

## Synthesis of Hexa(*p*-*tert*-butyl)hexa(carboxylic acid)calix[6]arene from Hexa(*p*-*tert*-butyl)hexa(ethyl ester)calix[6]arene

Nasriadi Dali<sup>\*1</sup>, Abd. Wahid Wahab<sup>2</sup>, Firdaus<sup>2</sup>, Maming<sup>2</sup>  
and Muhammad Nurdin<sup>1</sup>

<sup>1</sup>Department of Chemistry, Faculty of Mathematics and Natural Sciences,  
Universitas Halu Oleo, Kendari 93232 – Southeast Sulawesi, Indonesia

<sup>2</sup>Department of Chemistry, Faculty of Mathematics and Natural Sciences,  
Hasanuddin University, Makassar 90245 – South Sulawesi, Indonesia

**Abstract :** Hexa(*p*-*tert*-butyl)hexa(carboxylic acid)calix[6]arene was synthesized from hexa(*p*-*tert*-butyl)hexa(ethyl ester)calix[6]arene as a raw material. The target compound obtained by hydrolyzing hexa(*p*-*tert*-butyl)hexa(ethyl ester)calix[6]arene in aqueous KOH-ethanol 96%. Synthesis products were identified and characterized by melting point, thin layer chromatography (TLC), FTIR, <sup>1</sup>H-NMR and <sup>13</sup>C-NMR spectrometer. Compound of hexa(*p*-*tert*-butyl)hexa (carboxylic acid)calix[6]arene was obtained as a white solid (62.38% recovery), a melting point of 326-328 °C, and TLC (SiO<sub>2</sub>, ethanol : ethyl acetate = 1 : 1 v/v, R<sub>f</sub> = 0.93).

**Keywords:** calix[6]arene, synthesis, hydrolysis, characterization.

### Introduction

Calix[n]arene is a macrocyclic molecules obtained from the hydroxy alkylation or condensation *p*-alkylphenols and formaldehyde under alkaline conditions<sup>1</sup>. Conformational structure of calix[n]arene may be different because rotation around methylene bridge is not difficult. Unit phenol or its derivatives in the structure of calix[n]arene can be rotated on the axis of rotation of the oxygen generating conformation cone, partial cone, and alternate<sup>2</sup>. This conformational structure having a hydrophobic cavity that can hold small molecules or ions, so that the calix[n]arene can act as a host molecule<sup>3</sup>.

Derivatives of calix[n]arenes was obtained by substituting the H atoms in the OH groups at the bottom of the annulus ring or replacing *tert*-butyl group at the top of the annular ring with the other groups. Replacement groups at the bottom of the annular ring calix[n]arene have been reported by researchers, such as hexa(ester)calix[6]arene<sup>4</sup>, tetrakis(ethoxycarbonylmethoxy)calix[4]arene<sup>5</sup>, tetra(carboxylic)-calix[4]arene<sup>6</sup>, tri(ethoxycarbonylmethoxy)tri(hydroxy)calix[6]arene<sup>7</sup>, and tetra(propenyloxy)calix[4]arene<sup>3</sup>. Similarly, the replacement groups at the top of the annulus ring calix[n]arene have been reported by researchers, such as tetra(*p*-propenyl)calix[4]arene, tetra(allyloxy)calix[4]arene<sup>3</sup>, carboxylic, amines and amides groups<sup>8</sup>.

Calix[n]arene can have different selectivity when the functional groups above and below the annulus ring modified. For example, ester derivatives of compounds of calix[n]arene used as electrochemical sensors. Hexamer ester used as ionophores cation K, Rb, Sr, and Cs. Tetramer ester is selective to alkali metal ions and amine ligands. Phosphine oxide compound calix[n]arene was used as extractant of radioactive elements from

nuclear waste. These compounds, especially tetramer, also ion selective binding of  $\text{Ag}^+$  and alkali metal ions when used in ion selective electrode (ISE)<sup>9</sup> and as antioxidant activity, in vitro antimicrobial screening against bacterial and fungal strains<sup>10</sup>. Carboxylic acid derivative compounds calix[n]arene is selective for the ion  $\text{Fe}^{3+}$  and  $\text{Ni}^{2+}$  through the bulk liquid membrane 1,2-dichloroethane<sup>6</sup>. Derivative compounds tetra (sulfonato) tetra (alkoxy)calix[4]arene, (*p*-alkenyl)calix[4]arene, and (*p*-haloalkyl)calix[4]arene is quite selective on metal cation  $\text{Pb}^{2+}$  and  $\text{Cr}^{3+}$  in the column system<sup>3</sup>.

