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SYNTHESIS AND X-RAY INVESTIGATION OF NITROCALIX[4]QUINONE

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The method of selective oxidation of simply accessible dihydroxy-dipropoxycalix[4]arene to nitrocalixmonoquinone by mixture of 75% nitric acid and glacial acetic acid was developed. The nitrocalixmonoquinone is prospective as synthone for design of optical sensors and redox-sensitive bio-active compounds. The nitrocalix[4]monoquinone exist a partial cone conformation.

СИНТЕЗ ТА РЕНТГЕНОСТРУКТУРНЕ ДОСЛІДЖЕННЯ НІТРОКАЛІКС[4]ХІНОНУ

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Розроблений метод селективного окиснення легкодоступного дигідроксидипропоксикалікс[4]арену сумішшю 75% азотної та льодяної оцтової кислоти, яке приводить до утворення нітрокалікс[4]монохінону — синтону для отримання оптичних сенсорів та редокс-чутливих біологічно активних речовин. Молекула нітрокалікс[4]монохінону існує в конформації частковий конус.

СИНТЕЗ И РЕНТГЕНОСТРУКТУРНОЕ ИССЛЕДОВАНИЕ НИТРОКАЛИКС[4]ХИНОНА

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Разработан метод селективного окисления легкодоступного дигидроксидипропоксикалікс[4]арена смесью 75% азотной и ледяной уксусной кислот, которое приводит к нитрокалікс[4]монохинону — синтону для получения оптических сенсоров и редокс-чувствительных биологически активных веществ. Молекула нитрокалікс[4]монохинона существует в конформации частичный конус.

Introduction

Calixarenes containing benzoquinone chromophores (calixquinones) are promising building blocks for rational design of various bio-active compounds, chemosensors, NLO materials, etc [1, 2].

Calixquinones which change their color upon the complexation, are promising as ionophores and optical sensors [3, 4, 5]. For example, compounds 1 (Fig. 1) were used as redox-active ionophores for selective recognition of cesium and rubidium cations [6]. Absorption maximum in UV-spectra of calixdiquinone 2, functionalized with complexating amide groups at the lower rim of macrocycle, is significantly shifted in a process of selective anion binding [7]. Calixquinone derivative 3 containing macrocyclic crown-ether system change its coloration as a result of selective calcium complexation [8].

Synthesis and properties of calixarenes containing mainly two or four quinone groups were described in literature [9, 10]. But, there are only few work dedicated to synthesis of calix[4]monoquinones [11, 12, 13]. We report here the synthesis and spatial structure of calix[4]monoquinone 5 bearing reactive nitro-group at the wide rim capable to subsequent.

Results and discussion

Phenolic ring oxidation of dihydroxy- and tetrahydroxy-calix[4]arenes is principal method of calix[4]quinones synthesis. Products of total oxidation — diquinones and tetraquinones — are mainly obtained by these routes. Toxic and expensive tallium nitrate or triflate are usually used as oxidizing agents [14, 15]. It was described only few examples of the formation of nitrated calixquinones at the conditions of nitration reaction [16]. Oxidation of calixarenes to quinones by other reagents wasn't developed.

We have found conditions of selective oxidation of one phenolic fragment of dihydroxy-dipropoxycalix[4]arene 4 by the mixture of 75% nitric acid and glacial acetic acid. Calixmonoquinone 5 is afforded by this reaction (Scheme). The reaction was carried out at 0-5°C. Double change of reaction mixture color from yellow to dark purple and to orange is observed.

