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Rigid Tetranitroresorcinarenes

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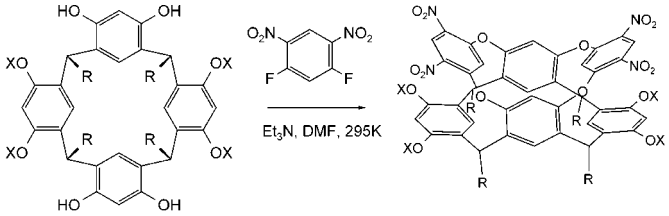
ABSTRACT



o-Alkylation of C_{2V}-symmetrical resorcinarene tetraesters 2 with 2 equiv of 1,3-difluoro-4,6-dinitrobenzene readily affords conformationally rigid octanitro resorcinarene 3, which is a potential scaffold for the design of supramolecular structures.

Calixarenes and resorcinarenes are readily available molecular platforms that have been successfully used for the synthesis of receptors as well as self-assembling structures such as capsules and boxes.[1] Especially promising are nitrated derivatives of calixarenes and cavitands as precursors of the corresponding amines to which various functional groups can be appended through acylations and alkylations of the amino groups. For instance, starting from tetranitrocalix[4]arene tetraethers,[2] calix[4]arenetetraurea derivatives were prepared that formed dimeric hydrogen-bonded capsules[3] and were powerful anion receptors.[4] On the other hand, the reduction and acylation of resorcinarene-based octanitrocavitands afforded self-folding molecular containers forming kinetically stable inclusion complexes with complementary neutral and charged organic guests.[5]

Herein we report a simple and efficient synthesis of novel type of rigid tetranitro derivatives of resorcinarenes **3** through bridging of the opposite hydroxy groups in tetrasubstituted derivatives **2** with 1,3-difluoro-4,6-dinitro-benzene.

Tetrasubstituted resorcinarenes of type **2** are easily prepared by selective acylation of the parent octols **1** with arylsulfonyl, dialkoxy phosphoryl, and benzoyl chlorides.[6] The structure of compounds **2** was established by NMR methods and single-crystal X-ray analysis. Namely, it was shown that C_{2V}-symmetrical resorcinarene tetraarylsulfonates adopt in the crystalline state the boat conformation in which the unsubstituted resorcinol rings are parallel while diacylated ones are nearly coplanar.[7] Molecular modeling (MMX force

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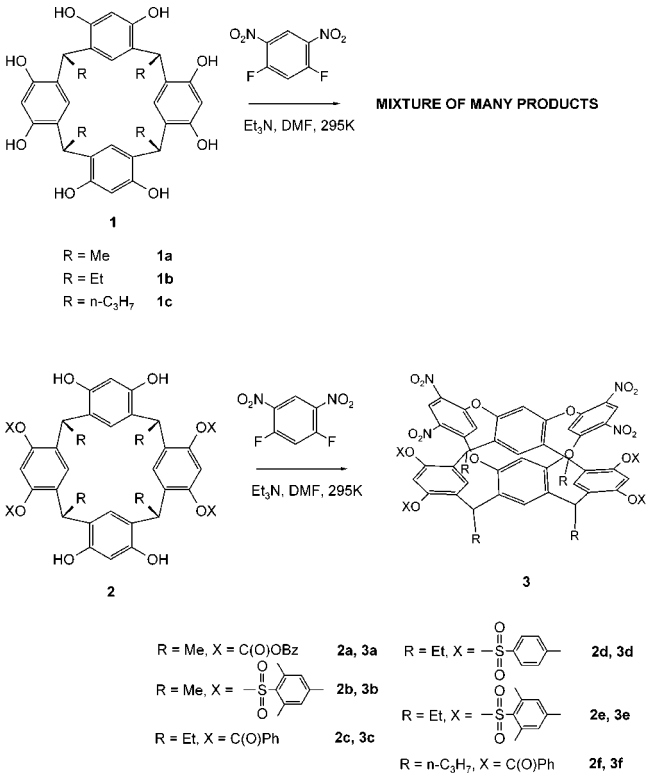
Scheme 1



field[8]) suggested that a meta-substituted benzene ring would be an ideal spacer for bridging the opposite hydroxy groups in such a conformation.[9]

