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Phosphorylation of *p-tert*-Butylthiocalix[4]arene: Reaction with Phosphorus Trichloride.

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Abstract: The synthesis of the first phosphorylated derivatives of *p-tert*-butylthiocalix[4]arene was achieved by reaction with phosphorus trichloride. The product containing two cyclic P(III) atoms is not hydrolytically stable. The *flattened 1,2-alternate* conformation of a P(IV) derivative was established by ^{1}H, ^{13}C, ^{31}P NMR experiments and X-ray analysis. © 1999 Elsevier Science Ltd. All rights reserved.

In recent years supramolecular chemistry has been drawn to the calix[n]arenes due to their ability to act as pre-organizing complexing agents, carriers and potential biomimics as well as being able to undergo multiple functionalization.[1,2] The insertion of phosphorus containing moieties into calix[n]arenes allows extension of the possibilities for engineering of supramolecular systems.[3,4] We are currently studying the phosphorylation of thiocalix[4]arene **1**, which was recently synthesized in a satisfactory yield by the condensation of *tert*-butylphenol and sulfur under basic conditions at elevated temperatures.[5] Of course, the presence of the four sulfur atoms could bring new features into the chemical behavior of calixarenes.

In the present paper the first synthesis and structural analysis of phosphorylated thiocalix[4]arenes in the solution and crystalline state are reported. Phosphorus trichloride was chosen as the phosphorylation reagent because the P-Cl compounds are very useful starting materials for further transformations.

The phosphorylation of **1** by PCl_3 with the commonly used procedure (toluene, NEt_3 (excess), room temperature) yields a single product which shows an intense (100%) peak in the MALDI spectrum at m/z 848.[6] In the ^{31}P NMR spectrum of the reaction mixture one resonance at δ 170.2 is observed. This value is in the range for three-coordinate phosphorus. The comparison with the ^{31}P chemical shifts of model compounds **3a** (δ 168.4) and **3b** (δ 170.4)[7] suggest the formation of cyclic chlorophosphite **2** (Scheme 1). However, during attempts at isolation, **2** decomposed to give free *p-tert*-butylthiocalix[4]arene, as well as other unidentified products. So the product obtained is less hydrolytically stable than corresponding cyclic chlorophosphite of *p-tert*-butylcalix[4]arene.[8] The influence of a sulfur atom in the dioxathiophosphocin ring system may be responsible for such behavior (due to P-S interactions).

Using a slightly modified literature procedure [9] we reacted **1** with the excess of PCl_3 in *p*-bromotoluene without base at elevated temperatures.[10] After dilution of the reaction mixture with hexane, a colorless, crystalline precipitate was formed after 12 h (Scheme 1). These crystals were found to be a complex of

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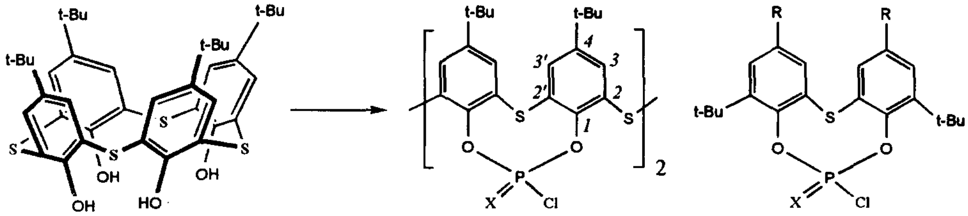
phosphorylated thiocalixarene **4** with *p*-bromotoluene (stoichiometry 2:1) according ^{1}H NMR and X-ray data. The formation of chlorophosphate **4** instead of the expected compound **2** indicates that the initially formed chlorophosphite readily undergoes oxidation by air.



