Note

A single step preparation of p-sulphonated calixarenes

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Calix[n]arene sulphonylic acids (n=4, 6, 8) have been prepared by direct ipso-substitution of respective p-tert-butylcalix[n]arenes and their methyl ethers.

Calixarenes are macrocyclic compounds containing a cavity that can be used to recognize metal ions, anions or neutral molecules.1 By appropriate functionalization, they can be expected to mimic the actions of enzymes as well as to synthesize new molecular or metallo receptors.2 One of the most important requirements of a metallo receptor is their solubility in water or aquo-organic solvents. A few water soluble calix[n]arenes3 have been reported in the literature and amongst them, the ones containing the sulphonylic acid group at the para position of the phenolic unit of calixarenes are the most important for their excellent metal ion extractant qualities.4 Sulphonated calixarenes have been obtained by de tert-butylation of readily available p-tert-butylcalix[n]arenes followed by their reaction with conc. sulphuric acid, chlorosulphonic acid or sulphur trioxide.5 The yields of sulphonated calix[n]arenes are therefore dependent upon the yields obtained at each step of the synthetic strategy and such a course normally results in significant losses. In this note, we report an efficient one-step one-pot sulphonation of p-tert-butylcalix[n]arenes which provide p-sulphonated calix[n]arenes in 60-70% yields (Scheme I).

Sulphonation of benzenoid substrates bearing p-tert-butyl groups have been investigated earlier and it has been observed to lead to substantial isomerization and dealkylations. Studies on sulphonation of tert-butyl phenol have also been extensively carried out by Cerfontain6 who have determined it to be a reversible reaction as observed in other aromatic substrates. In the present work, sulphonation of p-tert-butylicalixarene seems to occur via ipso-substitution7 to yield p-sulphonated calixarenes. The driving force
of the reaction appears to be the formation of butene via cyclopentadienyl cation as reported earlier. The isolated product indicates that the macrocyclic ring was stable under the conditions employed.

### Experimental Section

NMR spectra were recorded on a 300 MHz Bruker DPX 300 instrument; IR spectra on a Nicolet Protegé 460 spectrometer in KBr disks; mass spectra on a Jeol SX-102 spectrometer and C, H, N analysis was obtained by using a Perkin-Elmer 240C elemental analyzer.

**General procedure for the preparation of para-sulphonated calix[n]arenes.** Sulphuric acid (15 mL) was taken in 100 mL round bottom flask and p-tert butylcalix[n]arene (0.5 g) was added to it. The reaction mixture was stirred for 6-18 hr (in the case of calix[n]arene methyl ether reaction required 40 hr for completion) at 70-80°C and the reaction was monitored by taking an aliquot of reaction mixture and adding it to water. The reaction was considered complete when no water insoluble material was detected. The reaction mixture was then added to water (100 mL) and neutralized with NaCO₃. The reaction mixture was filtered and pH of filtrate solution was adjusted to 7.5-8.0 with Na₂CO₃ solution. The solution was filtered again and the residue washed with water. Combined filtrate was distilled under vacuum. The residue obtained was dissolved in water (10 mL) and precipitated by addition of ethanol to give 60-70% of the para-sulphonated calix[n]arenes.

The reaction mixture could also be worked up by adding the reaction mixture to saturated sodium chloride solution, when the sodium salt of the p-sulphonated calix[n]arene methyl ether (e.g. in the case of p-tert-butylcalix[n]arene methyl ether) separated out. The reaction mixture was filtered to give p-sulphonated calix[n]arene methyl ether which was recrystallized with water/methanol to give pure p-sulphonated calix[n]arene methyl ether.

Alternatively, p-tert-butylcalix[6]arene methyl ether (1 g) was taken in a round bottom flask and 30 mL of conc. sulphuric acid was added to it. The mixture was warmed to 70°C for 4 hr and then kept at 5-10°C for 30 days. It was worked up as above to give the hexasulphonated calix[6]arene methyl ether.