Simultaneously with oxidation, a nitration of para-position phenolic rings is occurred. As the result a mixture of nitrocalix[4]arene-monoquinone 5 and dinitrocalix[4]arene 6 is formed. The compounds were separated by column chromatography (silica gel L 35/100, dry chloroform). Analogous technique of

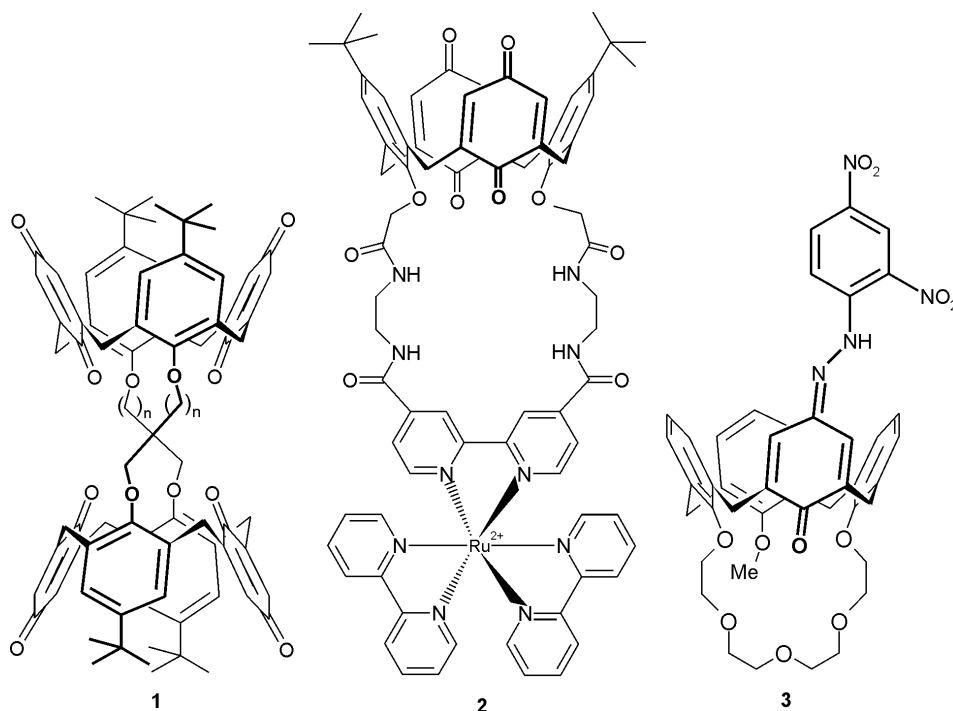


Figure 1

dinitrocalix[4]arene 6 obtaining was described in the literature, but any data about formation of calixquinone was not presented [17].

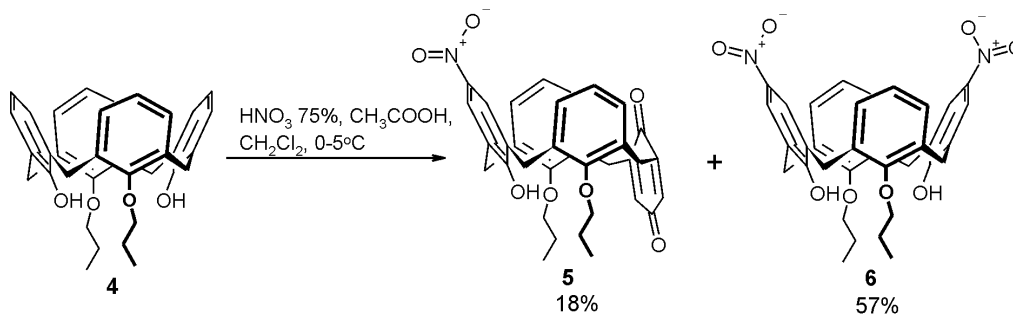
The structure of dinitro-dipropoxycalix[4]arene 6 with C_{2v} symmetry is proved by the ^1H NMR spectrum. It contains the characteristic signals: downfield singlet of hydroxyl groups (δ 9,46 ppm), which form intramolecular hydrogen bonds OHOPr, singlet (δ 8,05 ppm.), doublet (δ 6,99 ppm 7,6 Hz) and triplet (δ 6,85 ppm 7,6 Hz) of aromatic hydrogen atoms; pair of doublets spin system AB of axial (δ 4,28 ppm 13,3 Hz) and equatorial (δ 3,54 ppm 13,3 Hz) protons of methylene spacers. Like other dialkoxycalixarenes [18], dinitrocalixarene 6 adopts in solutions a pinched cone conformation. This is confirmed by the 0,74 ppm difference between axial and equatorial protons of the macrocyclic methylene groups [19].

