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Syntheses and Crystal Structure of Calix[4]quinone

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Calix[4]quinone and other functionalized calixarenes were synthesized in high yields. The crystal structure of the calix[4]-quinone was determined by the X-ray diffraction method.

Calixarenes, which are accessible from base-catalyzed condensation of p-substituted phenols with formaldehyde, are a sort of metacyclophane. These compounds have lately attracted considerable attention because their potential as enzyme mimics has been suggested.1)

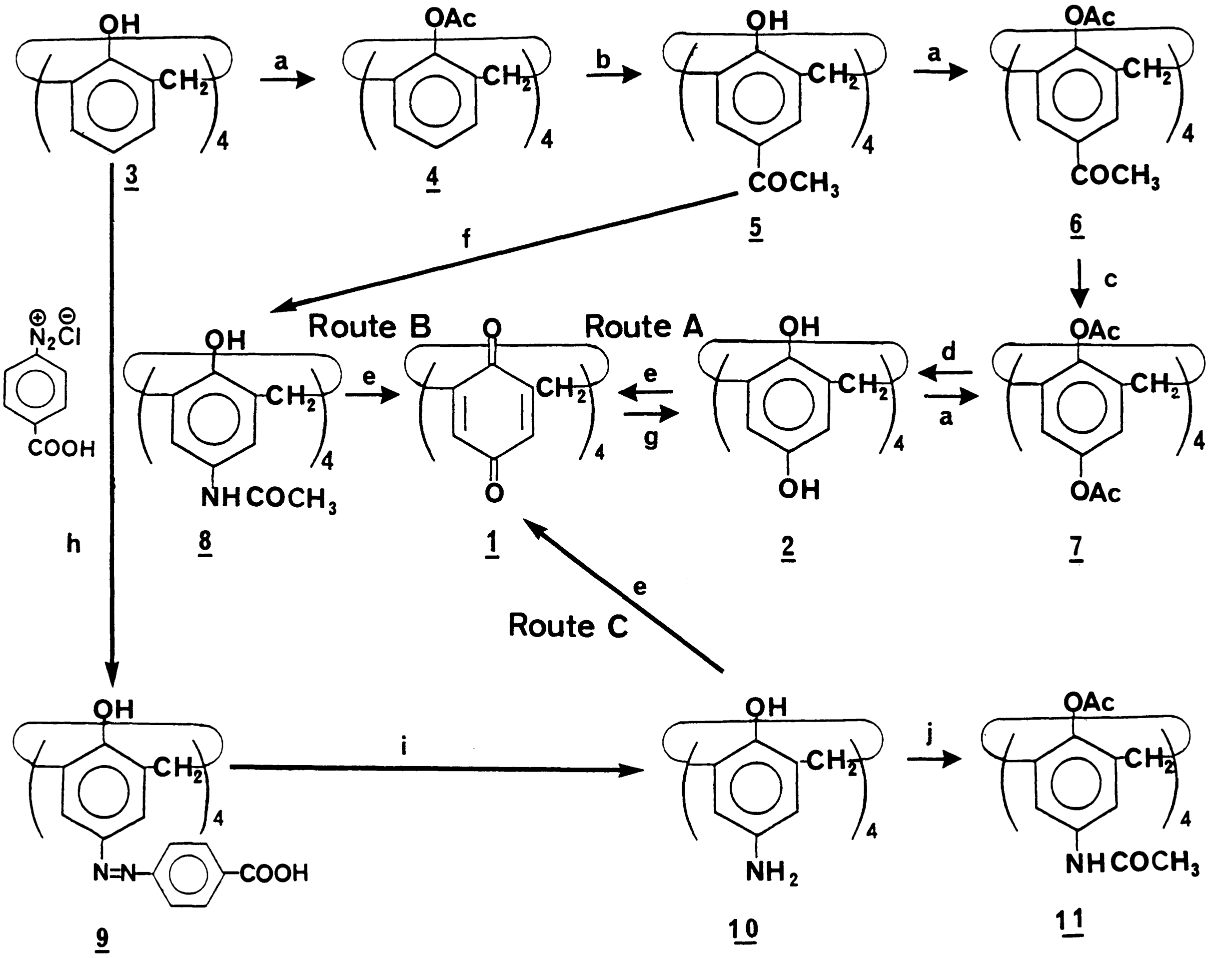
Since the first paper of Gutsche for calixarenes2) was issued, we have been studying on the syntheses of various calixarenes and on their character.3) And, we have also been searching a new redox system. If calix[4]quinone4)(1), which is a sort of calixarene comprising cyclic arrays of p-quinone residues attached by methylene groups, is synthesized readily from an available p-tert-butylcalix[4]-arene, it must form a new redox system and must become a new compound which is able to form a charge-transfer complex. Thus, we finally found the convenient synthesis of calix[4]quinone 1. We wish to report here its synthetic method and crystal stucture.