Indeed, the reaction of resorcinarene tetraesters **2** with 2 equiv of the highly reactive 1,3-difluoro-3,5-dinitrobenzene in DMF in the presence of Et_3N as a base afforded bis-bridged tetranitro derivatives **3** in 66−89% yield.[10] Compounds **3** were purified by simple recrystallization and characterized by NMR spectroscopy and single-crystal X-ray analysis. The high yield of the bridging is caused by the high preorganization of the four hydroxy groups for the reaction, since the analogous reaction with resorcinarene octols resulted in an unseparable mixture of products that could not be characterized. The alkylation of **2** with 1 equiv of 1,3-difluoro-4,6-dinitrobenzene resulted in a 1:1 mixture of **3** and the starting material, with no trace of the mono-bridged compound being detected. The latter suggests that the introduction of one *m*-phenylene spacer facilitates the bridging of the remaining pair of the hydroxy groups. Unfortunately, all attempts for bridging opposite hydroxy groups of **2** by 2,6-dichloropyridine and 2,6-difluoropyridine (DMF, Et_3N, or *i*-Pr_2NEt) resulted only in the reisolation of the starting materials.

The ^1H NMR spectrum of resorcinarene tetramesityl sulfonate **2e** in $CDCl_3$ at 295 K contains one doublet of doublets for the methine protons of the bridges, four singlets for the protons of the resorcinol rings, one singlet for the aromatic protons of the mesityl rings, and a broadened singlet for the protons of the hydroxy groups (Figure 1a). The ^1H NMR spectrum of the parent doubly bridged derivative **3e** (Figure 1b) contains similar signals for the resorcarene signals while no resonance of hydroxy groups is observed. Two additional singlets appear at 8.68 and 4.73 ppm, which correspond to the protons of the 1,3-dinitrophenyl bridges, in ortho and meta positions to the nitro groups. The unusually high field chemical shift of the latter can be explained by the shielding effect of the resorcinol rings of the resorcinarene skeleton (see the X-ray structure in Figure 2). The ^1H NMR spectrum of **3e** did not change considerably upon decreasing the temperature to 233 K. This is in contrast to the parent tetrasulfonate **2e**, which exists at lower temperature as a hydrogen-bonded dimer of C_2-symmetrical conformers. The other compounds **3** exhibited ^1H NMR patterns and low-temperature behavior similar to those of **3e**.

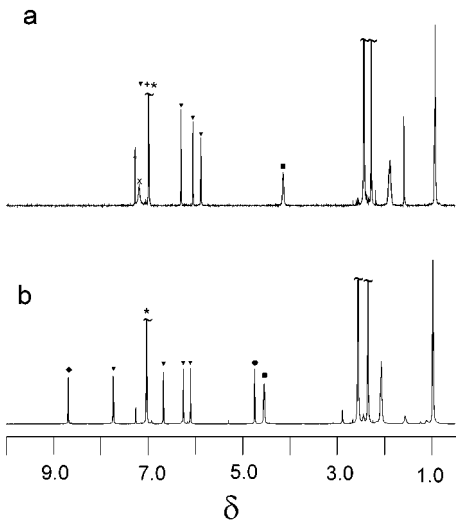


Figure 1. ^1H NMR spectra in $CDCl_3$ (295 K, 600 MHz): (a) tetrasulfonate **2e**; (b) bisbridged tetranitro derivative **3e**. (■) Methine protons of the bridges. (▼) Protons of the resorcinol rings. (∗) Aromatic protons of mesitylsulfonate fragments. (×) Protons of the hydroxy groups. (♦) Protons in positions ortho to the nitro groups. (●) Protons in positions meta to the nitro groups.

Very surprisingly standard MALDI-TOF and ES-MS techniques failed to give molecular peaks for compounds **3**. The addition of AgOTf to the samples also did not afford any interpretable mass spectra. The GPC analysis of a chloroform solution revealed that molecules **3** are monomeric. To acquire the absolute structural proof for the compounds **3**, single-crystal X-ray analysis was performed. Numerous attempts to grow diffraction quality crystals of **3** were hitherto unsuccessful. Finally, slow evaporation of the solution of **3f** in a three-component solvent system (MeOH/CH_2Cl_2/MeCN) gave transparent crystals, which despite their instability without the mother liquor and mechanical fragility, were suitable for X-ray crystallographic study.[11,12]

(8) PCMODEL is distributed by Serena Software, Dr. Kevin E. Gilbert, P.O. 3076, Bloomington, IN 47402.