1

2 X = lone pair
4 X= O

3a X = lone pair, R = Me
3b X = lone pair, R = t-Bu
5 X= O, R = Me

Scheme 1

The structure of **4** was established by ^{1}H NMR (the absence of an OH resonance), ^{31}P NMR and mass-spectrometry methods.[11] Such fully substituted macrocycles containing two phosphorus atoms in the rings can form a mixture of isomers due to different orientations of substituents at phosphorus. However, the ^{31}P NMR spectrum of **4** shows only one signal at δ -4.16 (^{31}P shift of model compound **5** is –9.49 ppm[7]), which indicates that only one isomer is formed. The conformation of the macrocycle in solution has been studied by ^{1}H and ^{13}C NMR. In fact, a few conformations for such *bis-(O,O-*phosphorus)-bridged compounds are possible: *cone, flattened cone, 1,2-alternate and flattened 1,2-alternate*. The ^{1}H NMR spectrum of **4** is more complicated than that of the parent macrocycle **1** which is in a *cone* conformation [12] and displays three singlets at δ 1.22 (*tert*-Bu), 7.64 (two aromatic protons) and 9.60 (OH).[5]

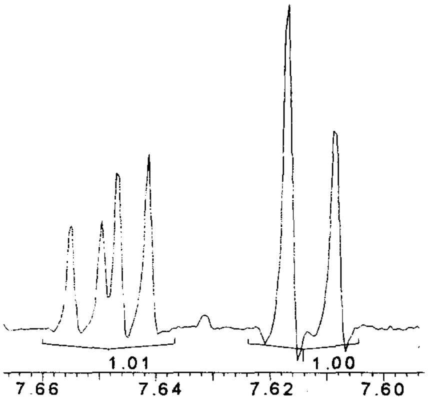


Figure 1. Portion of the ^{1}H NMR spectrum of **3** in CDCl$_3$. Coupling constant data: δ 7.613 ($^4J_{HH}$ = 2.5 Hz, $^5J_{PH}$ not observed), 7.648 ($^4J_{HH}$ = 2.5 Hz, $^5J_{PH}$ = 1.6 Hz).

In the product **4** the *tert*-butyl resonance is also a singlet at δ 1.37 while the aromatic protons appear as an AB spin system. So, the protons of the aromatic ring are not equivalent. Their resonances at δ 7.61 and 7.65 are two doublets ($^4J_{HH}$ = 2.5 Hz) and are shown on Figure 1. However, one of the doublets is additionally split to give a doublet of doublets due to phosphorus coupling with $^5J_{PH}$ = 1.6 Hz. These data indicate that product **4** adopts a *1,2-alternate* or *flattened 1,2-alternate* conformation in CDCl$_3$ solution. The ^{13}C{^{1}H} NMR spectrum also supports this conclusion. Carbon atoms 2 – 2′ as well as 3 – 3′ are inequivalent and appear as two singlets[11] in each case (numbering is shown on Scheme 1). The spectrum recorded without ^{1}H decoupling shows that C,H coupling constants are also different for both pairs of chemically equivalent carbon atoms. For example, C3 and C3′ atoms: $^1J_{CH}$ are 161.2 and 163.2 Hz, $^3J_{CH}$ are 8.0 and 8.6 Hz,[11] respectively.

The solid state structure of **4** has been elucidated by a single crystal X-ray crystallographic study.[13] The ORTEP structure of **4** is represented in Figure 2 together with numbering scheme of the asymmetric part. The shape of the calixarene platform deviates from an ideal *1,2-alternate* and may be defined as a centrosymmetrical *flattened 1,2-alternate* conformation, in which two diametrically opposite benzene rings are nearly parallel to the plane of the sulfur bridge atoms (main plane). This structure may also be rationalized as a (uo, u, do, d) conformation according Gutsche.[14] The dihedral angles from the main plane to the aromatic rings are 77.1 (plane 1, C2-C7), 13.0 (plane 2, C9-C14). The geometry of the phosphoryl groups of **4** are similar to that of ordinary phosphoryl compounds.[15] The average bond distances P1-O1, P1-O7, P1-O14, P1-Cl1 are 1.46(1), 1.57(1), 1.58(1), 1.972(6) Å, respectively. Bond angles at phosphorus atoms are in the range of 101-118°.

