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1,3,5-Cycloheptatrienyl Derivatives of Calix[4]- and Calix[6]arenes and their Corresponding Tropylium Salts

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Abstract: Tetrakis-(p-cycloheptatrienyl-7)calix[4]arene and hexakis-(p-cycloheptatrienyl-7)calix [6]arene have been synthesized. The oxidation affords calixarenes with four or six positively charged substituents at the upper rim. Whereas the cycloheptatrienyl substituent has little influence on the conformational flexibility of the macrocycle, the tropylium substituents reduce the interconversional barrier.

Calixarenes are a readily available and important class of macrocycles in supramolecular chemistry. Numerous potential applications of calixarene derivatives as specific ligands for cations, anions, and as a host of neutral compounds have been reported. [1,2,3]

In order to develop specifically acting receptors based on the calixarene architecture, lower and upper rim functionalization can be carried out. Whereas the substitution at the phenolic oxygen is easy to achieve, methods of direct modification at the upper rim are rare. Mostly, calixarenes protected at the lower rim were used.[4, 5]

Our particular interest was the direct introduction of a group at the upper rim which accomplishes the following tasks:

- a flexible conformation of the substituent itself in order to create a second clock on the NMR time scale beside the macrocycle itself,
- photoactivity in order to change the properties of the calixarene in response to light,
- reactivity at the upper rim, which could be suitable for further functionalization.

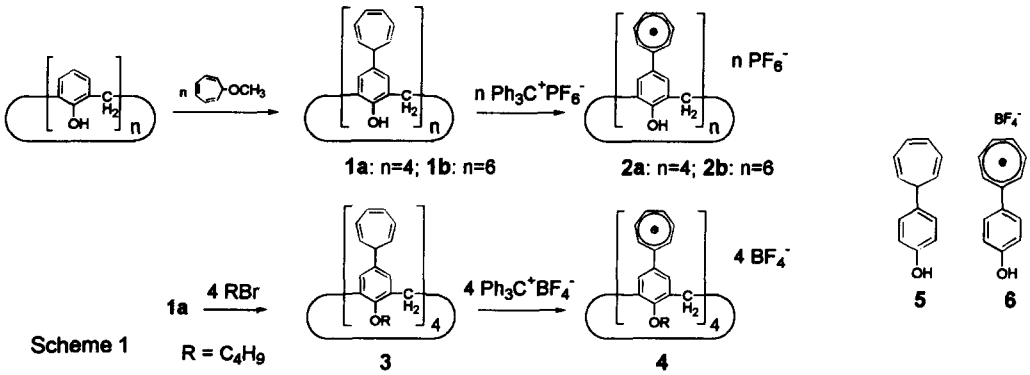
We have chosen the cyloheptatrienyl group as a substituent because:

- the ring inversion of the boat-shaped seven-membered ring can easily be followed by means of NMR spectroscopy,[6]
- the 1,7-hydrogen shift in the excited state of aryl cycloheptatrienes [7] might lead to drastical changes of the conformation at the upper rim of the macrocycle,
- the cyloheptatriene can easily be transformed into the tropylium substituent by thermal or photo-initiated oxidation, changing the electronic properties of the substituent and the colour of the macrocycle,[8,9]
- the tropylium substituent can be used for further derivatization of the calixarene by nucleophilic reactions.[10]

The synthetic approach is outlined in Scheme 1.[11]

According to the ^{1}H NMR spectra, **1** exhibits the interconversion of two cone conformations. Two broad

singlets for the $ArCH_2Ar$ protons are observed. The well-resolved doublet signals of the different protons of the methylene bridge at 3.2 and 4.6 ppm reveal that the cone conformation is immobilized by the butyl group in **3**, just as it is observed with other calix[4]arenes.[1] The cycloheptatrienyl substituent has no or only little influence on the conformational properties of the calixarenes.

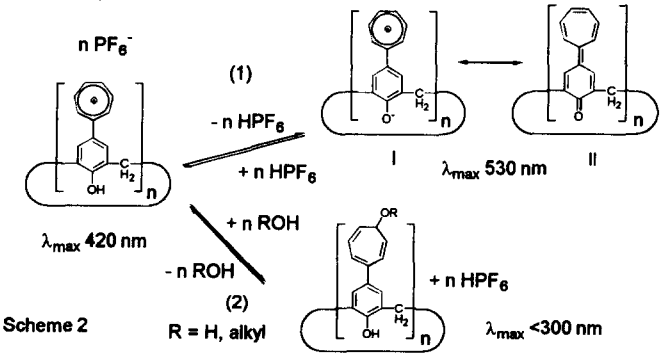


Scheme 1

An interesting aspect is the conformation of the cycloheptatriene ring. Usually, the interconversion of the boat conformers is very fast on the NMR time scale. Therefore, the NMR spectrum of **5** exhibits a well-resolved triplet for H_7. But in the calixarene derivative **1a**, the signal of the proton at the position 7 and also the other ring protons are relatively broad singlets. This indicates that the activation barrier of the ring conversion in the seven-membered ring is increased by binding at the macrocycle. In the immobilized cone structure of **3**, the cycloheptatriene ring exhibits resolved signals of the ring protons.

