



## NOTE

### Synthesis of 25-(Thioalkyl-alkoxy)-*p*-*tert*butylcalix[4]arene in One Reaction System

BINGQING CAO\*, QIBIN HUANG and MOLIN QING

State Key Laboratory of NBC Protection for Civilian, Beijing 102205, P.R. China

\*Corresponding author: Tel: +86 10 66758621; Fax: +86 10 69760246; E-mail: caobingqing961@sohu.com

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25-(Thioalkyl-alkoxy)-*p*-*tert*butylcalix[4]arene with self-assembled monolayers character was synthesized by two steps nucleophilic substitute reaction in NaH-THF phase with *p*-*tert*butylcalix[4]arene and dibromodecane. The structure of product was characterized by FT-IR, <sup>1</sup>H NMR, <sup>13</sup>C NMR and MALDI-TOF-MS.

**Keywords:** Calixaren, Sodium hydride, Synthesis, Self-assembled monolayers.

Recently, more and more attention has been paid to the study on the surface self-assembly of calixarene due to its specific three-dimensional structure and pre-organized three-dimensional hydrophobic cavities as recognition sites. The assembly of host calixarene molecules can be directed on the surface of colloid, SiO<sub>2</sub>, gold or other metals through bonding, hydrophobic interactions, or non-covalent weak interactions to form a mono- or multi-layer self-assembly system, which shows promise for wide applications in molecular recognition, chemical sensor, phase transfer catalysis, enzyme mimetics<sup>1,2</sup>. In this study, 25-(thioalkyl-alkoxy)-*p*-*tert*-butylcalix[4]arene, which is capable of self-assembling, was synthesized from *p*-*tert*-butylcalix[4]arene in NaH-THF system, as illustrated in **Scheme-I**.

Reagents of *p*-*tert*-butylcalix[4]arene and 1,10-dibromodecane were obtained from Alfa Aesar China Co., Ltd. Sodium hydride, tetrahydrofuran, dichloromethane, potassium hydroxide and acetone were obtained from Beijing Chemical Plant. Tetrahydrofuran was dried by distillation in the presence of sodium hydride before use.

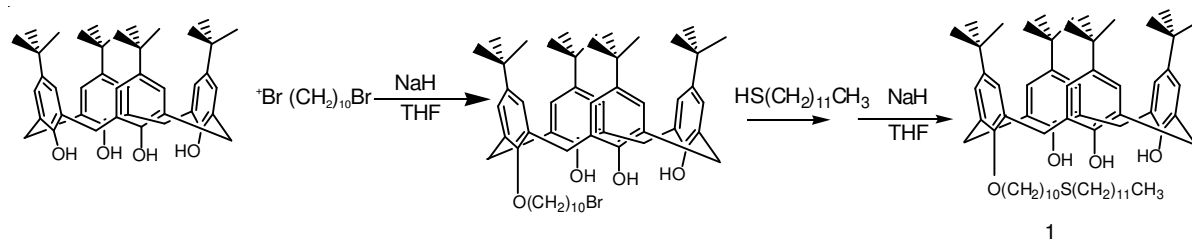
<sup>1</sup>H NMR and <sup>13</sup>C NMR spectra were recorded on a Bruker 600 MHz NMR spectrometer, with CDCl<sub>3</sub> or DMSO-*d*<sub>6</sub> as a solvent and TMS as internal standard. The infrared (IR) spectra of samples (prepared as KBr pellets) were recorded on a Bio-Rad FTS-185 Fourier transform IR spectrometer, with a spectral range of 4000-400 cm<sup>-1</sup> (KBr). Mass spectra were recorded on a BIFLEX-III MALDI-TOF-MS spectrometer (Bruker Daltonics Inc., USA).

**Synthesis:** 1.3 g (0.002 mol) of *p*-*tert*-butylcalix[4]arene, 0.0530 g (0.0022 mol) of sodium hydride and 30 mL of dried tetrahydrofuran were added into a 250 mL two-mouth flask

and a reflux condenser with a drying tube containing anhydrous CaCl<sub>2</sub> was mounted to the flask. Reflux was performed by a magnetic stirrer under the protection of N<sub>2</sub> for 1 h to obtain white turbid liquid. Then, 1.200 g (0.004 mol) of 1,10-dibromodecane was added into the mixture and reflux was performed for another 3 h. TLC monitoring was conducted during reflux. After the raw materials were depleted, 0.4848 g (0.0024 mol) of dodecyl mercaptan, 0.0530 g (0.0022 mol) of sodium hydride and 50 mL of dried tetrahydrofuran were added into the flask. The reaction almost ended after 8 h. Tetrahydrofuran in the mixture was removed by vacuum distillation and 100 mL of CH<sub>2</sub>Cl<sub>2</sub> and 25 mL of water were added for demixing. The obtained water phase was subject to extraction using CH<sub>2</sub>Cl<sub>2</sub> (2 × 10 mL) and the obtained organic layers were mixed. CH<sub>2</sub>Cl<sub>2</sub> was removed from anhydrous MgSO<sub>4</sub> by evaporation. The residue was rinsed using anhydrous ethanol (2 × 10 mL) to obtain light-yellow solid. The product was treated with a chromatographic silica gel column (80-100 mesh) using dichloromethane-petroleum ether (2:3) as a developing solvent. The solvent was removed by evaporation. The product was treated by recrystallization in acetone to obtain white solid **1**, which was then vacuum-dried at 60 °C for 24 h. The final product weighed 1.6327 g and the yield was 83.92 %.

