

NOTE**Mechanochemical Synthesis of *p*-Nitro Calix[6]arene**

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A novel procedure was developed for the synthesis of *p*-nitro calix[6]arenes from *p*-*tert*-butyl calix[6]arene by mechanical activation. Mixture of *p*-*tert*-butyl calix[6]arene dissolved in dichloromethane, glacial acetic acid and anhydrous HNO₃ was subjected to intense mechanical activation/agitation in planetary ball mill. The nitro substituted calix[6]arene with 97 % purity and 75 % yield was formed within 2.5 h which otherwise takes several hours to complete the reaction.

Key Words: Mechanical activation, Nitration, Calix[n]arenes, CH₃COOH/HNO₃.

Calix[n]arenes are unique category of macromolecules that can complex cations and neutral molecules. The base induced reaction between *p*-alkyl phenol and formaldehyde leads to the formation of cyclic oligomers which are known as calixarenes. Selective functionalization of lower or upper rim of calixarenes requires specific reagents and experimental conditions¹. Introduction of a nitro group at the wide rim or narrow rim facilitates a main path way for N-substituted calixarenes. Calix[4]arenes substitute with amide functional groups on the upper rim acts as a ligand for the extraction of lanthanides and actinides². Shinkai *et al.*³ reported the synthesis of *p*-nitro-calix[6]arene by ipso substitution of nitro group on *p*-*tert*-butyl substituted calixarenes, but the overall yields were low⁴⁻⁶. Mild nitrating agent such as KNO₃/AlCl₃, silver nitrate and 63 % HNO₃ were tried in the synthesis of nitro calix[4]arenes^{7,8}. The selective ipso nitration was found to occur in partially etherified calixarenes⁹. Recently Zolfigol *et al.*¹⁰ applied the grinding technique for nitration of aromatic compounds in the presence of silica and sulfuric acid. In the present study the mechanical activation technique was attempted to introduce nitro groups on *p*-*tert*-butyl calix[6]arene as shown in Fig. 1.

The chemicals used in the present study are of AnalaR grade and were procured from Merck. The *p*-*tert*-butyl calix[6]arene and nitro substituted calix[6]arenes were characterized using FTIR, ¹H NMR, ¹³C NMR, CHNS elemental analyzer and HPLC, LCMS-ES⁻ for molecular ion peak determination. A planetary mill with agate bowl and balls (Model-pulverisette 5 supplied by M/s Fritsch, Germany) was employed for mechanical activation/agitation. Planetary mills are very effective for grinding, mixing and homogenizing emulsions and pastes. For each experiment, the ratio of

the reactants mixture to balls was maintained at 1:4 by weight. The dia of the agate ball used is 20 mm and the bowl contains fifteen such balls. All the experiments were performed at ambient temperature and at the rotation speed of 200 rpm.