## Experimental Details

### Chemicals

The starting materials, hexa(*p*-*tert*-butyl)hexa(ethylester)calix[6]arene (synthesized)<sup>4</sup>; potassium hydroxide (Merck); ethanol (Merck); hydrochloric acid (Merck); chloroform (Merck), and distilled water. All solvents were obtained from commercial sources and used without further treatment.

### Spectroscopic Measurements

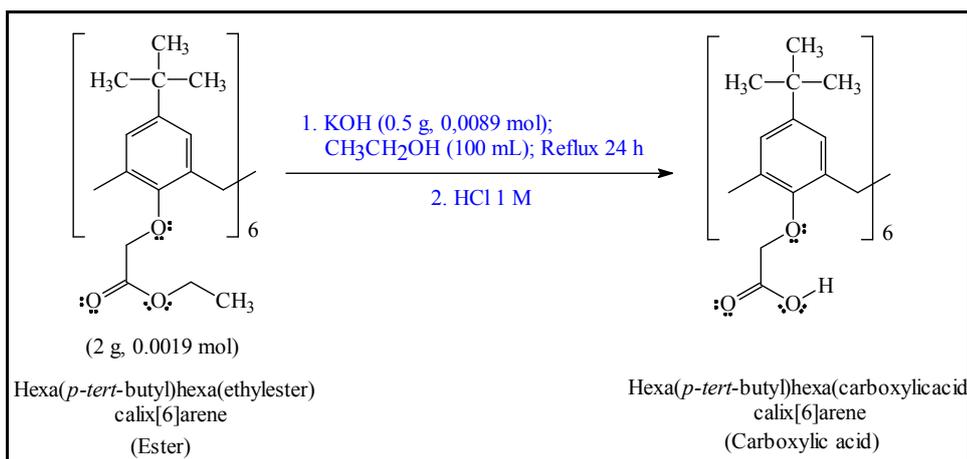
FTIR spectra were obtained on a Shimadzu Prestige-21 spectrometer. <sup>1</sup>H and <sup>13</sup>C-NMR spectra were measured on a JEOL ECX500 FTNMR spectrometer with  $\text{CDCl}_3$  as solvent and tetramethylsilane (TMS) as the internal standard.