The transformation of the cycloheptatriene ring into the tropylium ring strongly influences the flexibility of the macrocyclic ring. The methylene bridge protons of **2a** and **2b** are no longer split into two signals but appear as one relatively sharp singlet indicating the fast interconversion of two cone conformations.

The conversion of **1** to **2** does not only alter the steric situation at the upper rim but should also strongly influence the acidity of the phenolic hydroxy group due to the electron acceptor properties of the tropylium substituent (equilibrium (1)). This reaction competes with the pseudo acid-base equilibrium (2) of the tropylium cation itself (scheme 2).[12]



Scheme 2

Equilibrium (1) is connected with a bathochromic shift of the absorption band (λ_{max} 435 nm in acetonitrile).[12] This shift can be attributed to the formation of a quinarenone I/II.[5,13] Accordingly, compound **4** does not show any pH dependent bathochromic shift. The two equilibria are dependent on the concentration of the tropylium salt in a different manner. It can be seen from Fig. 1 that the ratio of the quinarenone derivative to the tropylium salt is increased with decreased concentration of **2**. This holds true both in water and in alcohols, and demonstrates the acid strength of **2**. In contrast to **6**, **2** behaves as a weak elektrolyte in polar solvents. Equilibrium (1) predominates.

Also, adding of water to solutions of **2** in acetonitrile causes dissociation (Fig. 2).

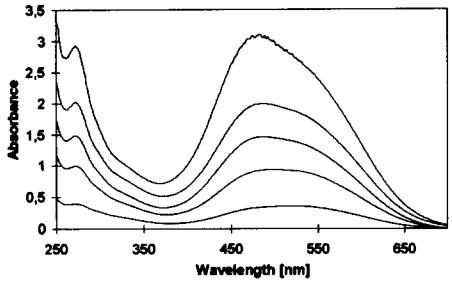


Fig. 1 **2b** in water solution at different concentration

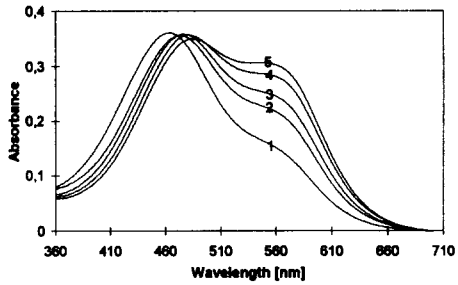


Fig. 2 Addition of water (mol/l) to a solution of **2b** in acetonitrile solution (1= 0; 2= 0.2; 3= 0.5;4= 0.9; 5= 1.3)

The stronger acidic and non nucleophilic 1,1,1,3,3,3-hexafluoropropan-2-ol (HFP) suppresses both the dissociation of the phenolic OH group and the solvent reaction. Therefore, the absorption spectra of the tropylium salts are not influenced by (1) or (2).

Surprisingly, urea is able to shift the long wavelength absorption band even in HFP (Fig. 3). This may be explained by the strong interaction of urea with the acidic OH groups of **2** leading to the dissociation of the OH groups.

Also, solvent molecules (toluene, ether, acetonitrile) are strongly complexed by **2a** and **2b**, respectively. This may explain the phenomenon, that a saturated solution of **2** can be used in order to make solutions of **2** in solvents such as water, toluene and dichloromethane in which the compounds itself are not soluble.

In conclusion, calixarenes with cycloheptatriene and tropylium substituents are easily prepared in a direct way. The new derivatives exhibit new interesting properties which may be useful for binding studies. Investigation of the new compounds as chromogenic hosts and of reactions of the tropylium substituent to increase the cavity of the macrocycle is currently in progress.

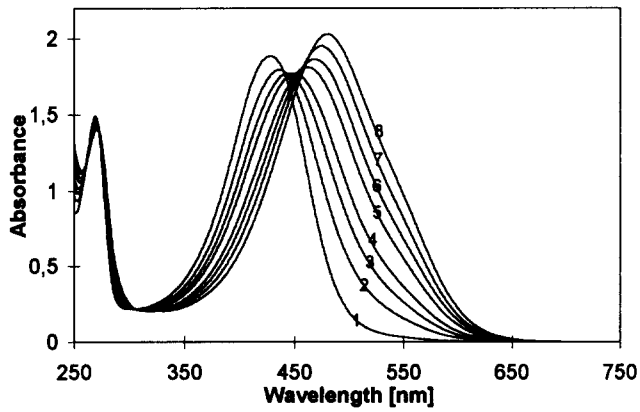


Fig. 3. Different concentrations of urea (x0.1 mol/l) added to a solution of **2b** in HFP (1= 0; 2= 0.2; 3= 0.5; 4= 0.8; 5=1.6; 6= 2.3; 7=3.5; 8=5.3)

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In memory of Prof. Dr. D. Cech, Berlin