^1H NMR spectrum of calixquinone 5, which adopt a partial cone conformation is more complicated (Fig. 2). Hydrogen atoms of nitrophenol and quinone rings are appeared as singlets at δ 8,07 and 6,69 ppm correspondingly. Protons of alkylated phenolic rings are revealed as pair of overlaping doublets at δ 6,70 ppm and triplet at δ 6,87 ppm. Equatorial and axial hydro-

gen atoms of methylene spacer are revealed as two pair of doublets at δ 3,43 and 3,45 ppm (13,4 and 13,8 Hz) and δ 3,88 and 4,20 ppm (13,4 and 13,8 Hz). It is suggested that three benzene rings are disposed oppositely to quinone fragment relatively to the plane of methylene groups. It is known [20], that quinone ring can easily rotate around Ar-CH₂-Quin bonds even at -60°C. Protons, of OCH₂ groups are diastereotopic and appeared as two multiplets at δ 3,75 and 3,86 ppm.

Difference in chemical shifts between axial and equatorial protons, which determines mutual orientation (syn or anti) of neighboring aromatic fragments of macrocyclic skeleton is 0,75 ppm in CDCl₃ solution and 0,34 ppm in more polar dimethylsulfoxide. It is shown that conformation of molecule is influenced by nature of solvent. Detailed spatial structure of calixquinone 5 was investigated by the X-ray analysis (Fig. 3).

Dihedral angles between methylene groups' plane and quasiparallel alkylated phenolic rings of macrocycle are equal 111,10° and 102,73° (Planes of these rings form angle of 33,87°). Quinone ring is turned and form an angle of 103,31°. Nitrophenolic ring forms more obtuse angle of 138,43°. Partial rotation of last ring is probably caused by intramolecular hydrogen bond



