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A Novel De-*tert*-butylation of *p*-*tert*-Butylcalix[n]arenes

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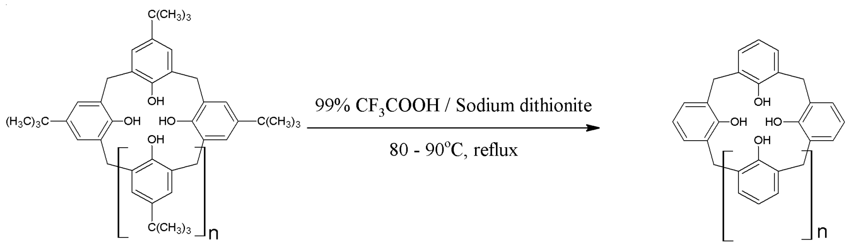
A facile de-*tert*-butylation method was developed for the synthesis of calix[n]arenes. A mixture of *p*-*tert*-butylcalix[n]arene, sodium dithionite and tri-fluoro acetic acid were refluxed at 80-90 ºC for 24 h. The calix[n]arenes with yields ranging from 80-92 % was achieved.

Key Words: De-alkylation, Calix[n]arene, Trifluoro acetic acid, *p*-*tert*-Butyl calix[n]arene.

INTRODUCTION

Calix[n]arenes are the cyclic oligomers of *p*-substituted phenol and formaldehyde[1]. The non modified calixarenes can form coordinate complexes with alkaline and alkaline earth metals. The functionalized calixarenes at lower and wide rim were used as electrochemical and optical sensors, chiral recognition devices, modifiers, catalysts, ion scavengers, phase transfer agents, ligand for transition metals[2-4]. The selective functionalization of calixarenes at wide and narrow rim was a challenging task. Though ipso electrophilic substitution of *p*-alkyl calixarenes with nitro and sulfonate groups was successful, in certain cases[5-7], the oxidized products are obtained. After successful de-*tert*-butylation of *p*-*tert*-butyl calix[n]arenes, the functional groups like nitro, amino, oxime, sulfonic, acetyl, alkyl, halo, carbonyl and allylic groups[8-10] could be introduced at wide rim of the calixarenes. Thus the de-*tert*-butylation was mandatory prior to the modification at wide rim of the calixarene. Saleh and Tashtoush[11,12] reported several catalyzed de-*tert*-butylation reagents such as Lewis acids, metal oxides, mineral acids, natural clays and nafion-H for substituted arenes. Completely or partially de-*tert*-butylated calix[4]arene was obtained by refluxing the *p*-*tert*-butyl calix[4]arene with nafion-H in toluene[13]. The Lewis acid (*i.e.*, $AlCl_3$) catalyzed de-*tert*-butylation at upper rim of *p*-*tert*-butyl calix[n]arenes was reported[14-16]. Even though the reaction is simple, the variation in reaction conditions was observed to have huge impact on the yield of reaction product. However no attempts were made for de-*tert*-butylation of *p*-*tert*-butyl calix[n]arenes with trifluoro acetic acid/sodium dithionite media. First time a novel de-*tert*-butylation method was developed to obtain calix[n]arene. The de-*tert*-butylation of *p*-*tert*-butyl calix[n]arenes was shown in **Scheme-I**. The main advantages of the present de-*tert*-butylation method are high reaction yields (80-92 %) and simplicity of isolation.



If n=1, p-t-butyl calix[4]arene
n=3, p-t-butyl calix[6]arene
n=5, p-t-butyl calix[8]arene

If n=1, Calix[4]arene
n=3, Calix[6]arene
n=5, Calix[8]arene

Scheme-I

EXPERIMENTAL

The chemicals *viz. p-tert*-butyl phenol, formaldehyde, *para* formaldehyde, trifluoro acetic acid and other solvents used during extraction and purification were pure grade and obtained from Merck. The liquid state ^{1}H NMR and DEPT NMR spectra were recorded at room temperature with a Bruker Avance-500 MHz spectrometer. The ^{13}C NMR CP-MAS spectra were recorded with a Bruker Avance 300 MHz. Samples were packed in 2.5 mm diameter ZrO_2 rotors and spun at 7 kHz speed. TENSOR series of FTIR-spectrophotometer, CHNS analyzer (EURO vector) was used for characterization. The molecular weight was determined by LCMS (Agilent Technologies) Electron Spray Ionization method.