As shown in Scheme 1, three possible routes A, B, and C were taken into account for the synthesis of 1. Route A is as follows: Acetylation of calix[4]-arene(3) was carried out along the method of Gutsche and Lin to afford 25,26,27,28-tetraacetoxycalix[4]arene(4).5) Although the Fries rearrangement of 37,38,39,40,41,42-hexaacetoxycalix[6]arene in chlorobenzene had been reported not to take place,6) we could carry out the Fries rearrangement of 4 in nitrobenzene and obtained 5,11,17,23-tetraacetyl-25,26,27,28-tetrahydroxycalix[4]arene(5) in an excellent yield. Acetylcalix[4]arene(5) was allowed to react with acetic anhydride in the presence of sodium acetate to give 5,11,17,23-tetraacetyl-25,26,27,28-tetra-acetoxycalix[4]arene(6) in a 76% yield. The Baeyer-Villiger oxidation of 6 to 5,11,17,23,25,26,27,28-octaacetoxycalix[4]arene(7) required prolonged shaking(25 d) at room temperature for completion. The hydrolysis of 7 under basic conditions proceeded smoothly to produce calix[4]hydroquinone(2) in a 95% yield. The calix[4]-

hydroquinone 2 was oxidized readily with ferric chloride to yield the desired compound 1 in an 89% yield.[7)]

Route B is as follows: The reaction of 5 with sodium azide in acetic acid in the presence of conc. sulfuric acid gave 5,11,17,23-tetraacetoamido-25,26,27,28-tetrahydroxycalix[4]arene(8) in a 75% yield. This compound was converted into 1 by ferric chloride in a 52% yield.

Route C is most convenient and therefore described below in detail. A solution of p-carboxybenzenediazonium chloride,[8)] which was prepared from p-aminobenzoic acid(1.37 g, 10 mmol), sodium nitrite, and hydrochloric acid, in 25 ml of water, was added slowly into a cold(5 °C) solution of calix[4]arene(3)(1.0 g, 2.36 mmol) and sodium acetate$\cdot 3H_2O$(4.08 g, 30 mmol) in MeOH-DMF(26 ml, 5:8 v/v) to give a red suspension. After allowing to stand for 2 h, the suspension was acidified with 0.25% HCl(150 ml). The mixture was warmed at 60 °C for 30 min to yield a solid, which was filtered and washed with water and MeOH. The resulting moist paste of the azo-compound was dissolved in an aq solution of NaOH(2.0 g in 200 ml



(a) Ac_2O, AcONa, reflux; (b) $AlCl_3$, $C_6H_5NO_2$, 70 °C; (c) $C_6H_5CO_2H$, $CHCl_3$, r.t.; (d) aq NaOH, dioxane; (e) $FeCl_3$, K_2CrO_4, AcOH; (f) NaN_3, H_2SO_4, AcOH, 60 °C; (g) aq $Na_2S_2O_4$, $CHCl_3$, reflux; (h) p-$HOCOC_6H_4\overset{+}{N}_2Cl^-$; (i) $Na_2S_2O_4$, aq NaOH, 90°C; (j) Ac_2O, C_5H_5N.