Scheme

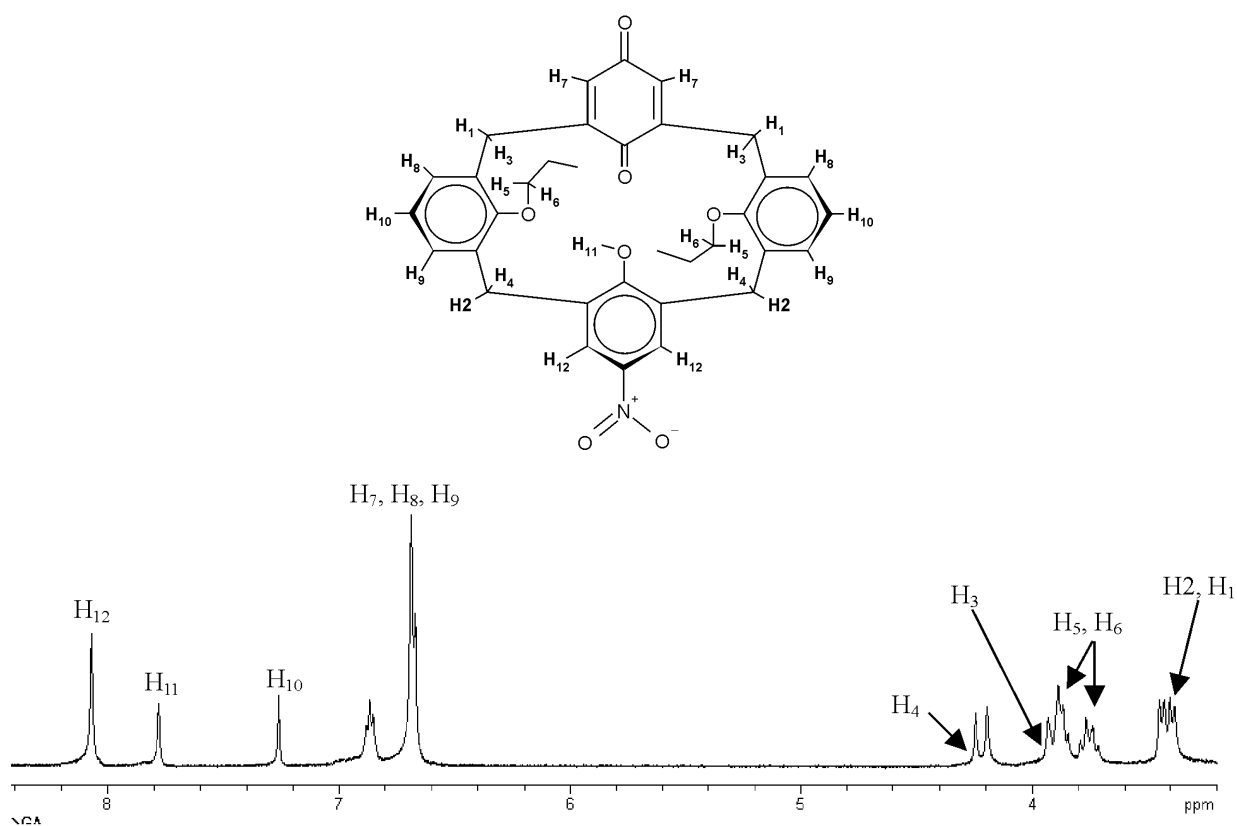


Figure 2. ^1H NMR spectrum of characteristic signals calixquinone 5 in CDCl_3 , 300 K.

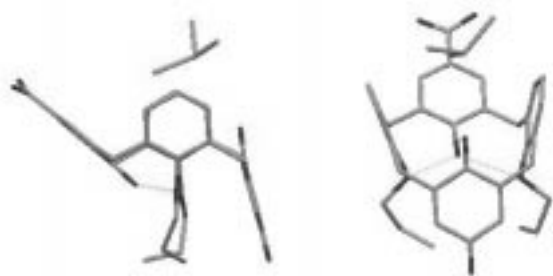


Figure 3. Molecular structure of calixquinone 5. (Two side projections. Hydrogen atoms aren't shown for clarity).

formation between the hydroxyl groups and propoxy fragments (distances $\text{O} \cdots \text{O}$ are equal 2,655 and 2,906 Å). A disordered on two position chloroform molecule is included into macrocyclic cavity. $\text{Cl} \cdots \pi$ interactions are indicated by spatial orientation and short distances (3,510 and 3,424 Å) between chlorine atoms and benzene rings. The shortest distances between oxygen atom of the quinone ring and the carbon atom of the chloroform are 3,366 Å and indicate $\text{C}=\text{O} \cdots \text{H}-\text{C}$ interaction (Fig. 4).

The electrostatic interaction between positively charged nitrogen of the nitro group and oxygen of