### Synthesis

The starting materials (2 g, 0.0019 mol) was mixed with potassium hydroxide (0.5 g, 0.0089 mol) and then dissolved in ethanol 96% (100 mL). The mixture was refluxed at a temperature of 78°C for 24 h. The reaction mixture was cooled to room temperature. The solution was acidified with HCl 1 M. The precipitate was filtered and then washed with HCl 1 M and distilled water, then dried in the desiccator. The solid is recrystallized from ethanol. The white solid was identified and characterized by melting point, TLC, IR, <sup>1</sup>H and <sup>13</sup>C-NMR spectrometer. Yield: 1.2476 g (62.38 %); mp 326 – 328 °C; TLC ( $\text{SiO}_2$ , ethanol : ethyl acetate = 1:1 v/v,  $R_f$  = 0.93); FTIR (KBr)  $\nu_{\text{max}}$  ( $\text{cm}^{-1}$ ): 3429,43 (OH acid), 1757,15 (C=O acid), 1298,09 (COC alkyl aryl ether), 1062,78 (RCO alkyl aryl ether), 1600,92 and 1467,83 (C=C aromatic), 1190,08 (C-O aromatic), 879,54 and 723,31 (CH OOP aromatic), 2954,95, 2920,23, and 2850,79 (CH saturated aliphatic), 1386,82 ( $\text{CH}_3$  aliphatic), 1363,67 ( $\text{CH}_2$  aliphatic); <sup>1</sup>H-NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta_{\text{H}}$  (ppm): 10,3785 [(s, 1H) (OH-1\*)], 6,9638 [(s, 1H) (ArH-34/36)], 4,5357 [(s, 2H) ( $\text{CH}_2\text{O}-2''$ )], 4,7071 [(d, 2H,  $J$  = 12,9 Hz) (Ar $\text{CH}_2$ Ar-32, *endo*)], 3,4313 [(d, 2H,  $J$  = 12,9 Hz) (Ar $\text{CH}_2$ Ar-2, *ekso*)], 0,9622 [(s, 9H) ( $\text{C}(\text{CH}_3)_3-2'$ )]; <sup>13</sup>C-NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta_{\text{C}}$  (ppm): 169,6231 [(CO<sub>2</sub>H) (C-1'')], 153,2751 [(CO aril) (C-37)], 146,6262 [(C-*para* aril) (C-35)], 132,9196 [(C-*ortho* aril) (C-1/C-33)], 126,4717 [(C-*meta* aril) (C-34/C-36)], 70,8060 [(OCH<sub>2</sub>CO<sub>2</sub>H) (C-2'')], 34,0739 [(C(CH<sub>3</sub>)<sub>3</sub>) (C-1')], 31,3746 [(C(CH<sub>3</sub>)<sub>3</sub>) (C-2')], and 31,6131 [(Ar $\text{CH}_2$ Ar) (C-2/C-32)].

## Results and Discussion

Target compound of hexa(*p*-*tert*-butyl)hexa(carboxylicacid)calix[6]arene was obtained by hydrolyzing hexa(*p*-*tert*-butyl)hexa(ethylester)calix[6]arene in aqueous KOH-ethanol 96% (Figure 1)<sup>11</sup>. Synthesis product was obtained as a white solid substance (62.38% recovery), a melting point of 326-328 °C, TLC ( $\text{SiO}_2$ , ethanol:ethyl acetate = 1:1 v/v,  $R_f$  = 0.93).



**Figure 1. Hydrolysis of hexa(*p-tert-butyl*)hexa(ethylester)calix[6]arene**

The FTIR spectrum synthesis product showed an absorption band at 3429.43 cm<sup>-1</sup> (OH stretching) of the carboxylic acid. The hydroxyl stretching band of the monomer carboxylic acid spectrum is located at higher frequencies (3500-3200 cm<sup>-1</sup>)<sup>12-14</sup>. Strong absorption band that appeared at 1757.15 cm<sup>-1</sup> indicate the presence of the C=O stretching vibrations of the carboxylic acid that different absorption bands of origin as ester carbonyl compounds. Both of these data indicate that the ester group has been hydrolyzed to carboxylic acids. Both of these data are also supported by the data of <sup>1</sup>H and <sup>13</sup>C-NMR product synthesis. The signal at δ<sub>H</sub> 10.3785 ppm (s, 1H) derived from carboxylic acid proton (OH-1\*). An acid proton in the <sup>1</sup>H-NMR spectrum appear at about δ<sub>H</sub> 10-13 ppm<sup>15</sup>. The signal at δ<sub>C</sub> 169.6231 ppm derived from carbonyl carbon (C-1) that binds the OH groups carboxylic acid (C-O<sub>2</sub>H). Carbon chemical shifts ranges for carboxylic acid derivatives is δ<sub>C</sub> 1600-1800 ppm<sup>16</sup>.