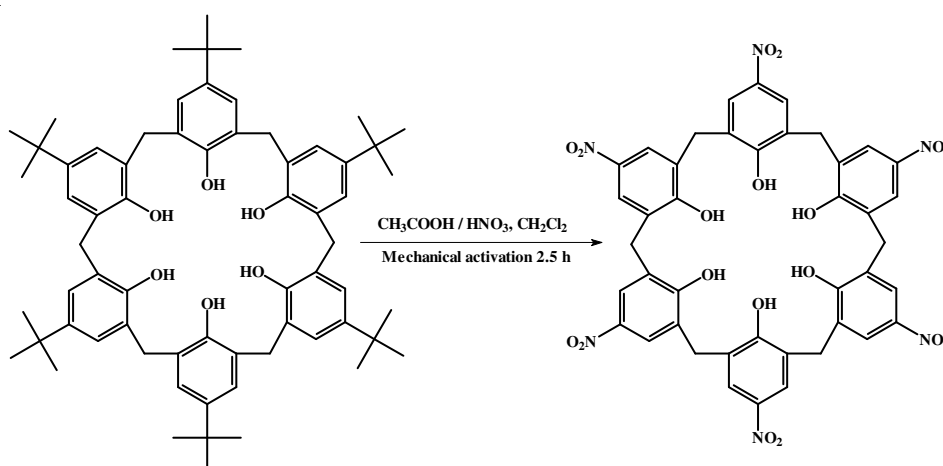


Fig. 1. Synthetic path way for nitration of *p*-nitro-calix[6]arene

Preparation of anhydrous HNO₃: Anhydrous nitric acid was prepared as per the method suggested by Coon¹¹. 265 mL of 70 % nitric acid was taken in a separating funnel and 235 mL of 96 % sulfuric acid was added to nitric acid solution. The aqueous acid mixture was extracted with 500 mL portion of dichloromethane. Each extraction was carried out by shaking the aqueous-dichloromethane vigorously for several minutes and allowed to separate. The dichloromethane extracts were collected separately and the contents were cooled to -60 to -80 °C. The 100 % anhydrous nitric acid crystals were isolated by filtration. This anhydrous HNO₃ was stored in calcium chloride-ice mixture to avoid the decomposition.

Synthesis of *p*-tert-butyl calix[6]arene: The *p*-tert-butyl calix[6]arene was synthesized using *p*-*t*-butyl phenol and formaldehyde in KOH media according to the procedure suggested by Gutsche *et al.*¹². The melting point and purity of the compound as estimated by HPLC was 370-372 °C and 97 %, respectively. The spectral data obtained was found to match with the literature data¹². Yield 80 %; m.p. 370-372 °C; LCMS-ESI (M-1)⁺ 971.5; ¹H NMR (500 MHz, CDCl₃) δ (ppm) 1.25 (s, 54H, -C(CH₃)₃), 3.4 to 4.3 (d, 12H, -CH₂), 10.5 (s, 3H, -OH), 9.6 (s, 3H, -OH); ¹³C NMR (500 MHz, pyridine-d₅) δ (ppm) 150.9, 144.4, 129.9, 127.3, 35.4, 33.8, 32; DEPT-NMR (500 MHz, pyridine-d₅) δ (ppm) 151, 129.9, 127 (aromatic ring -CH), 33.8 (bridged methylene -CH₂), 35.4 32.7 (*tert*-butyl, -CH₃); ¹³C NMR CP-MAS (300 MHz) δ (ppm) 147.9, 144.7, 127.7, 125.5, 34.0, 33.6, 32.4.

Synthesis of *p*-nitro-calix[6]arene: 1 g of *p*-tert-butyl calix[6]arene was taken in agate bowl containing agate balls and dissolved in 10 mL of dichloromethane. Further, mixture of 20 mL of glacial acetic acid and 10 mL of 100 % HNO₃ was

added and the contents were mechanically activated/agitated at room temperature for 2.5 h. The progress of the reaction was monitored using TLC. After completion of the reaction, the agate bowls and balls are washed with double distilled water. The collected pale yellow solid was washed with ethanol and kept in vacuum oven at 10 mmHg at 100 °C to obtain pure *p*-nitro-calix[6]arene. The purity of the *p*-nitro-calix[6]arene was estimated using HPLC and found to be 97 %. Yield 75 %, melting point ≥ 250 °C; FTIR (KBr, ν_{\max} , cm^{-1}): 3461, 1588, 1513, 1415 and 1346. LCMS-ES⁻: C₄₂H₃₀N₆O₁₈. 2CH₃OH, $m/z = 971.8$; Elemental analysis calculated (%): C, 58.54; H, 3.63; N, 8.13; found (%): C, 59; H, 3.71; N, 7.98. ¹H NMR (pyridine-d₅, δ); 8.1(12H, s, ArH), 4.2 (12H, s, ArCH₂Ar). ¹³C NMR (pyridine-d₅, δ); 158, 141, 124, 122, 31.3. ¹³C NMR CP-MASS: 159, 138,123, 119, 30.8.

ACKNOWLEDGEMENTS

One of the authors K. Chennakesavulu, Senior Research Fellow is grateful to Council of Scientific and Industrial Research (CSIR), New Delhi, India for financial support. The authors are grateful to SAIF, IIT Madras during the characterization of materials.

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(Received: 14 August 2009;

Accepted: 2 March 2010)

AJC-8497