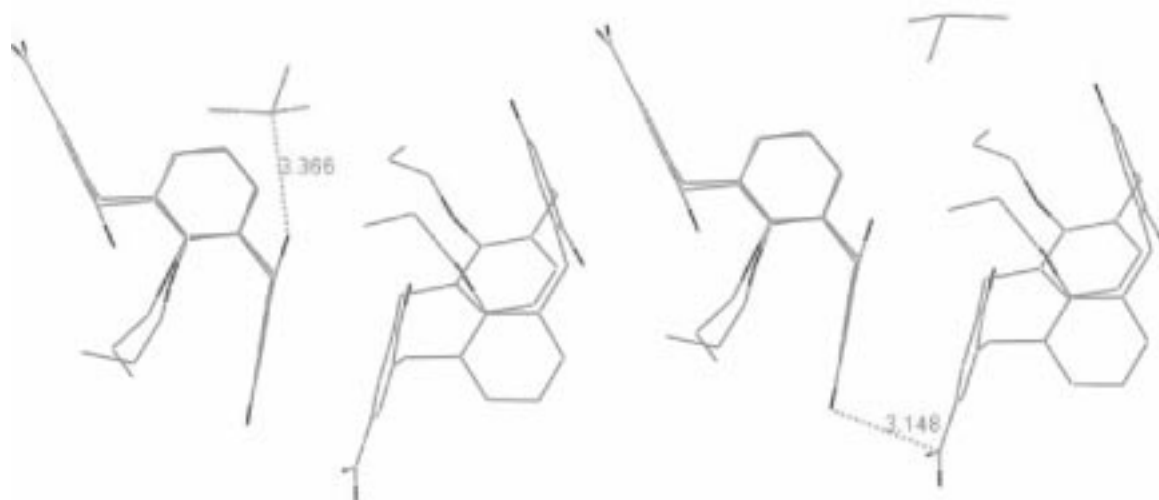


Figure 4. Crystal structure of calixquinone 5.

quinone ring (distance $N \cdots O$ is equal 3,148 Å) are the most strong interaction in the crystal state (Fig. 4). Rods are formed due to these interactions. Quinone and *p*-nitrophenolic rings of adjacent molecules are disposed almost parallel one to another (dihedral angle is 6,28°). But, despite on short distances between them (shortest distances $C \cdots C$ are equal 3,552 and 3,574 Å), π - π interactions are not observed, because rings are located not opposite one to another.

Nitrocalixquinone 5 is orange crystal compound, soluble in most organic solvents. UV-spectrum recorded in the tetrahydrofurane solution contains two intensive absorption bands with λ_{\max} 249 nm (ϵ 922 L/mol · cm) and λ_{\max} 327 nm (ϵ 922, 1500 L/mol · cm).

Summary

The method of selective oxidation of simply accessible dihydroxy-dipropoxycalix[4]arene to nitrocalixmonoquinone by mixture of 75% nitric acid and glacial acetic acid was developed. The nitrocalixmonoquinone is prospective as synthone for design of optical sensors and redox-sensitive bio-active compounds.

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Experimental part

IR spectra were recorded at Specord M-80 spectrometer; UV-spectra were recorded at a spectrophotometer Shimadzu UV 3100; ^1H NMR spectra were recorded on "Varian-300" spectrometer at 299,943 MHz (TMS as internal standard). Dipropoxycalix[4]arene was obtained correspondingly the literature procedures [21]. Nitration reaction was carried out at anhydrous conditions.

Nitration of 25,27-dipropoxycalix[4]arene 4.

To a vigorously stirred cooled to 2°C solution of 25,27-dipropoxycalix[4]arene 4 (0,51 g, 1 mmol) in methylene chloride (25 ml) was added a mixture of 75% nitric acid (1,5 ml) and glacial acetic acid (1,5 ml). The colour of the reaction mixture turned to dark purple after 5-10 min. Over less than 1 minute the colour of the mixture changed to orange. The reaction mixture was diluted with water (100 ml) after 10 minutes. The water layer was washed with methylene chloride (2x15 ml). The combined organic layers were washed with 1% solution of sodium carbonate (15 ml) and twice with brine (2 x 20 ml). Then it was dried upon Na_2SO_4 over night. Solvent was removed in vacuum (10 mm, 50°C). Residue was refluxed in methanol during 3 hours. After cooling to room temperature, precipitate of mixture 5 and 6 was filtered and dried

on air. The mixture was separated by preparative column chromatography (silica gel, L 35/100, dry CHCl_3). R_f: 0,25 (5), 0,55 (6).

5-Nitro-17,18-dioxo-26-hydroxy-25,27-dipropoxycalix[4]arene 5.

