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# *Notes*

## From a Novel Silyl *p-tert*-Butylcalix[4]arene Triether to Mono-*O*-alkyl Substitution: A Unique, Efficient, and Selective Route to Mono-O-substituted Calix[4]arenes

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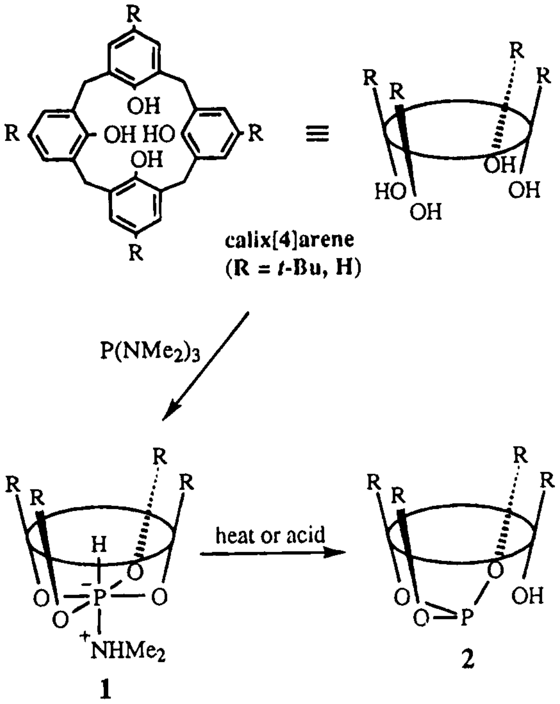
*Summary: The reaction of p-tert-butylcalix[4]arene with either tris(dimethylamino)methylsilane or trichloromethylsilane yields **3**, a novel silyl triether derivative with a pendent phenolic group, which should serve as a valuable precursor to substituted calix[4]arenes. We demonstrate its utility in the high-yield synthesis of the mono-O-methylated p-tert-butylcalix[4]arene **6** via O-methyl silyl compound **5**.*

The compounds commonly referred to as calixarenes are an important class of molecules due, in large part, to the cavity shape of many of the derivatives.[2] In addition, the ability to carry out functionalization at both the "upper" and "lower" rims allows for variation of the shape of the cavity. We have recently found that steric constraints of the calix[4]arene framework result in novel transformations of phosphorus at the base of the "basket" (Scheme 1).[3] During the course of our study of the insertion of other main-group elements into the calix[4]arene framework, we have synthesized a novel silyl triether derivative with a pendent phenolic group. We believe that this compound will serve as a useful precursor to a variety of substituted calix[4]arenes. For example, it has become increasingly important to be able to selectively functionalize the oxygens at the lower rim,[4] and only recently have routes been developed to mono-O-substituted calix[4]arenes.[5] However, these methods resulted in low yields and/or contamination with higher substituted products which many times necessitated chromatographic separation. We herein report a new route to mono-O-substituted calix[4]arenes via a silyl triether which avoids these problems.

**Scheme 1**



### Experimental Section

All reactions and manipulations were carried out under an atmosphere of nitrogen in a Vacuum Atmospheres dry box or using standard Schlenk techniques, unless otherwise indicated. Solvents were dried using standard procedures and distilled under a nitrogen atmosphere and either used immediately or stored in the drybox prior to use. Glassware was oven-dried at 140 °C overnight prior to use. The reagents tris(dimethylamino)methylsilane, butyllithium (1.6 M in hexane), methyl trifluoromethanesulfonate, tetrabutylammonium fluoride (1.0 M in THF), methyltrichlorosilane, and triethylamine were purchased commercially and used without further purification except for triethylamine, which was distilled under nitrogen prior to use; *p-tert*-butylcalix[4]arene·toluene was

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synthesized by literature methods.[6] All NMR spectra were recorded on an IBM/Bruker WP200SY multinuclear NMR spectrometer (equipped with a Tecmag computer system) resonating at 200.132 ($^1$H) MHz. $^1$H resonances were measured relative to residual proton solvent peaks and referenced to $Me_4Si$. Melting points were obtained in nitrogen-filled tubes on a Mel-Temp capillary apparatus and are uncorrected. Elemental analyses were obtained from E + R Microanalytical Laboratories, Inc., Corona, NY, or on a Carlo Erba Strumentazione Model 1106 elemental analyzer.

