

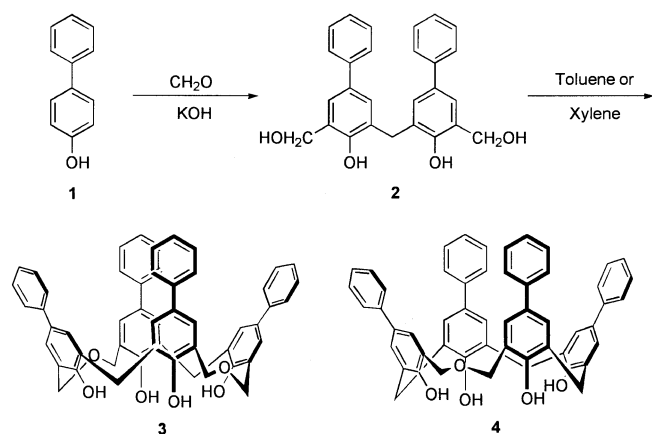
Facile Synthesis of *p*-Phenyl Homooxacalix[4]arenes

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Calixarenes are synthetic macrocycles available in a variety of ring sizes and are of interest both as complexation hosts for ions and molecules and as frameworks for elaborating more complex structures and have received a great deal of attention in recent years.¹⁻³ In contrast to the calix[4]arenes, homooxacalix[4]arenes, containing extra oxygens in the macrocyclic ring, have received little attention mainly because they can only be synthesized in relatively low yield. *p*-*t*-Butyl dihomooxacalix[4]arene was obtained as a minor product (20% yield) from the direct base-catalyzed condensation reaction of *p*-*t*-butylphenol and formaldehyde⁴ and then the yield was enhanced up to 25%.⁵ *p*-*t*-Butyl tetrahomodioxacalix[4]arene was prepared by Gutsche in 44% yield from the dehydration of bishydroxymethylated dimer of *p*-*t*-butylphenol in xylene.⁶ There have only been limited studies for the conformation and metal-binding properties of dihomooxa- and tetrahomodioxacalix[4]arene derivatives.⁷⁻¹⁴ In this communication the facile synthesis of two *p*-phenyl homooxacalix[4]arenes which have deep cavity as shown in following scheme was described.



Scheme

When the mixture of *p*-phenylphenol and 35% formaldehyde was stirred for 4 days at 40 °C in the presence of potassium hydroxide, the dimer diol **2** was prepared in 55% yield using the published procedures.^{15,16} Compound **2** (3.02 g, 7.32 mmole) was refluxed in toluene (180 mL) for 20 h to remove water in a Dean-Stark moisture trap. After cooling to room temperature, small amount (less than 100 mg) of toluene insoluble material was filtered off. The residue, obtained by removal of solvent, was purified by recrystallization from toluene to afford the tetrahomodioxacalix[4]arene **3** in 69% yield.¹⁷ An additional pure product was obtained from the flash chromatographic separation (eluent was 3:5 mixture of