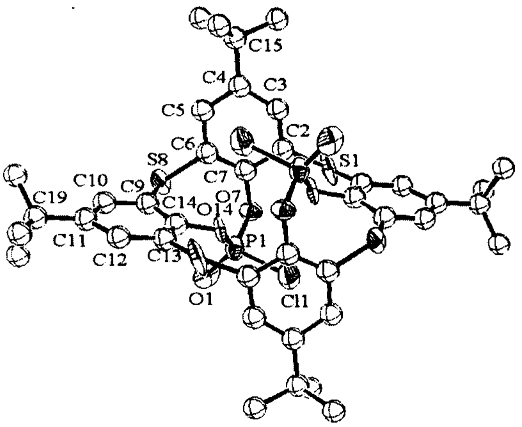


Figure 2. Crystalstructure of **4**. H atoms and the solvent molecule have been omitted.

The two eight-membered rings have a *twisted tub* conformation.[16] The atoms forming the floor of the tub (O14, C7, C6, C14) are coplanar within ±0.017 Å. Atoms P1, O7, S8, C9 are displaced from this plane in the same direction by distances of 1.239(5), 1.016(9), 1.235(4) and 0.58(1) Å, respectively. X-ray data indicates the existence of weak P-S interactions in **4** because P-S distance of 3.22(1) Å across these rings are shorter than the sum of the van der Waals radii for sulfur and phosphorus of 3.65 Å[17] and compares with 3.114-3.177 Å for dioxathiophospacin ring systems containing tertacoordinated phosphorus atoms (for example, **5**) in which such bonding interactions have been observed.[7] It should be also mentioned the interaction between the π-system of the benzene ring (C2 – C7) and the Cl1′ atom (distance between ring plane and chlorine atom is 3.22(1) Å).

In conclusion, the synthesis of the first phosphorylated thiocalix[4]arenes has been achieved. The solid state structural analysis revealed that **4** adopts *flattened 1,2-alternate* conformation. The rigidity of the molecular structure of compound **4** and spectral data obtained indicate the same conformation in solution.

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REFERENCES AND NOTES

1. (a) Gutsche, C.D. *Calixarenes*: Monographs in Supramolecular Chemistry Vol.1; Stoddart J.F. Ed., The Royal Society of Chemistry, Cambridge and London, 1989; (b) *Calixarenes. A versatile class of macrocyclic compounds.* (Eds. J.Vicent, V.Bohmer), Kluver, Dordrecht, 1991