**Calix[4]arene-p-sulphonate.** Following the general procedure described above, calix[4]arene-p-sulphonate was obtained in 66% yield, mp > 300°C; IR (KBr, cm⁻¹): 1051, 1191 (SO₃), 1420, 3541 (OH); ¹H NMR (D₂O, δ): 3.90 (8H, ArCH₂Ar), 7.45 (8H, s, ArH); ¹³C NMR (D₂O, δ): 32.61, 126.22, 129.83, 132.45, 158.44; DEPT-135 NMR (D₂O, δ): 32.5 (CH₂), 126.17 (CH); MS-FAB: m/z 832 (M⁺). Found: C, 33.09; H, 3.34. Calc. for C₅₆H₁₆O₈S₄Na₅·8H₂O: C, 32.94; H, 3.36%.

**Calix[6]arene-p-sulphonate.** Following the general procedure described above, calix[6]arene-p-sulphonate was obtained in 59% yield, mp > 300°C; IR (KBr, cm⁻¹): 1048, 1118, 1190 (SO₃), 1416, 3491 (OH); ¹H NMR (D₂O, δ): 3.92 (12H, s, ArCH₂Ar), 7.50 (12H, s, ArH); ¹³C NMR (D₂O, δ): 34.85, 128.91, 133.54, 136.57, 136.54; DEPT-135 NMR (D₂O, δ): 32.2 (CH₂), 126.3 (CH); MS-FAB: m/z 1249 (M⁺). Found: C, 31.45; H, 3.58. Calc. for C₄₂H₂₆O₂₄S₆Na₂·15H₂O: C, 31.39; H, 3.51%.

**Calix[8]arene-p-sulphonate.** Following the general procedure described above, calix[8]arene-p-sulphonate was obtained in 63% yield, mp > 300°C; IR (KBr, cm⁻¹): 1051, 1185, (SO₃), 1472, 3446 (OH); ¹H NMR (D₂O, δ): 4.05 (16H, s, ArCH₂Ar), 7.58 (16H, s, ArH); ¹³C NMR (D₂O, δ): 32.47, 126.68, 129.14, 134.22, 156.71; DEPT-135 NMR: 32.6 (CH₂), 126.6 (CH). Found: C, 32.1; H, 3.4. Calc. for C₅₀H₃₂O₃₂S₄Na₁₂·20H₂O: C, 31.88; H, 3.62%.

**Tetrasodiumtetramethoxyxalic[4]arene-p-sulphonate.** The sulphonation was carried out as per the general procedure. The time required for completion of reaction was 36 hr, yield 63%; mp > 300°C; IR (KBr, cm⁻¹): 1146 (SO), 1206, 1456; ¹H NMR (D₂O, δ): 3.63-3.91 (m, 20H, ArCH₂Ar and OMe), 7.44 (s, 8H, ArH); MS-FAB: m/z: 889 (M⁺). Found: C, 40.13; H, 3.59. Calc. for C₆₀H₴₀O₁₆S₄Na₁₂·3H₂O (943): C, 40.76; H, 3.63%.

**Hexasodiumhexamethoxyxalic[6]arene-p-sulphonate.** The sulphonation was carried out as per the general procedure. The time required for completion of reaction was 40 hr to give white crystalline compound, yield 67%, mp > 300°C; IR (KBr, cm⁻¹): 982, 1086, 1208; ¹H NMR (D₂O, δ): 3.32 (s, 18H, OCH₃), 3.45 (s, 12H, ArCH₂Ar), 7.48 (s, 12H, ArH). Found: C, 40.1; H, 3.75%. Calc. for C₅₈H₳₂O₳₂S₆Na₃·5H₂O (1423): C, 40.5; H, 3.68%.

**Octasodiumoctamethoxyxalic[8]arene-p-sulphonate.** The sulphonation was carried out as per the general procedure. The time required for completion of reaction was 40 hr, yield 62%, mp > 300°C; IR (KBr, cm⁻¹): 1402, 1162 (SO), 1114; ¹H NMR (TFA-d, δ): 3.15 (s, 24H, OCH₃), 3.93 (s, 16H, ArCH₂Ar), 7.22 (s, 16H, ArH). Found: C, 39.83; H, 3.6. Calc. for C₆₈H₳₂O₳₂S₆Na₈·8H₂O (1921.6): C, 40.00; H, 3.77%.
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References
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