The FTIR spectrum synthesis products also showed a group C=C aromatic ring (1600.92 and 1467.83 cm<sup>-1</sup>), C-O aromatic (1190.08 cm<sup>-1</sup>), and C-H out-of-plane deformation of aromatic substitution-*para* (879.54 and 723.31 cm<sup>-1</sup>). All three of these data shows that the synthesis product contains of the aromatic ring. All three of these data is also supported by the data of <sup>1</sup>H and <sup>13</sup>C-NMR synthesis product. The signal at δ<sub>H</sub> 6.9638 ppm (s, 1H) derived from proton aryl (ArH-34/36). Signals aryl carbon atoms (C-aryl) are spread into four δ<sub>C</sub> price. First, the carbon atom C-37 shows the most downfield signal at the δ<sub>C</sub> 153.2751 ppm (CO aryl) than other aryl carbon because it binds oxygen directly from the OCH<sub>2</sub>CO<sub>2</sub>H group. Second, carbon C-35 absorption signal at the δ<sub>C</sub> 146.6262 ppm binding *tert-butyl* group at the *para* position (C-*para* aryl). Third, carbon absorption signal C-1/C-33 in the *ortho* position appears on δ<sub>C</sub> 132.9196 ppm (C-*ortho* aryl). Fourth, carbon absorption signal C-34/C-36 at the *meta* position appears on δ<sub>C</sub> 126.4717 ppm (C-*meta* aryl).

The FTIR spectrum synthesis products also showed three absorption bands at 2954.95, 2920.23, and 2850.79 cm<sup>-1</sup> derived from C-H saturated stretch vibration from the group *tert-butyl*, -C(CH<sub>3</sub>)<sub>3</sub>. The C-H saturation absorption band is also in accordance with the presence of an absorption band at 1363.67 cm<sup>-1</sup> of a methylene group, -CH<sub>2</sub>-, and a methyl group, -CH<sub>3</sub>, which absorbs at 1386.82 cm<sup>-1</sup>. All three of these data is also supported by the data of <sup>1</sup>H and <sup>13</sup>C-NMR synthesis product. The signal at δ<sub>H</sub> 4.5357 ppm (s, 2H) derived from proton methoxy methylene (CH<sub>2</sub>O-2"). The signal at δ<sub>H</sub> 4.7071 ppm (d, 2H, *J* = 12.9 Hz) comes from the breakdown of the proton resonance methylene bridge (ArCH<sub>2</sub>Ar-32, endo) by another bridge methylene protons (ArCH<sub>2</sub>Ar-2, exo) whose signal also appears at δ<sub>H</sub> 3.4313 ppm (d, 2H, *J* = 12.9 Hz). Singlet proton absorption signals with the highest abundance appears on δ<sub>H</sub> 0.9622 ppm (s, 9H) is derived from *tert-butyl* (C(CH<sub>3</sub>)<sub>3</sub>-2'). Group upfield carbon uptake is derived from the alkyl groups. The methylene carbon (OCH<sub>2</sub>CO<sub>2</sub>H) absorption signal appears on δ<sub>C</sub> 70.8060 ppm (C-2"). Three strong absorption signals on δ<sub>C</sub> 34.0739, 31.3746, and 31.6131 ppm respectively derived from the carbon resonance quarterner of *tert-butyl* (C-1'), -CH<sub>3</sub> (C-2'), and ArCH<sub>2</sub>Ar (C-2/C-32).

The FTIR spectrum synthesis products also showed a moderate absorption band at 1298.09 cm<sup>-1</sup> derived from the C-O-C stretching vibration in the an alkyl aryl ether. Strong absorption band at 1062.78 cm<sup>-1</sup> derived from R-C-O stretching vibration in the an alkyl aryl ether. Both of these data are also supported by the data of <sup>1</sup>H and <sup>13</sup>C-NMR synthesis product. The signal at δ<sub>H</sub> 4.5357 ppm (s, 2H) derived from protons of methylene

methoxy [(2'') -CH<sub>2</sub>O-C- (37)]. The signal at  $\delta_c$  153.2751 ppm derived from carbon aryl [(37) -C-O-CH<sub>2</sub>- (2'')]. The carbon of methylene methoxy [(2'') -CH<sub>2</sub>O-C- (37)] absorption signal appears on  $\delta_c$  70.8060 ppm (C-2'').

Thus, absorption that appeared in the FTIR, <sup>1</sup>H and <sup>13</sup>C-NMR spectrum synthesis product is consistent with the carbon framework and structure 5,11,17,23,29,35-hexakis(*p*-*tert*-butyl)-37,38,39,40,41,42-hexa(carboxymethoxy)calix[6]arene (Figure 2).