Orange-yellow crystal compound: yield 0,1 g (18%), melt. point 210-212°C. ^1H NMR (δ , ppm, CDCl_3): 1,08 (t, $J = 7,4$ Hz, 6H, O- CH_2 - CH_2 - CH_3), 1,81-1,92 (m, 4H, O- CH_2 - CH_2 - CH_3), 3,43 (d, $J = 13,4$ Hz, 2H, $\text{ArCH}_{\text{eq}}\text{Quin}$), 3,45 (d, $J = 13,8$ Hz, 2H, $\text{ArCH}_{\text{eq}}\text{Ar-NO}_2$), 3,70-3,80 and 3,83-3,91 (two m, 4H, O- CH_2 - CH_2 - CH_3 diastereotopic), 3,88 (d, $J = 13,4$ Hz, 4H, $\text{ArCH}_{\text{ax}}\text{Quin}$), 4,20 (d, $J = 13,8$ Hz, 2H, $\text{ArCH}_{\text{ax}}\text{Ar-NO}_2$), 6,69 (brd, $J = 5,0$ Hz, 4H+2H, ArH, QuinH), 6,87 (t, $J = 5,0$ Hz, 2H, Ar), 7,78 (s, 1H, OH), 8,07 (s, 2H, ArH- NO_2). IR (KBr, cm^{-1}): ν_{symNO_2} 1332, ν_{asymNO_2} 1511, $\nu_{\text{C=O}}$ 1650, ν_{OH} 3205; IR (CHCl_3 , cm^{-1}): ν_{symNO_2} 1338, ν_{asymNO_2} 1522, $\nu_{\text{C=O}}$ 1658, ν_{OH} 3300. UV: λ_{\max} 249, 327 nm (ϵ 922, 1500 L/mol · cm). Calculated for $\text{C}_{34}\text{H}_{33}\text{NO}_7$, %: C — 71,94, H — 5,86, N — 2,47. Found, %: C — 71,27, H — 5,43, N — 2,50.

5,17-Dinitro-26,28-dihydroxy-265,27-dipropoxycalix[4]arene 6.

Pale-yellow crystal compound: yield 0,34 g (57%), melt. point 328-330°C. ^1H NMR (δ , ppm, CDCl_3): 1,33 (t, $J = 7,5$ Hz, 6H, O- CH_2 - CH_2 - CH_3), 2,03-2,16 (m, 4H, O- CH_2 - CH_2 - CH_3), 3,54 (d, $J = 13,3$ Hz, 4H, $\text{ArCH}_{\text{eq}}\text{Ar}$), 4,02 (t, $J = 6,3$ Hz, 4H, O- CH_2 - CH_2 - CH_3), 4,28 (d, $J = 13,3$ Hz, 4H, $\text{ArCH}_{\text{ax}}\text{Ar}$), 6,85 (t, $J = 7,6$ Hz, 2H, Ar), 6,99 (d, $J = 7,6$ Hz, 4H ArH), 8,05 (s, 4H, ArH- NO_2), 9,46 (s, 2H, OH). Physical constant and ^1H NMR spectrum are identical to literature referenced [17, 22].

X-Ray investigation.

Monocrystal of quinone 5 was obtained by slow evaporation of chloroform solution. Crystal data for 5: $\text{C}_{34}\text{H}_{33}\text{NO}_7 \cdot 0,5\text{CHCl}_3$; Mr = 627,37; orange-yellow, crystal size 0,80 x 0,46 x 0,1 mm, monoclinic $\text{P}2_1/\text{c}$, $a = 9,9900(3)$ Å, $b = 19,0300(8)$ Å, $c = 16,4390(7)$ Å, $\alpha = 90^\circ$, $\beta = 98,446(2)^\circ$, $\gamma = 90^\circ$, $V = 3091,32$ Å³, $Z = 4$, $\rho_{\text{calc}} = 1,126$ g/cm³; $2\theta_{\text{max}} = 46,5^\circ$. Intensity data were collected at 100(2)K on a Nonius Kap-paCCD diffractometer using Mo- $\text{K}\alpha$ radiation ($\lambda = 0,71073$ Å). Lorentz and polarization corrections were applied and diffracted data were not corrected for absorption [23]. Structure was solved and refined using SHELXS-97 [24] and SHELXL-97 [24] respectively. Hydrogen atoms were calculated to their idealized positions and were refined as riding atoms. The final values of R-factors are $R_1 = 0,0491$ for 4041 reflections [$I > 2\sigma(I)$] and 0,0858 for all 6298 data. Residual electron density was between 0,441 and -0,458 eÅ⁻³.

Spatial atom disposition shown at the pictures was created with Mercury program.

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