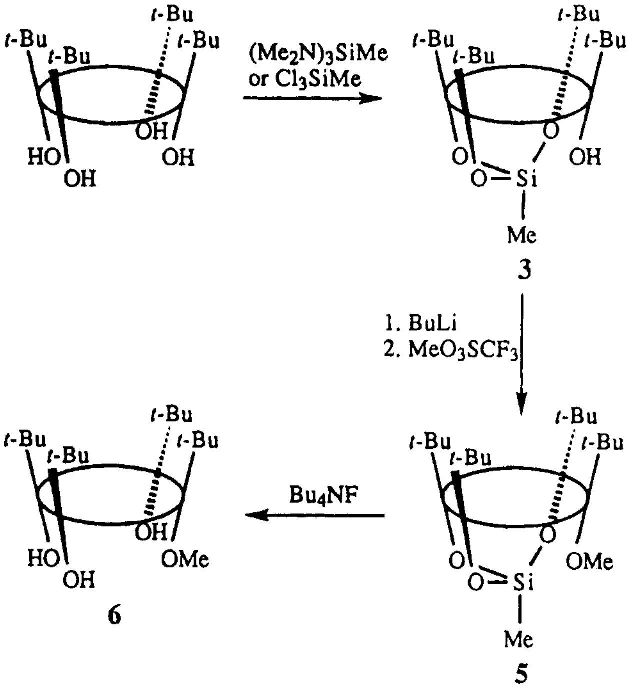
**Synthesis of 3 via Tris(dimethylamino)methylsilane.** A stirred suspension of *p-tert*-butylcalix[4]arene·toluene (1.3 g, 1.8 mmol) in benzene (100 mL) was treated dropwise with tris(dimethylamino)methylsilane (2.1 mL, 10 mmol). This stirred mixture was refluxed for 8 h under a sweep of nitrogen. The volatiles were then pumped off and the residue redissolved in benzene and again pumped to dryness. This is the most efficient way to remove the last traces of the initial silane. The product was washed with hexane and allowed to dry, yielding **3** as a white, air-stable solid (1.1 g, 91%), mp 330–332 °C. This product is sufficiently pure for further reactions; analytically pure samples can be obtained by recrystallization from benzene/hexane. Anal. Calcd for $C_{45}H_{56}O_4Si$: C, 78.44; H, 8.19. Found: C, 78.23; H, 8.40. $^1$H NMR ($CDCl_3$): $\delta$ −0.35 (s, 3 H), 1.25 (s, 9 H), 1.30 (s, 9 H), 1.31 (s, 18 H), 3.42 (d, $^2J_{HH}$ = 14 Hz, 2 H), 3.78 (d, $^2J_{HH}$ = 17 Hz, 2 H), 4.20 (d, $^2J_{HH}$ = 17 Hz, 2 H), 4.42 (d, $^2J_{HH}$ = 14 Hz, 2 H), 4.59 (s, OH, 1 H), 7.07, 7.10, 7.11, 7.12 (8 H total aromatic). $\nu_{OH}$ (Nujol mull) = 3580 cm$^{-1}$.

**Synthesis of 3 via Methyltrichlorosilane.** To a stirred suspension of *p-tert*-butylcalix[4]arene·toluene (10.0 g, 13.5 mmol) in benzene (400 mL) was added triethylamine (6.4 mL, 46 mmol) via syringe. After 2 min of stirring, the resulting mixture was treated dropwise with methyltrichlorosilane (3.4 mL, 29 mmol). Stirring was continued overnight. The mixture was then filtered, the salts were washed once with benzene (30 mL), and the volatiles were pumped off from the filtrate. The resulting solid was washed twice with hexane (50 mL total), yielding spectroscopically pure **3** (6.5 g, 70%).