(9) For bridging of resorcarene tetrasulfonates through the aminomethylation with suitable diamines, see: (a) Shivanyuk, A.; Schmidt, C.; Böhmer, V.; Paulus, E. F.; Lukin, O. V.; Vogt, W. *J. Am. Chem. Soc*. **1998**, *120*, 4319−4326. (b) Arnott, G.; Bulman Page, P. C.; Heaney, H.; Hunter, R.; Sampler, E. P. *Synlett* **2001**, 412−414.

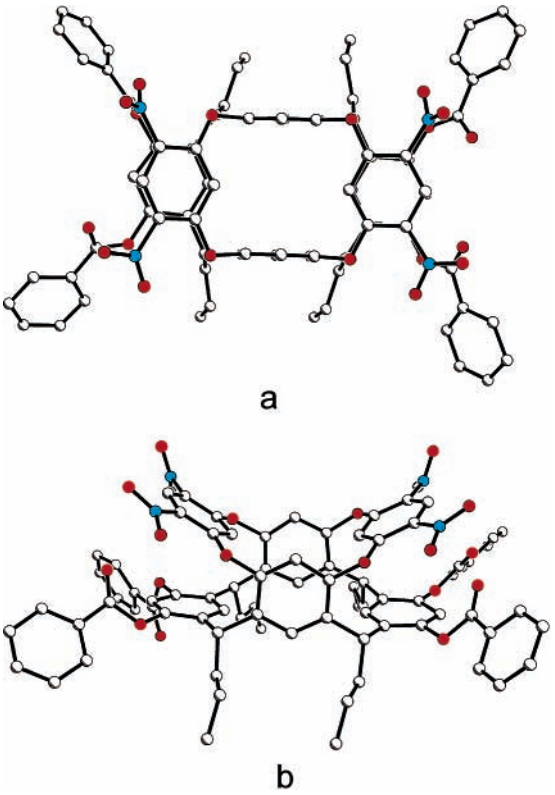


Figure 2. Single-crystal X-ray structure of compound **3f**: (a) top view; (b) side view.

In the crystalline state molecule **3f** has an initially anticipated monomeric structure. The resorcinarene skeleton adopts a boat conformation in which two acylated resorcinol rings are nearly parallel (dihedral angle 172.3°). Two *m*-dinitrophenyl rings bridge opposite parallel resorcinol rings (dihedral angle 7.1°) and assume with each other the dihedral angle of 145.8°. Thus, the two parallel resorcinol rings and two bridging *m*-dinitrophenyl rings form oxygen-bridged calix[4]arenes[13] in 1,3-alternate conformation.[14] The hydrogens in positions meta to the nitro groups are pointing toward the resorcinol rings of the resorcinarene skeleton. The distances between these protons and the centers of the unsubstituted resorcinol rings (3.0 Å) show that they should be subjected to strong magnetic shielding, in accordance with their corresponding upfield signals in the ^{1}H NMR spectra of compounds **3**. The dinitrophenyl rings in **3f** are nearly parallel to the diacylated resorcinol rings (dihedral angles 28.0° and 27.6°). The distances between the centers of these rings are 3.5 Å, suggesting probable intramolecular $\pi-\pi$ interactions. The three carbonyl groups of the benzoyl residues are pointing in the same direction toward the *m*-dinitrophenyl linkers. The distances between these electron-rich carbonyl oxygens and the positively charged nitrogens of the nitro groups are between 2.8 and 3.2 Å, suggesting intramolecular dipole−dipole attractions. Molecule **3f** has no intramolecular cavity, and the voids of the crystal are filled with severely disordered solvent that could not be identified from the electron density map. This disorder, added to the poor quality and instability of the crystal, are the main cause for the high final *R*-values.

