 mmol) were dissolved in anhyd acetone (100 mL), and the solution was stirred at the reflux temperature for 12 h in the presence of K_2CO_3 (846 mg, 6.12 mmol). The workup was similar to that described above. The residue was subjected to column chromatography (silica gel (Wakogel C-300), dichloromethane:*n*-hexane = 2:1 v/v): mp 194–196 °C dec, yield 47%; IR (Nujol) ν_{OH} 3250 cm^{-1}; ^{1}H NMR ($CDCl_3$, 24 °C) δ 1.11, 1.27 and 1.28 (*t*-Bu, s each, 18H each), 3.05, 3.45, 3.60, 3.83, 4.03, and 4.52 ($ArCH_2Ar$, d, d, m, d, d, d, J = 15.2, 13.5, 15.0, 13.5, 13.8 Hz, 1H, 1H, 6H, 1H, 1H, 2H) 5.42 ($ArCH_2O$, s, 4H), 6.76, 7.05–7.18 and 7.39 (ArH, s, m and s, 2H, 10H and 4H), 8.10 and 8.80 (OH, s each, 2H and 2H). Anal. Calcd for $C_{74}H_{90}O_6 \cdot 0.35CHCl_3$: C, 79.93; H, 8.15. Found: C, 79.78; H, 8.29.

5,11,17,23,29,35-Hexa-*tert*-butyl-37,38,40,41-tetrahydroxy-39,42-(*m*-xylylenedioxy)calix[6]arene (1,4-bridged calix[6]-arene, 11). Compound 1 (1.0 g, 1.03 mmol) was treated with oil-dispersed NaH (247 mg, 6.18 mmol) in THF (90 mL)–DMF (10 mL), and then α,α'-dibromo-*m*-xylene (326 mg, 1.24 mmol)

was added. The reaction mixture was refluxed for 12 h. The workup was similar to that described for **9**. The residue was subjected to column chromatography (silica gel (Wakogel C-300), chloroform): mp 151–153 °C, yield 71%; IR (Nujol) ν_{OH} 3300 cm^{-1}; ^1H NMR ($CDCl_3$, 24 °C) δ 1.19 and 1.26 (*t*-Bu, s each, 18H and 36H), 3.31, 3.48, 4.18, and 4.31 ($ArCH_2Ar$, d each, J = 13.7 Hz for 3.31 and 4.18 and J = 13.4 Hz for 3.48 and 4.31, 2H, 4H, 2H, and 4H), 5.28 ($ArCH_2O$, s, 4H), 7.0–7.2 and 8.51 (ArH, m and s, 14H and 2H), 9.03 (OH, s, 4H). Anal. Calcd for $C_{74}H_{90}O_6 \cdot 0.15CHCl_3$: C, 81.45; H, 8.31. Found: C, 81.32; H, 8.32.

5,11,17,23,29,35-Hexa-*tert*-butyl-37,38,39,40-tetramethoxy-41,42-(*o*-xylylenedioxy)calix[6]arene (1,2-bridged tetra-O-methylated calix[6]arene, 12). Compound **10** (180 mg, 0.17 mmol) was treated with oil-dispersed NaH (54 mg, 1.34 mmol) in THF (30 mL)–DMF (3 mL), and then MeI (0.13 mL, 2.02 mmol) was added. The reaction mixture was refluxed for 12 h. The workup was similar to that described for **9**. Dilution of the chloroform solution with methanol gave **12** as a white powder precipitate: mp 136–138 °C, yield 90%; IR (Nujol) no ν_{OH}; ^1H NMR ($CDCl_3$, 24 °C) δ 1.11, 1.13 and 1.23 (*t*-Bu, s each, 18H each), 2.82 and 3.49 (OCH_3, s each, 6H each), 2.83, 3.49 and 3.7–4.0 ($ArCH_2Ar$, m, 12H), 4.2–4.3 ($ArCH_2O$, m, 4H), 6.7–7.1 (ArH, m, 16H). Anal. Calcd for $C_{78}H_{98}O_6$: C, 82.79; H, 8.73. Found: C, 82.43; H, 9.10.

5,11,17,23,29,35-Hexa-*tert*-butyl-37,38,40,41-tetramethoxy-39,42-(*m*-xylylenedioxy)calix[6]arene (1,4-bridged tetra-O-methylated calix[6]arene, 13). Compound **13** was synthesized in a manner similar to that described for **12**. The product was purified by recrystallization from chloroform–methanol: mp 239–242 °C, yield 87%; IR (Nujol) no ν_{OH}; ^1H NMR ($CDCl_3$, 24 °C) δ 0.93 and 1.43 (*t*-Bu, s each, 36H and 18H), 3.42 (OCH_3, s, 12H), 3.1–3.8 and 4.25 ($ArCH_2Ar$, m and s, 8H and 4H), 4.3–4.6 ($ArCH_2O$, m, 4H), 5.49, 6.84, 6.91, 7.18, and 7.35 (ArH, s, d, d, s, and s, J = 2.2 Hz for 6.84 and 6.94, 1H, 4H, 4H, 3H, and 4H). Anal. Calcd for $C_{78}H_{98}O_6 \cdot 3CH_3OH$: C, 79.24; H, 9.03. Found: C, 79.42; H, 9.23.