chloroform and hexane) of the residue which was resulted by the evaporation of solvent from the combined solution of filtrate and washing. The total yield was 79%. A faint spot of the compound **4** was shown on the TLC analysis of crude product, however, the isolation of compound **4** was not successful. When benzene was used as solvent, there was very faint spot corresponding to **3** with no indication of formation **4**. The structure of compound **3** was confirmed by ¹H, ¹³C NMR, mass spectral analyses and elemental analysis. Compound **3** shows a temperature dependent ¹H NMR spectrum. The methylenic proton displayed at -50 °C in chloroform appears as a set of AB quartet at δ 4.53, 3.77 with *J*-13.9 Hz arising from ArCH₂Ar and two singlets at δ 4.76, 4.75 arising from ArCH₂O. When the temperature was raised, the spectrum became less well resolved and at -25 °C, AB quartet from ArCH₂Ar collapsed into two broad singlets and peaks from ArCH₂O protons collapsed into singlet. At room temperature, two broad singlets from ArCH₂Ar protons appeared as a singlet at δ 4.13. The ¹³C NMR spectrum of **3** showed twelve peaks from aromatic carbons and single peak each from ArCH₂O carbons and ArCH₂Ar carbons, respectively. These spectral data are commensurated with the proposed structure of **3**. Molecular ion peak at 788 in mass spectrum also supports the structure. When the similar reaction was tried with xylene instead of toluene, crude product showed two major spots on TLC analysis. Flash chromatographic separation (eluent was 3:5 mixture of chloroform and hexane) of the crude product afforded the compound **3** and **4** in 59% and 8% yield respectively. When the same reaction was carried out with the reduced amount of xylene (100 mL), the yield of **4** was increased to 36%. If the solvent was changed from xylene to mesitylene, the TLC of crude product showed very complex spots and there was no spot corresponding to the **3**. The structure of compound **4** was confirmed by NMR spectra, mass spectra and elemental analysis.¹⁸ In the ¹H NMR spectrum of **4**, at room temperature the protons from methylene bridge showed two singlets in the ratio of 4:6, which became two singlets at δ 5.31, 4.75 arising from ArCH₂O protons and three doublets at δ 4.43, 3.81 and 3.77 arising from ArCH₂Ar protons at -50 °C. ¹³C NMR spectrum showed 18 peaks (20 expected) from aromatic carbons, one peak from ArCH₂O bridge methylene carbons and one peak from ArCH₂Ar bridge carbons as expected. Mass spectrum showed molecular ion peak at *m/e* 758. In this study, we have provided an efficient method for the synthesis of *p*-phenyl homooxacalix[4]arenes which have deep cavity, and we are currently studying the use of these compounds for inclusion hosts.

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17. mp 236-237 °C: ¹H NMR (CDCl₃, 25 °C) δ 9.32 (s, 4, OH), 7.60-7.26 (m, 28, ArH), 4.78 (s, 8, OCH₂Ar), 4.13 (s, 4, ArCH₂Ar) [(at -50 °C) 4.76 (s, 4, OCH₂Ar), 4.75 (s, 4, OCH₂Ar), 4.53 (d, 2, ArCH₂Ar, *J*=13.9 Hz), 3.77 (d, 2, ArCH₂Ar, *J*=13.9 Hz)]; ¹³C NMR (CDCl₃) δ 152.37, 140.59, 133.95, 129.64, 128.70, 127.96, 127.00, 126.83, 126.80, 123.33 (Ar), 71.71 (OCH₂Ar), 31.18 (ArCH₂Ar); FAB MS 788 (M⁺) (Calcd. M⁺ 788); Anal. Calcd for C₅₄H₄₄O₆: C, 82.21; H, 5.62. Found: C, 82.22; H, 5.64.
18. mp 267 °C (decompose): ¹H NMR (CDCl₃, 25 °C) δ 10.04 (s, 2, OH), 9.48 (s, 2, OH), 7.58-7.23 m, 28, ArH), 4.78 (br.s, 4, OCH₂Ar), 4.09 (br.s, 6, ArCH₂Ar) [(at -50 °C) 5.31 (br.s, 2, OCH₂Ar), 4.75 (br.s, 2, OCH₂Ar), 4.43 (d, 2, ArCH₂Ar, *J*=14.1 Hz), 3.81 (d, 2, ArCH₂Ar, *J*=14.1 Hz), 3.77 (d, 2, ArCH₂Ar, *J*=14.1 Hz)]; ¹³C NMR (CDCl₃) δ 152.58, 148.96, 140.90, 135.67, 133.91, 129.69, 128.70, 128.61, 128.37, 128.29, 128.06, 128.01, 127.80, 127.06, 126.83, 126.80, 126.79, 122.85 (Ar), 71.09 (OCH₂Ar), 32.46, 31.89 (ArCH₂Ar); FAB MS 758 (M⁺) (Calcd. M⁺ 758); Anal. Calcd for C₅₃H₄₂O₅: C, 83.88; H, 5.58. Found: C, 83.76; H, 5.58.