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Facile Synthesis of *p-tert*-Butylthiacalix[4]arene by the Reaction of *p-tert*-Butylphenol with Elemental Sulfur in the Presence of a Base

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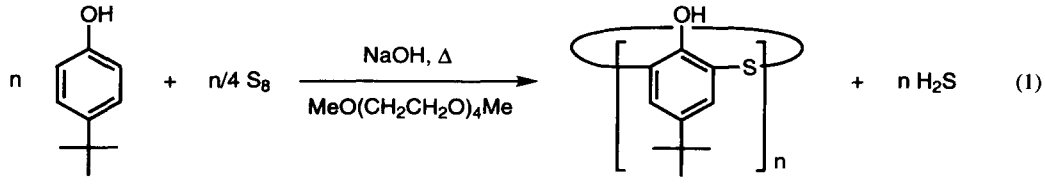
Abstract: *p-tert*-Butylthiacalix[4]arene, in which the four methylene bridges of *p-tert*-butylcalix[4]-arene are replaced by sulfide linkages, is conveniently synthesized in a single step (54%) by heating a mixture of *p-tert*-butylphenol, elemental sulfur S_8, and NaOH in tetraethylene glycol dimethyl ether with concomitant removal of the resulting hydrogen sulfide. © 1997 Elsevier Science Ltd.

Calix[n]arenes are macrocycles comprising phenolic and methylene units which can readily be assembled by the base-catalyzed condensation of *p*-alkylphenols with formaldehyde.[1,2] Various modifications of the parent calixarenes are also available both at the phenolic hydroxy groups and at the *p*-positions; the ready availability as well as the unique complexation characteristics have invoked intensive interests in such methylene-linked cyclic oligophenols as host molecules in the last fifteen years. Although replacement of the methylene units by hetero atom linkages such as -O-, -S-, and -NR- would provide the calixarene analogues of quite interest because of the varied cavity sizes and the additional binding sites provided by the hetero atoms, such modifications have so far been quite difficult to carry out in substantial quantities.[2] In fact, to the best of our knowledge, the only one precedent of the synthesis of this class of heterocycles was briefly reported in a conference abstract paper by Sone and his coworkers where they prepared *via* stepwise processes the analogues of *p-tert*-butylcalix-[4]arene in which one to four of the methylene linkages were replaced by sulfides bridges.[3] Thus, *p-tert*-butylthiacalix[4]arene **1** was obtained in poor yield by cyclization of a linear tetramer[4] with sulfur dichloride.

Since it has long been known that the treatment of phenols with sulfur at elevated temperatures under basic conditions affords a complex mixture of phenol oligomers joined by sulfide bonds at the *o*-, *o'*-, and/or *p*-positions of the phenol moieties,[5,6] we wondered if any conditions could be found for the preferential, not to say selective, formation of the sulfur-linked cyclic oligophenols of particular ring sizes. Herein we report that this has actually been realized by finding out a simple procedure, though not optimized, to obtain the thiacalix[4]arene **1** in a satisfactory yield (eq. 1).

In a typical procedure, a mixture of *p-tert*-butylphenol (64.5 g, 0.43 mol), elemental sulfur S_8 (27.5 g, 0.86 mol), and NaOH (8.86 g, 0.215 mol) in tetraethylene glycol dimethyl ether (19 ml) was stirred under nitro-



1 n = 4 **3** n = 6
2 n = 5

gen. The stirred mixture was heated gradually to 230 °C over a period of 4 hr and kept at this temperature for a further 3 hr with concomitant removal of the evolving hydrogen sulfide with a slow stream of nitrogen. The resulting dark red product was cooled to ambient temperature and diluted with toluene and ether, and then 1/2 M aq. sulfuric acid solution was added with stirring to give a suspension. The precipitate was collected by filtration, recrystallized from chloroform and dried *in vacuo* (100 °C, 4 hr) to give an essentially pure sample of **1** (30.3 g, 39% based on the *p-tert*-butylphenol) as confirmed by elemental analysis and spectral data.[7] The mother liquor of the recrystallization was concentrated *in vacuo*, and chromatography of the residue on silica gel (hexane : $CHCl_3$ 4 : 6) afforded additional **1** (11.5 g, 15%), the combined yield of **1** amounting to 54% which compares very well with the reported yields of conventional calixarenes.[1,2]

The organic phase from the filtration of the above suspension contained a complex mixture of seemingly sulfurized phenol oligomers as judged by HPLC as previous papers mentioned.[6] However, close scrutiny of the effluent fractions of silica-gel column chromatography (hexane : $CHCl_3$ 4 : 6) by HPLC and FD MS suggested the existence of *p-tert*-butylthiacalix[n]arenes where $n \geq 5$, among which small samples of **2** (n = 5) and **3** (n = 6) were obtainable by MPLC and confirmed as such by spectral data,[8] and efforts are now underway to improve the yields of these particular products.

Alkali metal hydroxides examined for the sulfurization of *p-tert*-butylphenol included LiOH, NaOH, KOH, and CsOH, among which NaOH gave the best result in terms of the yield of **1**; this may suggest that sodium cation acts as a template for the formation of the thiacalix[4]arene **1**. The rather high melting point of **1** seems to be a common property of many calixarenes of high symmetry with free hydroxy groups capable of hydrogen bonding.[1,2] The ^1H and ^{13}C NMR spectra of **1** are uncomplicated[7] and quite similar to those of the parent *p-tert*-butylcalix[4]arene except lacking the signals due to methylene moiety, indicating the structural resemblance of the two calix[4]arenes. However, the hydrogen bonding of **1** seems somewhat loosened compared to that of the calix[4]arene itself as judged by the characteristic IR and NMR absorptions due to phenolic hydroxy functionality of **1**[7] with that of the latter (IR(KBr) 3138 cm^{-1}; ^1H NMR ($CDCl_3$) δ 10.34). Recrystallization of **1** from various solvents forms crystals as 1 : 1 inclusion complexes, which do not lose the guests at ambient temperature under vacuum for 2 hr; examples of such guests include chloroform, acetone, methylcyclohexane, cyclohexane, decalin, and 1,4-dioxane.

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7. **1**: Colorless prisms (from $CHCl_3$) mp 320–322 °C; FD MS m/z 720 (M^+); IR (KBr) 3324, 2962 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.22 (36H, s), 7.64 (8H, s), and 9.60 (4H, s); ^{13}C NMR ($CDCl_3$) δ 31.3 ($C(\underline{C}H_3)_3$), 34.2 ($\underline{C}(CH_3)_3$), and 120.5, 136.4, 144.7 and 155.6 (Ar). Calcd for $C_{40}H_{48}O_4S_4$: C, 66.62; H, 6.71; S, 17.79. Found: C, 66.37; H, 6.57; S, 17.50.
8. **2**: FD MS m/z 900 (M^+); ^1H NMR ($CDCl_3$) δ 1.21 (45H, s), 7.47 (10H, s), OH protons (5H) were not detected. ^{13}C NMR ($CDCl_3$) δ 31.3 ($C(\underline{C}H_3)_3$), 34.2 ($\underline{C}(CH_3)_3$), and 119.6, 133.6, 144.1 and 154.3 (Ar).

   3: FD MS m/z 1080 (M^+); ^1H NMR ($CDCl_3$) δ 1.23 (54H, s) 7.59 (12H, s), 9.18 (6H, s); ^{13}C NMR ($CDCl_3$) δ 31.3 ($C(\underline{C}H_3)_3$), 34.2 ($\underline{C}(CH_3)_3$), and 120.4, 135.4, 144.4 and 155.3 (Ar).

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