Scheme 1.

of water) and reduced with sodium hydrosulfite(7.0 g, 40 mmol) for 1 h at 90 °C to give a white suspension. It was then cooled rapidly to 20 °C, filtered, and washed with water to give white powder of 5,11,17,23-tetraamino-25,26,27,28-tetrahydroxycalix[4]arene(10), which was dried at room temperature under reduced pressure to yield a pale blue solid(1.15 g). The white moist paste of calixarene 10 was dissolved in acetic acid(50 ml) and warmed at 50 °C. Into this solution, a solution of ferric chloride(4.9 g, 30 mmol) in 18% HCl(20 ml) was added. The reaction mixture was stirred for 15 min to give a yellow suspension. It was poured into a solution of potassium dichromate(2.94 g) and conc. H_2SO_4(7.7 ml) in 130 ml of water, and heated at 80-90 °C. After 15 min, the solution was cooled to 15 °C to precipitate a yellow solid(1)(1.08 g, 95%). The analytical sample of 1 was obtained by recrystallization from THF; dp 250 °C.

Calix[4]quinone 1 was reduced with sodium hydrosulfite to 2 in a 93% yield.

Calixarene 10 was converted by the treatment with acetic anhydride in pyridine into 5,11,17,23-tetraacetylamido-25,26,27,28-tetraacetoxycalix[4]arene(11) in a 73% yield.

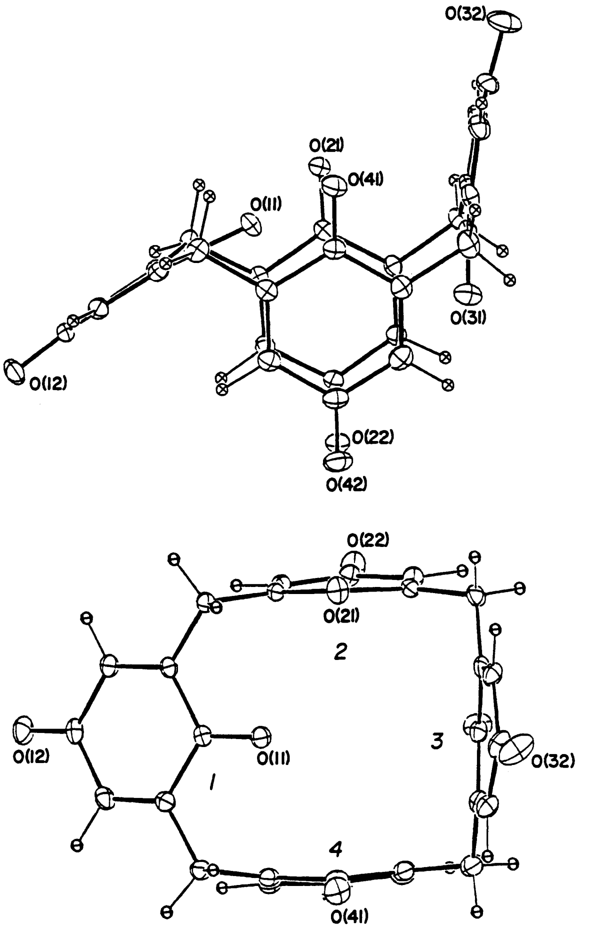


Fig. 1. ORTEP drawings of the molecular structure of calix[4]quinone 1.