In conclusion, C_{2V}-symmetrical tetraesters of resorcinarenes **2** are ideally preorganized for intramolecular bridging

(10) **General Procedure for Synthesis of 3.** Triethylamine (310 μL, 2.22 mmol) was added to a solution of tetraprotected resorcinarene **2** (1.86 × 10^{-4} mol) and 1,5-difluoro-2,4-dinitrobenzene (169 mg, 7.84 × 10^{-4} mol) in 6 mL of DMF. The mixture was stirred at room temperature for 15 h and was concentrated in vacuo. The residue was dissolved in the minimum amount of CH_2Cl_2 and was added to 30 mL of MeOH. The precipitate was filtered, washed with 3 × 15 mL of MeOH, and dried in vacuo, to give the desired product **3** as an amorphous powder. Compounds **3** were recrystallized from CH_2Cl_2/EtOH. **Tetranitroresorcinarenetetrabenzyl carbonate 3a.** Yield: 61%. White solid: mp 205−208 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 1.59 (d, J = 7.2 Hz, 12H), 4.71 (q, J = 7.2 Hz, 4H), 4.96 (s, 2H), 5.20 (d, J = 11.9 Hz, 4H), 5.25 (d, J = 11.9 Hz, 4H). 6.03 (s, 2H), 6.66 (s, 2H), 6.91 (s, 2H), 7.39 (m, 12H), 7.46 (d, J = 8.0 Hz, 8H), 7.79 (2H, s), 8.88 (2H, s). IR (KBr, disc, cm^{-1}): 1767, 1619, 1593, 1531, 1491, 1456. **Tetranitroresorcinarenetetramesitylsulfonate 3b.** Yield: 66%. Yellowish solid: mp 229−231 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 1.62 (d, J = 7.1 Hz, 12H), 2.33 (s, 12H), 2.53 (s, 24H), 4.63 (s, 2H), 4.78 (q, J = 7.1 Hz, 4H), 6.09 (s, 2H), 6.15 (s, 2H), 6.59 (s, 4H), 7.01 (s, 8H), 7.80 (s, 2H), 8.66 (s, 2H).^{13}C NMR (150 MHz, $CDCl_3$) δ 20.09, 21.63, 23.04, 32.26, 105.29, 117.26, 118.23, 126.94, 128.77, 129.77, 130.67, 131.36, 132.54, 136.74, 136.92, 140.44, 144.75, 145.96, 150.68, 155.36. IR (KBr, disc, cm^{-1}): 1619, 1602, 1534, 1489, 1399, 1354. **Tetranitroresorcinarenetetrabenzoate 3c.** Yield: 68%. Yellowish solid: mp 248−251 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.01 (t, J = 7.3 Hz, 12H), 2.05 (m, 4H), 2.19 (m, 4H), 4.55 (t, J = 7.6 Hz, 4H), 4.85 (s, 2H), 6.23 (s, 2H), 6.64 (s, 2H), 6.94 (s, 2H), 7.53 (t, J = 7.7 Hz, 8H), 7.65 (t, J = 7.5 Hz, 8H), 7.84 (s, 2H), 8.14 (d, J = 7.5 Hz, 8H), 8.91 (s, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 12.83, 27.87, 39.02, 105.60, 118.55, 118.74, 126.52, 128.86, 129.09, 129.30, 130.63, 131.25, 133.14, 134.57, 135.50, 147.45, 151.19, 155.68, 164.63. IR (KBr, disc, cm^{-1}): 1744, 1618, 1599, 1532, 1490. **Tetranitroresorcinarenetetratosylate 3d.** Yield: 83%. Yellowish solid: mp > 250 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 0.94 (t, J = 7.3 Hz, 12H), 1.93 (m, 4H), 2.02 (m, 4H), 2, 48 (s, 12H), 4.44 (dd, J = 5.2, 9.6 Hz, 4H), 4.61 (s, 2H), 6.04 (s, 2H), 6.49 (s, 2H), 6.62 (s, 2H), 7.43 (d, J = 8.3 Hz, 8H), 7.68 (s, 2H), 7.82 (d, J = 8.4 Hz, 2H), 8.70 (s, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 12.84, 22.26, 27.04, 38.92, 104.99, 115.70, 118.86, 126.01, 128.58, 129.31, 129.96, 130.74, 130.89, 133.10, 134.61, 134.92, 146.31, 146.57, 151.24, 155.39. IR (KBr, disc, cm^{-1}): 1618, 1597, 1534, 1489, 1354. **Tetranitroresorcinarenetetramesitylsulfonate 3e.** Yield: 69%. Yellowish solid: mp 210−215 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 0.96 (t, J = 7.2 Hz, 12H), 2.07 (quintet, J = 7.4 Hz, 8H), 2.33 (s, 12H), 2.55 (s, 24H), 4.53 (m, 4H), 4.73 (s, 2H), 6.08 (s, 2H), 6.25 (s, 2H), 6.64 (s, 2H), 7.01 (s, 8H), 7.72 (s, 2H), 8.68 (s, 2H). IR (KBr, disc, cm^{-1}): 1619, 1604, 1537, 1488, 1401. **Tetranitroresorcinarenetetrabenzoate 3f.** Yield: 89%. White solid: mp >250 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 0.89 (t, J = 7.3 Hz, 12H), 1.33 (m, 4H), 1.41 (m, 4H), 1.97 (m, 4H), 2.15 (m, 4H), 4.63 (t, J = 7.6 Hz, 4H), 4.87 (s, 2H), 6.21 (s, 2H), 6.65 (s, 2H), 6.89 (s, 2H), 7.53 (t, J = 7.9 Hz, 8H), 7.64 (t, J = 7.4 Hz, 4H), 7.81 (s, 2H), 8.14 (d, J = 7.3 Hz, 8H), 8.90 (s, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 14.56, 21.24, 36.78, 37.17, 105.53, 118.61, 118.81, 126.51, 128.83, 129.01, 129.50, 129.28, 130.63, 131.23, 133.55, 134.57, 133.30, 147.28, 151.19, 155.66, 164.69. IR (KBr, disc, cm^{-1}): 1745, 1619, 1600, 1532, 1490.