**Synthesis of 5.** In an inert atmosphere, a solution of **3** (200 mg, 0.290 mmol) in benzene (8 mL) was treated dropwise with butyllithium (1.6 M in hexane, 208 $\mu$L, 0.33 mmol). After 3 h, methyl trifluoromethanesulfonate (46 $\mu$L, 0.41 mmol) was added dropwise and the resulting mixture stirred overnight. After filtration, the volatiles were pumped off from the filtrate and the resulting solid washed with hexane to yield **5** as a white, air-stable solid (203 mg, 100%), mp 295–297 °C. This product is sufficiently pure for further reactions; analytically pure samples can be obtained by recrystallization from toluene, which yields a 1:1 complex with toluene. Anal. Calcd for $C_{46}H_{58}O_4Si{\cdot}C_7H_8$: C, 80.05; H, 8.37. Found: C, 79.75; H, 8.13. $^1$H NMR ($C_6D_6$): $\delta$ −0.18 (s, 3 H), 0.96 (s, 9 H), 1.21 (s, 9 H), 1.38 (s, 18 H), 2.76 (s, 3 H), 3.52 (d, $^2J_{HH}$ = 14 Hz, 2 H), 3.72 (d, $^2J_{HH}$ = 16 Hz, 2 H), 4.08 (d, $^2J_{HH}$ = 16 Hz, 2 H), 4.81 (d, $^2J_{HH}$ = 14 Hz, 2 H), 7.18–7.28 (m, 8 H total aromatic).

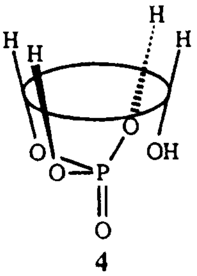
**Synthesis of 6.** A solution of **5** (165 mg, 0.235 mmol) in THF (4 mL) was treated dropwise with tetrabutylammonium fluoride (1.0 M in THF, 2.1 mL, 2.1 mmol) and stirred for 4 h. The resulting solution was poured into water. After extraction with ether, the organic layer was washed twice with water, acidified with dilute HCl, and washed again with water until the washings were neutral. The ether layer was then dried ($MgSO_4$) and filtered, and the solvent was pumped off to yield a slightly yellow product. Recrystallization ($CHCl_3$/MeOH) yielded white crystals of **5** (142 mg, 91%), mp 188–190 °C (lit. 186–188 °C). The $^1$H NMR spectrum agrees with that previously reported.[5b]

**Scheme 2**



## Results and Discussion

Treatment of *p-tert*-butylcalix[4]arene with an excess of tris(dimethylamino)methylsilane in refluxing benzene yields **3** in high yield (Scheme 2). A large excess of the silane is needed, as well as a sweep of nitrogen gas to remove the generated dimethylamine, in order to ensure complete reaction of *p-tert*-butylcalix[4]arene. The same product can be isolated (in somewhat lower yield) via the more usual reaction with methyltrichlorosilane and triethylamine. The identity of **3** is confirmed by its $^1$H NMR spectrum which shows three peaks in the *tert*-butyl region in a 1:1:2 ratio, a hydroxyl peak at $\delta$ 4.59, and a methyl (silyl) resonance at $\delta$ −0.35. In addition, the presence of four doublets for the methylene groups is consistent with the $C_s$ symmetry of **3**. We have not been able to obtain an X-ray crystal structure of **3**, so the conformation of the calix[4]arene backbone is not known for certain. However, the related phosphoryl compound **4** is known to have an approximate partial cone conformation.[3c,d] This, coupled with the fact that the $^1$H NMR spectra of **3** and **4** are very similar in the methylene region, suggests that **3** also adopts such a geometry.



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Since three of the four hydroxyl groups are essentially blocked by silicon in **3**, substitution at the remaining hydroxyl should be straightforward. Indeed, methylation of **3** gives **5**, which can be isolated in quantitative

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[6] (a) Gutsche, C. D.; Iqbal, M. *Org. Synth.* **1990**, *68*, 234. (b) Gutsche, C. D.; Iqbal, M.; Stewart, D. *J. Org. Chem.* **1986**, *51*, 742.

yield (Scheme 2). Moreover, the silyl group is easily cleaved by the usual treatment with fluoride, and the monomethylated calix[4]arene **6** is produced in excellent yield. The overall yield of **6** starting from the original calix[4]arene [via tris(dimethylamino)methylsilane] is 83%. This yield is significantly better than most previously reported syntheses of **6** and compares favorably with the most efficient synthesis reported (85%).[5b] However, that method involves tetramethylation of *p-tert*-butylcalix[4]arene, followed by partial demethylation; thus, different precursors are needed for each final product.

We believe that **3** will be an extremely useful starting material for a variety of O-substituted calix[4]arene derivatives, particularly since it avoids contamination from polysubstituted byproducts.

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