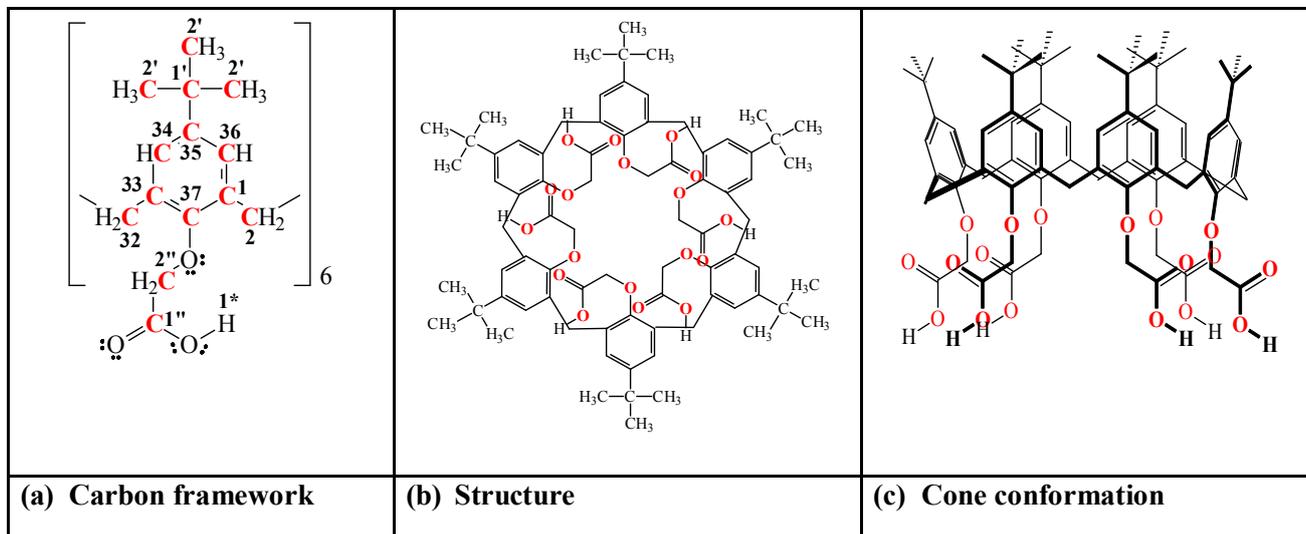


Figure 2. Structure of 5,11,17,23,29,35-hexakis(*p*-*tert*-butyl)-37,38,39,40,41,42-hexa(carboxymethoxy)calix [6]arene

## Conclusion

Synthesis hexa(*p*-*tert*-butyl)hexa(carboxylicacid)calix[6]arene from hexa(*p*-*tert*-butyl)hexa (ethylester) calix[6]arene as the initial raw material has been successfully carried through the reaction stage of ester hydrolysis in aqueous base. Synthesis product was obtained as a white solid (62.38% recovery), a melting point of 326-328°C, TLC (SiO<sub>2</sub>, ethanol : ethyl acetate = 1:1 v/v, R<sub>f</sub> = 0.93). The results of the analysis synthesis products with FTIR, <sup>1</sup>H and <sup>13</sup>C-NMR spectrometer showed that the synthesis product is a compound 5,11,17,23,29,35-hexakis(*p*-*tert*-butyl)-37,38,39,40,41,42-hexa(carboxymethoxy)calix[6]-arene.

## Acknowledgements

The author would like to thank the staff of Integrated Laboratory Chemistry Department, Faculty of Mathematics and Natural Sciences University of Hasanuddin Makassar and Chemical Research Center of Indonesian Institute of Sciences for its assistance in analyzing the sample by FTIR, <sup>1</sup>H and <sup>13</sup>C-NMR spectrometer.