(11) Crystallographic measurement at 295(2) K by a SMART Bruker diffractometer, with CCD detector, Mo Kα radiation (graphite monochromator, λ = 0.7107 Å) capillary with mother liquor. Structure solution by direct methods, full-matrix refinement versus F^2. No absorption correction was applied. Peaks of disordered solvent were treated as oxygen atoms and refined isotropically. $C_{80}H_{80}N_4O_{20}$·disordered solvent, monoclinic, $P2_1/n$, a = 22.191(9) Å, b = 15.293(7) Å, c = 22.85(1) Å, β = 106.303(8)°, Z = 4, V = 7445(6) Å^3, ρ = 1.279 g cm^{-3}, μ = 0.094 cm^{-1}, $2\theta_{max}$ = 56.66°, R1 = 0.106, wR2 = 0.271 (for 3094 reflections $I > 2\sigma(I)$), R_1 = 0.3773, wR_2 = 0.415 (for 14829 independent reflections), 968 parameters, S = 0.865, $\Delta\rho$ (max/min) = 0.754/−0.22 eÅ^{-3}.

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(13) For a recent review, see: König, B.; Fonseca, M. H. *Eur. J. Inorg. Chem.* **2000**, 2303−2310.

(14) The reaction of resorcinol and 1,3-dichloro-4,6-dinitrobenzene in 1:1 ratio was reported to give corresponding oxygen-bridged calix[4]arene in low yield; however, no crystallographic studies were undertaken on that compound: (a) Sommer, N.; Staab, H. A. *Tetrahedron Lett.* **1966**, 2837−2841. (b) Lehmann, F. *Tetrahedron* **1974**, *30*, 727−733. (c) Boros, E. E.; Andrews, C. W.; Davis, A. O. *J. Org. Chem.* **1996**, *61*, 2553−2555. (d) Bottino, F.; Foti, S.; Pappalardo, S. *Tetrahedron* **1976**, *32*, 2567−2570.

of their hydroxy groups with *m*-phenyl spacers. A simple and high yield reaction of **2** with 1,3-difluoro-4,6-dinitrobenzene gives novel rigid molecular platforms **3** possessing nitro groups and four protected hydroxy groups in an unprecedented arrangement. The chemical versatility of nitro groups, coupled with the wide range of protecting acyl groups used, strongly suggests that compounds **3** are highly promising molecular platforms for the synthesis of novel supramolecular systems.

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Supporting Information Available: Crystallographic data for **3f** (in CIF format). This material is available free of charge via the Internet at http://pubs.acs.org.

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