The structural characteristics of target compound were shown as below:

**<sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>):** 10.33 (s, 3H, OH), 7.257 (s, 4H, ArH), 7.047 (s, 4H, ArH), 5.291 (s, 1H, ArOCH<sub>2</sub>), 4.12 (t, 2H, OCH<sub>2</sub>), 2.507, 2.495, 2.48 2 (m, 4H, SCH<sub>2</sub>), 1.584, 1.370 (m, 16 H, OCH<sub>2</sub> (CH<sub>2</sub>)<sub>8</sub>CH<sub>2</sub>S), 1.280, (s, 18H, *t*-Bu-H) 1.270, 1.210 (m, 23H, SCH<sub>2</sub> (CH<sub>2</sub>)<sub>10</sub>CH<sub>3</sub>), 0.8929 (s, 18H,



Scheme-I

*t*-Bu-H), 0.869 (t, 3H, CH<sub>3</sub>); <sup>13</sup>C NMR δ: 146.685 (C-25), 144.383 (C-26, C-27, C-28), 77.212-77.76.787 (O-CH<sub>2</sub>), 34.004-31.396 (S-CH<sub>2</sub>); IR (KBr, ν<sub>max</sub>, cm<sup>-1</sup>): 3158.92 (OH), 1600, 1485 cm<sup>-1</sup>, (benzene ring-C), 1202 cm<sup>-1</sup> (CH<sub>2</sub>-O-CH<sub>2</sub>), 872 cm<sup>-1</sup> (benzene ring-H), 783 cm<sup>-1</sup> (CH<sub>2</sub>-S-CH<sub>2</sub>); MALDI-TOF-MS *m/z*: 1011.831 (M + Na<sup>+</sup>).

Attention has always been paid to calixarene derivatives which are used as building blocks for molecular assembly to realize the functionalization of supramolecular assembly. The long-chain hydrocarbylation of phenolic hydroxyl is a vital method for calixarene modification and introducing mercaptan, thioether, or other functional groups to obtain mercapto-alkoxy-calixarene derivatives that can be self-assembled to form a film on a gold substrate has been a hot topic of supramolecular assembly in recent years<sup>3-5</sup>. In this study, the reaction using the intermediates produced in the NaH-THF system lasted for approximately 16 h and the yield reached up to 84 %. The conventional K<sub>2</sub>CO<sub>3</sub>-CH<sub>3</sub>CN/CH<sub>3</sub>COCH<sub>3</sub> system was compared with the NaH-THF system in terms of yield and reaction time. The comparison results revealed that the K<sub>2</sub>CO<sub>3</sub>-CH<sub>3</sub>CN system is inferior to the NaH-THF system because of longer reaction time (> 48 h) and lower yield (67 %).

## Conclusion

Calixarene molecule has multiple phenolic hydroxyls, with significantly stronger acidity than phenol due to hydrogen bonding. Ghidini *et al.*<sup>6</sup> measured the pK<sub>a</sub> of water-soluble calix[4]arene by neutralization titration and found that its first dissociation constant was in the strongly acidic range. 25,26,27,28-Tetrahydroxy-calix[4]arene is prone to

dissociation and loses one proton easily, forming such resonant phenoxyl anion. The reaction with 1,10-dibromodecane belongs to typical base-catalyzed nucleophilic reaction. Using the K<sub>2</sub>CO<sub>3</sub>-CH<sub>3</sub>CN system, it is difficult for 25,26,27,28-tetrahydroxy *p*-*tert*-butylcalix[4]arene to be mono-substituted due to relatively weak alkalinity of K<sub>2</sub>CO<sub>3</sub>, so the reaction process takes a longer time and some dibrominated substances were produced. Nevertheless, the strong alkalinity of NaH in the NaH-THF system allows 25,26,27,28-tetrahydroxy *p*-*tert*-butylcalix[4]arene to be mono-substituted easily, thus greatly shortening reaction time and improving product purity. Therefore, the NaH-THF system is desirable for synthesis of 25-(thioalkyl-alkoxy)-*p*-*tert*-butylcalix[4]arene.

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