## References

1. Gutsche C.D. 1989. *Calixarenes: Monograph in Supramolecular Chemistry*. Royal Society of Chemistry, Cambridge.
2. Anonymous. 2013. *Calixarene*. (Online). (<http://en.wikipedia.org/wiki/Calixarene>, accessed March 18, 2016).
3. Kusumaningsih T., Jumina, Siswanta D., and Mustofa. 2010. Synthesis of Tetra-*p*-Propenyltetraester-calix[4]arene and Tetra-*p*-Propenyltetracarboxylicacid-calix[4]arene from *p*-*t*-Butylphenol. *Indonesian Journal of Chemistry*, 10(1):122-126.
4. Dali N., Wahab A.W., Firdaus, and Maming. 2015. Synthesis hexa(*p*-*tert*-butyl)hexa(ester)calix[6]arene from *p*-*tert*-butylcalix[6]arene. *Alchemy Science Research Journal of Chemistry*, 3(1): 103-109.

5. Dali N., Wahab A.W., Firdaus, and Maming. 2012. Synthesis of 5,11,17,23-tetrakis(*p*-*tert*-butyl)-25,26,27,28-tetrakis(ethoxycarbonylmethoxy)calix[4]arene from *p*-*tert*-butylcalix[4]arene. *dr. Aloei Saboe*, 1(2): 1-6.
6. Kadir A.N. 2014. Selectivity Transport Calixarene and Calixarene Carboxylic to Fe<sup>3+</sup> of the Mixture Fe, Ni, and Cr Through the Bulk Liquid Membrane 1,2-dichloroethane. *dr. Aloei Saboe*, 1(2): 1-6.
7. Dali N., Wahab A.W., Firdaus, and Maming. 2012. Synthesis of 5,11,17,23,29,35-hexa(*p*-*tert*-butyl)-37,39,41-tri(ethoxycarbonylmethoxy)-38,40,42-tri(hydroxy)calix[6]arene from *p*-*tert*-butylcalix[6]arene. *Science Journal of Chemistry & Chemical Education*, 1(2):110-115.
8. Gutsche C.D., Levine J.A., and Sujeeth P.K. 1985. Calixarene 17 Functionalized Calixarene: The Claisen Rearrangement Route. *The Journal of Organic Chemistry*, 50: 5802-5808.
9. O'Connor K.M., Henderson W., O'Neill E., Arrigan D.W.M., Harris S.J., McKervey M.A., and Syehla G. 1997. Calix[4]arenes in the Partial Cone Conformation as Ionphores in Silver Ion-Selective Electrodes. *Electroanalysis*, 9(4):311-315.
10. Kumar K.A., Jayarooma P., Kumar G.V. 2012. Comprehensive Review on the Chemistry of 1,3,4-Oxadiazoles and Their Applications. *International Journal of ChemTech Research*, 4(4):1782-1791.
11. Souane R. 2005. *Synthèse et propriétés complexantes vis-à-vis de l'ion uranyle de dérivés carboxyliques du p-tert-butyl-calix[6]arène*, Université Louis Pasteur de Strasbourg.
12. Lambert J.B., Gronert S., Shurvell H.F., and Lightner D.A. 2011. *Organic Structural Spectroscopy*. 2<sup>nd</sup> Edition. Pearson Prentice Hall, New Jersey.
13. Keerthiga R., Vijayalakshmi S., and Kaliyappan T. 2015. Metal Uptake Properties of Chelating Azo Polymeric Resin: Synthesis, Characterization and Biological Properties. *International Journal of ChemTech Research*, 7(7):2886-2893.
14. Maulidiyah, Cahyana A.H., Suwarso W.P., Nurdin M. 2015. Isolation and Structure Elucidation of Eumitrin A<sub>1</sub> from Lichen *Usnea blepharea* Motyka and Its Cytotoxic Activity. *International Journal of PharmTech Research*, 8(4):782-789.
15. Sastrohamidjojo H. 1992. *Infrared Spectroscopy*. 1<sup>st</sup> Edition. Liberty, Yogyakarta.
16. Kemp W. 1991. *Organic Spectroscopy*. 3<sup>rd</sup> Edition. Macmillan Education Ltd., London.

\*\*\*\*\*