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10. Kessler, H. Cycloheptatriene. In *Methoden der Organischen Chemie*, Vol V1d; Georg Thieme Verlag: Stuttgart, 1972, pp. 318 - 331.
11. *General:* For all new compounds satisfactory microanalysis were obtained. ^{1}H NMR, Bruker AM300, chemical shift in ppm (CHT= 1,3,5-cycloheptatrienyl; Tr= tropylium), UV-Vis, Shimadzu UV 2101PC. **1a**. 4H-calix[4]arene (0.1g, 0.24 mmol) and 7-methoxy-1,3,5-cycloheptatriene (0.19g, 1.6mmol) were dissolved in deaerated (argon bubbling) toluene (3 ml) . Three drops of acetic acid were added and the mixture was warmed at 50°C for 2 h. After stirring at room temperature for 20 h the solution was poured into methanol. The precipitated **1a** can be used for further reactions without purification. Purification was done by column chromatography (SiO_2, dichloromethane/hexane 1:1) affording pure **1a**. White powder. (0.11g; 60%). M.p.> 350°C. NMR (C_6D_6): 2.59(s, 4H, C_7H (CHT)); 3.22(br s, 4H, bridge CH_2); 4.26(br s, 4H, bridge CH_2); 5.03(m, 8H, C_1H, C_6H (CHT)); 5.99(m, 8H, C_2H, C_5H (CHT)); 6.50(m, 8H, C_3H, C_4H (CHT)); 6.79(s, 8H, Ar); 10.35(s, 4H, OH). **1b**. Same procedure than **1a**. 4H-calix[6]arene (0.5g, 8.8mmol) gave pure **1b** (0.86g, 91%). White powder. M.p.>350°C. NMR (C_6D_6): 2.83(br t, 6H, C_7H (CHT)); 3.81(br s, 12H, bridged CH_2); 5.35(m, 12H, C_1H, C_6H (CHT)); 6.10(m, 12H, C_2H, C_5H (CHT)); 6.59(m, 12H, C_3H, C_4H (CHT)); 7.08(s, 12H, Ar); 10.79(s, 6H, OH). **2a**. **1a** (0.16g, 0.2mmol) was dissolved in dichloromethane (5 ml). Trityl hexafluorophosphate (0.34g, 0.87 mmol) was added. The mixture was stirred for 10 h (rt), then 3h at 50°C. The precipitate was separated and washed with dichloromethane and ether yielding 0.15g (80%). Brown powder. Mp>350°C. NMR: (CD_3CN): 4.25 (br s, 8H, bridge CH_2); 8.00(s, 8H, Ar); 8.89(m, 16H, $C_{2,3,6,7}H$(Tr)); 9.21(m, 8H, $C_{4,5}H$(Tr)). **2b**. **2a** (0.2g, 0.17 mmol) in dichloromethane (200 ml) was treated with trityl hexafluorophosphate (0.44g, 1.1 mmol). Brown powder (0.32g, 91%). Mp>350°C. NMR(CD_3CN): 4,14(s, 12 H, bridged CH_2); 8.00(s, 12H, Ar); 8.74 (m, 24H, $C_{2,3,6,7}$(Tr); 9.29(m, 12 H, $C_{4,5}$(Tr). **3**. **1a** (0.1g, 0.13 mmol) and NaH (60% in oil) (0.3g, 7.5 mmol) was dissolved in DMF (10 ml). 1-Bromobutane (0.3g, 3mmol) was added. After 3 days at 70 °C the mixture was poured into methanol/water. By extracting with ether and purification by column chromatography (SiO_2, dichloromethane/hexane, 4:3) 0.17g (73%) pure **3** was obtained. White powder, Mp>360°C. NMR(C_6D_6): 1.01(t, 12H, CH_3); 1.43(m, 8H, CH_2); 2.01(m, 8H, CH_2); 2.78(br t, 4H, C_7H(CHT)); 3.20(br d, 4H, bridged CH_2); 4.61(br d, 4H, bridged CH_2); 5.32(m, 8H, C_1H, C_6H (CHT)); 6.10(m, 8H, C_2H, C_5H (CHT)); 6.55(m, 8H, C_3H, C_4H (CHT)); 6.89(s, 8H, Ar). ^{13}C-NMR(C_6D_6): 14.3 (C Bu^n); 19.7 (C Bu^n); 31.9 (bridged CH_2); 32.8 (C, Bu^n); 44.8 (C_7(CHT)); 75.4 (C, Bu^n); 124.6 ($C_{1,6}$(CHT)); 127.0 ($C_{2,5}$(CHT)); 131.1 ($C_{3,4}$(CHT)); 135.2 (3,5-Ar); 138.0 (4-Ar); **4**. **3** (0.05g, 0,05 mmol) were treated with trityl fluoroborate (0.08g, 0.25 mmol) in dichloromethane (5 ml). Brown powder (0.061g, 90%), Mp>360°C.NMR(CD_3CN): 1.06(t, 12H, CH_3); 1.56(m, 8H, CH_2); 2.00(m, 8H, CH_2); 3.62(br d, 4H, bridge CH_2); 4.18(t, 8H, CH_2); 4.68(br d, 4H, bridged CH_2); 7.52(s, 8H, Ar); 8.71(m, 16H, $C_{2,3,6,7}H$(Tr)); 8.89(m ($C_{4,5}$(Tr)).
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