5,11,17,23,29,35-Hexa-*tert*-butyl-37,38,39,40-tetramethoxy-41,42-dihydroxycalix[4]arene ($5_{1,2,3,4}$). Compound **12** (50 mg, 0.04 mmol) was treated with Me_3SiBr (100 μL × 2, 1.52 mmol) in anhyd chloroform (20 mL) at the reflux temperature for 24 h. Me_3SiBr was added in two portions at the beginning of the reaction and after 12 h. The workup was similar to that described for $3_{1,4}$. The residue was subjected to preparative TLC (silica gel (60 GF_{254}, Merck 7730, 0.75 mm), ethyl acetate:*n*-hexane = 1:6), and the spot with R_f = 0.60 was recovered: mp 122–124 °C, yield 17%; IR (Nujol) ν_{OH} 3180, 3370 cm^{-1}; ^1H NMR ($CDCl_3$, 24 °C) δ 1.05, 1.15 and 1.27 (*t*-Bu, s each, 18H each), 3.17 and 3.71 (OCH_3, s each, 6H each), 3.62, 3.80, 4.03, and 4.04 ($ArCH_2$, s each, 2H, 4H, 2H, and 4H), 6.80, 6.95, 7.03, and 7.06 (ArH, d, d, m, and s, J = 2.5 Hz for 6.80 and 6.95, 2H, 2H, 4H, and 4H), 9.03 (OH, s, 2H). Anal. Calcd for $C_{70}H_{92}O_6$: C, 81.67; H, 9.01. Found: C, 81.39; H, 9.12.

5,11,17,23,29,35-Hexa-*tert*-butyl-37,38,40,41-tetramethoxy-39,42-dihydroxycalix[6]arene ($5_{1,2,4,5}$) and 5,11,17,23,29,35-Hexa-*tert*-butyl-37,38,40-trimethoxy-39,41,42-trihydroxycalix[6]arene ($4_{1,2,4}$). Compound **13** (400 mg, 0.36 mmol) was treated with Me_3SiBr (114 μL × 2, 1.72 mmol) in anhyd chloroform (50 mL) in a manner similar to that described for $5_{1,2,3,4}$. The residue was subjected to preparative TLC (silica gel (60 GF_{254}, Merck 7730, 0.75 mm), chloroform). The spot at R_f = 0.30 was identified to be $5_{1,2,4,5}$ (yield 28%). The spot at R_f = 0.25 was identified to be $4_{1,2,4}$. $5_{1,2,4,5}$: R_f = 0.30, mp 275–277 °C dec (lit.[15] > 282 °C dec); ^1H NMR ($CDCl_3$, 24 °C) δ 0.94 and 1.18 (*t*-Bu, s each, 18H and 36H), 3.13 (OCH_3, s, 12H), 3.87 and 3.98 ($ArCH_2$, s each, 8H and 4H), 6.70 and 7.07 (ArH, s and m, 4H and 8H), 8.05 (OH, s, 2H). $4_{1,2,4}$: R_f = 0.25, mp 274–276 °C, yield 9%; IR (Nujol) ν_{OH} 3230, 3320, 3480 cm^{-1}; ^1H NMR ($CDCl_3$, 24 °C) δ 0.88, 1.09, 1.10, 1.14, 1.17, and 1.24 (*t*-Bu, s each, 9H each), 3.13, 3.29, and 3.34 (OCH_3, s each, 3H each), 3.82, 3.87, and 4.00 ($ArCH_2$, s, m, and s, 2H, 8H, and 2H), 6.60, 6.81, 6.83, 6.88, 6.93, 6.97, 6.99, 7.02, 7.07, 7.13, and 7.17 (ArH, d each, J = 2.2 Hz each, 1H, 1H, 1H, 1H, 1H, 1H, 2H, 1H, 1H, 1H, and 1H), 7.07, 7.66, and 9.03 (OH, s each, 1H each). Anal. Calcd for $C_{69}H_{90}O_6$: C, 81.61; H, 8.93. Found: C, 81.16; H, 8.92.

Miscellaneous. ^1H NMR, IR, and mass spectral measurements were carried out with a Bruker AC 250P spectrophotometer, a JASCO A-100 infrared spectrometer, and a HITACHI M-2500 mass spectrometer, respectively.