Synthesis of 5,11,17,23-tetra-*t*-butyl-25,26,27,28 tetrahydroxy-calix[4]arene (*p-tert*-butyl calix[4]arene): *p-tert*-Butyl calix[4]arene was synthesized and purified according to the Gutsche and Iqbal procedure[17]. Yield 70 %; m.p. 342-344 ºC; LCMS-ESI $(M-1)^+$ 647.5; ^{1}H NMR spectrum (500 MHz, pyridine-*d*$_5$) δ (ppm) 1.26 (s, 36H, $-C(CH_3)_3$), 4.2 (s, 8H, $ArCH_2Ar$), 7.3 (s, 8H, Ar-H), 8.6 (s, 4H, -OH); liquid state ^{13}C NMR spectrum (500 MHz, pyridine-*d*$_5$) δ (ppm) 149.9, 143.3, 128.4, 125.6, 33.9, 32.3, 31.4; DEPT NMR (500 MHz, pyridine-*d*$_5$) δ (ppm) 149.9, 128.4, 125.6 (aromatic ring -CH), 32.3 (bridged methylene $-CH_2$), 33.9, 31.4 (*t*-butyl, $-CH_3$); ^{13}C NMR CP-MAS (300 MHz) δ (ppm) 147, 144, 128, 125, 34, 32, 29.

5,11,17,23,29,35-Hexa-*t*-butyl-37,38,39,40,41,42-hexahydroxycalix[6]arene (*p-tert*-butyl calix[6]arene): *p-tert*-Butyl calix[6]arene was synthesized and purified according to the Gutsche and Stewart method[18]. Yield 80 %; m.p. 370-372 ºC; LCMS-ESI $(M-1)^+$ 971.5; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 1.25 (s, 54H, $-C(CH_3)_3$), 3.4-4.3 (d, 12H, $-CH_2$), 10.5 (s, 3H, -OH), 9.6 (s, 3H, -OH); ^{13}C NMR (500 MHz, pyridine-*d*$_5$) δ (ppm) 150.9, 144.4, 129.9, 127.3, 35.4, 33.8, 32; DEPT-NMR (500 MHz, pyridine-*d*$_5$) d (ppm) 151, 129.9, 127 (aromatic ring -CH), 33.8 (bridged methylene $-CH_2$), 35.4 32.7 (*t*-butyl, $-CH_3$); ^{13}C NMR CP-MAS (300 MHz) δ (ppm) 147.9, 144.7, 127.7, 125.5, 34.0, 33.6, 32.4.

Synthesis of 11,17,23,29,35,41,47-octa-*t*-butyl-49,50,51,52,53,54,55,56 octahydroxy alix[8]arene (*p*-*tert*-butyl calix[8]arene): *p*-*tert*-Butyl calix[8]arene was synthesized and purified according to the Munch method[19]. Yield 65 %; m.p. 416-418 ºC; LCMS-ESI $(M-1)^+$ 1297; ^1H NMR (500 MHz, $CDCl_3$) δ (ppm) 9.65 (s, 8H, -OH), 7.15 (s, 16H, Ar-H), 4.35 (d, 8H, Ar-CH_2), 3.5 (d, 8H, Ar-CH_2), 1.26 (s, 72H, -$C(CH_3)_3$); ^{13}C NMR (500 MHz, pyridine-d_5) δ (ppm) 151, 144.4,129.6, 126.7, 35, 33.4, 32.5 ; DEPT NMR (500 MHz, pyridine-d_5) δ (ppm) 151, 129.6, 126.7 (aromatic ring -CH), 33.4 (bridged methylene -CH_2), 35, 32.5 (*t*-butyl, -CH_3); ^{13}C NMR CP-MAS (300 MHz) δ (ppm) 147,143, 129, 124, 34, 31, 29.

