

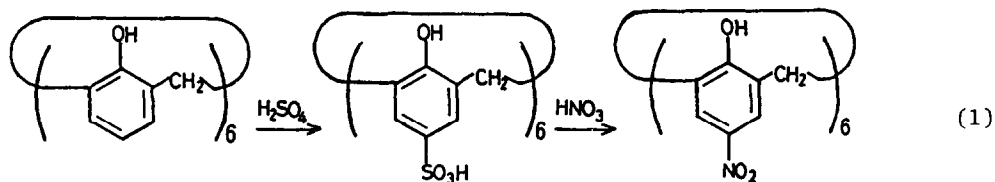
A NEW SYNTHESIS OF p-NITROCALIX[6]ARENE

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p-Nitrocalix[6]arene which possibly serves as a potential intermediate to derive functionalized calixarenes was synthesized for the first time.

The chemistry of cyclodextrins has occupied a central interest in host-guest chemistry in last two decades, and many functionalized cyclodextrins which can partly mimic the action of enzymes have been exploited.^{1,2)} Recently, Gutsche and co-workers³⁾ have reported on a series of new cyclic host molecules called "calixarenes" which possess a cylindrical architecture similar to cyclodextrins and are expected to be useful to design enzyme mimics in totally synthetic systems. In order to derive functionalized calixarenes nitrated calixarenes would play an important role as potential synthetic intermediates. Nitration of calixarenes was repeatedly attempted in the past, but it failed.^{4,5)} In fact, Gutsche describes in his recent review article⁵⁾ that attempts to obtain a nitration product have not been successful. We here report on the first successful method to synthesize the nitration product from calix[6]arene.

It is known that direct nitration mainly affords the decomposed products because the reaction conditions are too drastic.⁵⁾ We also attempted several direct nitration methods but failed. We have established that sulfonation of calix[6]arene gives calix[6]arenehexasulfonate in 75% yield.⁶⁾ We considered that the substitution of the sulfonate groups with the nitro groups should proceed under milder conditions without the formation of by-products (Eq. 1).



Calix[6]arene (5.0 g) was heated in 50 ml of conc. H_2SO_4 for 4 h at 80 °C. After cooling, the reaction mixture was diluted with 90 ml of cold water

and then treated with 61% HNO_3 (5.5 g) for 10 h at 0-5 °C. When the reaction mixture was diluted with water, a finely dispersed precipitate was observed. The precipitate was isolated by centrifugation and washed with water. It was dissolved in alkaline (NaOH) solution and treated with active charcoal. After filtration, NaOH was added (up to 5 wt%) to the filtrate in order to salt out the hexasodium salt. The salt was filtered, washed with NaCl solution, and dissolved in water. This aqueous solution was added dropwise into dil. HCl solution. The precipitate was recovered by centrifugation: yield (from calix-[6]arene) 15%, mp(dec) >300 °C. IR(KBr): ν_{OH} 3450 cm^{-1} , ν_{NO_2} 1330 and 1480 cm^{-1} . NMR($\text{Me}_2\text{SO}-d_6$): δ =3.98 (CH_2 , broad s, 12H), 8.10 (aromatic protons, broad s, 12H). Absorption spectrum in water: λ_{max} 318 nm at pH 2.00, 410 and 445 nm in 0.1 N NaOH (cf. λ_{max} of p-nitrophenol 316 nm at pH 2.00, 402 nm in 0.1 N NaOH). Found: C, 51.94; H, 3.32; N, 8.59%. Calcd for $(\text{C}_7\text{H}_5\text{NO}_3)_6 \cdot 4\text{H}_2\text{O}$: C, 51.53; H, 3.89; N, 8.59%.

When we carried out the direct nitration of calix[6]arene in chloroform, the i.r. spectrum of the product showed the $\nu_{\text{C=O}}$ peaks at 1710 and 1750 cm^{-1} . This indicates that the direct nitration accompanies the oxidation of calix-[6]arene. The first advantage of the present method is, therefore, that calix[6]arene is protected from the oxidation by introducing the sulfonate groups. In the direct nitration, it was very difficult to isolate a hexanitrated product from others (e.g., lower nitrated products). In the present method, on the other hand, the water-solubility of p-nitrocalix[6]-arene was largely different from sulfonate-containing, incompletely substituted products. This second advantage led to the successful isolation of pure p-nitrocalix[6]arene. Further characterizations and applications are now continued in this laboratory.

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