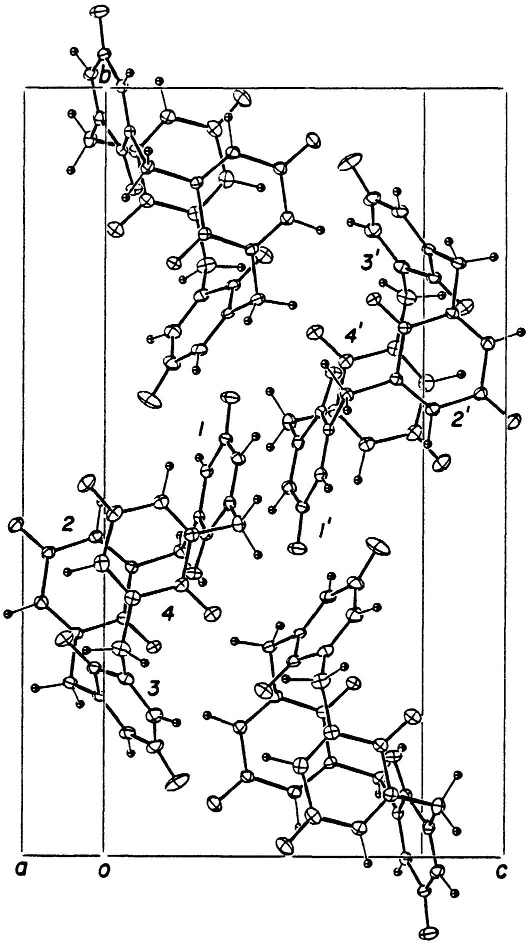


Fig. 2. Crystal structure of 1.

To elucidate the exact molecular structure of 1, X-ray crystal structure analysis has been carried out.[9)] Even though the crystallization was carried out in THF solution, the crystal lattice included no THF molecule. Figure 1 shows ORTEP drawing of the molecular structure of 1. Among the four quinone rings in the molecule, quinones *2* and *4* are parallel to each other with the carbonyl groups near to the bridging carbons in the overlapping positions. On the other hand, the quinones *1* and *3* are apart from the parallel position, dihedral angle between the rings being 49.7°, with the corresponding carbonyl groups in the opposite directions. The molecular structure indicates the conformational modification of 1 in the crystal structure from the probable D_{2d} structure with 1,3-alternate conformation instead of the corn-type C_{4v} structure. The fact may be attributed to a van der Waals interaction between the quinone *1* rings of neighboring molecules related by the crystallographic center of symmetry(Fig. 2).

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4) According to the IUPAC nomenclature, the name of this compound is pentacyclo-$[19,3,1,1,^{3,7}1,^{9,13}1,^{15,19}]$octacosa-3,6,9,12,15,18,21,24-octaene-5,11,17,23,25,26,27,28-octaone. The nomenclature of cyclophane family gives it the name of [1.1.1.1]metacyclophane-p-quinone.
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7) The quinone 1: mp 250 °C dec; IR(KBr) 1660, 1615, and 1296 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ=3.47(CH_2, s, 2H) and 6.70(-CH=C, s, 2H); ^{13}C NMR(DMSO-d_6) δ=28.9 (CH_2), 133.5(C=$\overset{*}{C}$H), 146.06(-$\overset{*}{C}$-CH_2), 185.1(C=O), and 186.8(C=O); Found: C, 69.56; H, 3.49%. Calcd for $C_{28}H_{16}O_8$: C, 70.00; H, 3.36%.
8) The diazonium chloride was prepared by the reported method with a slight modification: G. Schieman and W. Winkelmüller, Org. Synth., Coll. Vol. II, 299(1943).
9) Crystal data: $C_{28}H_{16}O_8$, F.W.=480.4, monoclinic, $P2_1/c$, a=9.046(1), b=21.955(1), c=11.366(1)Å, β=104.90(1)°, V=2181.3(2)Å^3, Z=4, D_o=1.462 g cm^{-3}, F(000)=992, μ(CuKα)=8.6 cm^{-1}. The X-ray diffraction data were collected on Rigaku automated four-circle diffractometer with Ni-filterd CuKα radiation. A total of 3236 independent reflections was collected up to 2θ=120° by the θ-2θ scan method, among which 2931 were observed reflections [$|F_o| \geq 3\sigma(F_o)$]. The crystal structure was solved by the direct method (SHELXS-86)[10)] and refined by the full-matrix least-squares method (XRAY-76)[11)] for the non-hydrogen atoms anisotropically and hydrogen atoms isotropically. The final R index is 0.050 for observed reflections.
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