Synthesis of 25,26,27,28-tetrahydroxycalix[4]arene(calix[4]arene): A mixture of *p*-*tert*-butyl calix[4]arene (2 g), 80 mL of 99 % trifluoro acetic acid and 100 mg of sodium dithionite was taken in two neck round bottomed flask. The contents of the flask are allowed to stir for 10 min at room temperature and refluxed for 24 h at 80-90 ºC by rota mantle. The reaction was monitored for each 3 h by either TLC (*n*-hexane/THF as eluent) or diminution of the *tert*-butyl peak in the NMR spectrum. At the end of the reaction, solvent was removed by vacuum evaporation. The residue was dissolved in chloroform and filtered to remove ($Na_2S_2O_4$). The excess chloroform in the filtrate was evaporated and the product was precipitated using CH_3OH. The crude product was recrystallized in CH_3OH-$CHCl_3$ to obtain the colourless crystals. Yield 92 %; m.p. 314-316 ºC; LCMS-ESI $(M-1)^+$ 423; anal. calcd. for $C_{28}H_{24}O_4$ (C, 79.22 %), (H, 5.70 %), found (C, 78.87 %), (H, 5.12 %); 1H NMR (500 MHz, $CDCl_3$) δ (ppm) 10.1 (s, 4H, -OH), 7.0 (d, 8H, Ar-H), 6.7 (t, 4H, Ar-H), 4.2 (s, 4H, Ar-CH_2) , 3.5 (s, 4H, Ar-CH_2); ^{13}C NMR (500 MHz, pyridine-d_5) δ (ppm) 150.3, 129.1, 121.4, 116, 31.7; DEPT NMR (500 MHz, pyridine-d_5) δ (ppm) 149.9,129.1, 121.4, 116 (aromatic ring -CH), 31.7 (bridged methylene -CH_2); ^{13}C NMR CP-MAS (300 MHz) δ (ppm) 151.6, 129, 122, 120, 31.6.

Synthesis of 37,38,39,40,41,42-hexa hydroxycalix[6]arene (calix[6]arene): A mixture of *p*-*tert*-butyl calix[6]arene (2 g), 80 mL of 99 % trifluoro acetic acid and 100 mg of sodium dithionite was placed in two neck round bottomed flask. The contents of the flask are allowed to stir for 10 min at room temperature and refluxed for 24 h at 80-90 ºC by rota mantle. The reaction was monitored for each 3 h by either TLC (*n*-hexane/THF as eluent) or diminution of the *tert*-butyl peak in the NMR spectrum. At the end of the reaction solvent was evaporated by vacuum evaporation. To remove ($Na_2S_2O_4$) residue was washed with methanol and ice water. The crude product was re-crystallized in CH_3OH-$CHCl_3$ to obtain colourless crystals. Yield 88 %; m.p. 415-417 ºC; LCMS-ESI $(M-1)^+$ 635; anal. calcd. for $C_{42}H_{36}O_6$ (C,79.22 %), (H, 5.70 %), found (C, 79.12 %), (H, 5.29 %); ^1H NMR (500 MHz, $CDCl_3$) δ (ppm) 10.3 (s, 6H, -OH), 7.1 (d, 12H, Ar-H), 6.8 (t, 12H, Ar-H), 3.8 (s, 12H, Ar-CH_2); ^{13}C NMR (500 MHz, DMSO-d_6) δ (ppm) 152.9, 128.8, 123.2, 120.3, 32.7. DEPT NMR (500 MHz, pyridine-d_5) δ (ppm) 152,128.8, 123.2, 120.3 (aromatic ring -CH), 32.7 (bridged methylene -CH_2); ^{13}C NMR CP-MAS (300 MHz) δ (ppm) 150, 128, 125, 120, 29.5.

Synthesis of 49,50,51,52,53,54,55,56-octhydroxycalix[8]arene (calix[8]arene): A mixture of *p-tert*-butyl calix[8]arene (2 g), 80 mL of 99 % trifluoro acetic acid and 100 mg of sodium dithionite is placed in two neck round bottomed flask. The contents of the flask are allowed to stir for 10 min at room temperature and refluxed for 24 h at 80-90 ºC by rota mantle. The reaction was monitored for each 3 h by either TLC (*n*-hexane/THF as eluent) or diminution of the *t*-butyl peak in the NMR spectrum. At the end of the reaction, solvent was removed by vacuum evaporation. To remove the $Na_2S_2O_4$, the residue was washed sequentially with chloroform, acetone and ether to obtain the final product with light gray colour. Yield 80 %; m.p. 373-375 ºC; LCMS-ESI $(M-1)^+$ 847; anal. calcd. for $C_{56}H_{48}O_8$ (C,79.22 %), (H, 5.70 %), found (C, 79.21 %), (H, 5.98 %); ^{1}H NMR (500 MHz, DMSO-d_6) δ (ppm) 8.8 (s, 8H, -OH), 6.9 (d, 16H, Ar-H), 6.6 (t, 8H, Ar-H), 3.8 (s, 16H, Ar-CH_2); ^{13}C NMR (500 MHz, pyridine-d_5) δ (ppm) 152, 128.8, 123.5, 120.4, 32.3; DEPT NMR (500 MHz, pyridine-d_5) δ (ppm) 149.9, 128.8, 123.5, 120.4 (aromatic ring -CH), 32.3 (bridged methylene -CH_2); ^{13}C NMR CP-MAS (300 MHz) δ (ppm) 148.6, 128.5, 120.4, 29.8.

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