2. Pochini, A.; Ungaro, R. *Comprehensive Supramolecular Chemistry, Vol. 2;* Atwood, J.L., Davies, J.E.D., MacNicol, D.D., Vögtle, F. Eds.; Pergamon: Oxford, 1996, 103-142.
3. Antipin, I.S.; Kazakova, E.Kh.; Habicher, W.D.; Konovalov, A.I. *Russian Chem. Rev.*, **1998**, *67*, 905-922.
4. (a) Neda, I.; Kaukorat, T.; Schmutzler, R.; *Main Grous Chemistry News.*, **1998**, *6*, 4-29; (b) Wieser, C.; Matt, D. *Platinum Metals Rev.*, **1998**, *42*, 11-16.
5. Kumagai, H.; Hasegava, M.; Miyanari, S.; Sugawa, S.; Sato, Y.; Hori, T.; Ueda, S.; Kamiyama, H.; Miyano, S. *Tetrahedron Lett.*, **1997**, *38*, 3971-3972.
6. *Synthesis of 2*: In an inert atmosphere, a stirred solution of **1** (0.36 g, 0.5 mmol) and triethylamine (0.242 g, 2.4 mmol) in toluene (10 mL) was treated dropwise with PCl_3 (0.138 g, 1.0 mmol). After stirring for 4 hr. at room temperature, the resulting reaction mixture shows one ^{31}P NMR resonance at δ 170.2 . MALDI m/z (%): 848 (100).
7. Sherlock, D.J.; Chandrasekaran, A.; Day, O.R.; Holmes, R.R. *Inorg.Chem.*, **1997**, *36*, 5082-5089.
8. Aleksiuk, O.; Grynszpan, F.; Biali. S.E. *J.Incl.Phen. Mol.Recogn*, **1994**, *19*, 237-256.
9. Mukmeneva, N.A.; Kadirova, V.Kh.; Zharkova, V.M.; Cherkasova, O.A. *J. Obshch. Khim.*, **1986**, *56*, 2267-2271.
10. *Synthesis of 4*: In typical procedure, a mixture of *p-tert*-butylthiocalix[4]arene (0.5 g, 0.69 mmol) and PCl_3 (0.4g, 2.9 mmol) in 15 ml of *p*-bromotoluene (or *p*-chlorotoluene) was stirred at 80°C for 1 hr in an inert atmosphere. The stirred mixture was then heated gradually to 180°C over period of 3 hr and kept at this temperature for a further 1 hr. The resulting product was cooled to 50°C and the excess of PCl_3 was removed *in vacuo*. A reaction mixture was diluted with hexane and a colorless, crystalline precipitate (0.3 g, 49%) was formed after 12 h. These crystals were found to be a complex of phosphorylated thiocalixarene **4** with *p*-bromotoluene (stoichiometry 2:1) as confirmed by spectral and X-ray data.
11. *Compound 4:* MS m/z (%): 880 (40) $[M^+]$, 845 (35) $[M^+ - Cl]$, 810 (32) $[M^+ - 2Cl]$; IR(KBr) 1305 cm^{-1} (P=O); ^1H NMR ($CDCl_3$, 300 MHz) δ 1.37 (36H, s), 7.61 (4H, d, $^4J_{HH}$ = 2.5 Hz) and 7.65 (4H, dd, $^4J_{HH}$ = 2.5 Hz, $^5J_{PH}$ = 1.6 Hz); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 31.3 ($C(\underline{C}H_3)_3$, $^1J_{CH}$ = 126.0 Hz, $^3J_{CH}$ = 5.0 Hz), 35.0 ($\underline{C}(CH_3)_3$, $^2J_{CH}$ = 4.0 Hz), 124.5 (C2(ar), $^3J_{PC}$ = 4.2 Hz), 125.2 (C2′(ar), $^3J_{PC}$ = 8.0 Hz), 132.2 (C3(ar), $^1J_{CH}$ = 161.2 Hz, $^3J_{CH}$ = 8.0 Hz), 132.2 (C3′(ar), $^1J_{CH}$ = 163.2 Hz, $^3J_{CH}$ = 8.6 Hz), 150.6 (C4(ar)), 150.9 (C1(ar), $^2J_{PC}$ = 10.6 Hz); ^{31}P NMR ($CDCl_3$, 162.0 MHz) δ - 4.16.
12. Acdas,Y.; Bringel, L.; Graf E.; Hosseini M.W.; Mislin G.; Pansanel, J.; Cian A.; Fischer J. *Tetrahedron Lett.*, **1998**, *39*, 2311-2314.
13. *X-ray analysis of 4:* $C_{40}H_{44}Cl_2O_6P_2S_4$ $0.5C_7H_7Br$, M = 1051.5 g mol^{-1}, colourless crystals. crystal size 0.1x0.2x0.3 mm, a = 9.821(2)Å, b = 10.538(4)Å, c = 12.166(4) Å, α = 93.46(3)°, ß = 97.94(2)°, γ = 96.56(2)°, V = 1235.2(6)$Å^3$, d_{calc}= 1.414 g cm^{-3}, Z = 1, μ = 11.52 cm $^{-1}$, T= 293°K, triclinic, space group P-1, Enraf-Nonius CAD4 diffractometer, ,MoK_α radiation, λ = 0.73073Å, scan mode ω-2θ, θ <26.3°, 8505 independent reflections, 1356 of which with $F>3\sigma(F)$, structure solved by direct methods (SIR-92, Altomare A., Cascarano G., Giacovazzo C., Viterbo D. Acta Cryst. **1991**, A47, P.744-748). The structural parameters (all non-carbon atoms anisotropic, all others isotropic) refined in a full-matrix technique with MolEN package (Straver L.H., Schierbeek A.J. MolEN. Structure Determination System. Vol.1. Program Description. Nonius B.V.1994. 180p.). Methyl and bromo groups of *p*-bromotoluene and *tert*-butyl groups were disordered and modelled in terms of two sets of disordered sites with equal occupancies. Hydrogen atoms were found from expected geometry and were not refined. The final value of R = 0.0767, R_ω=0.0879. Atomic coordinates and e.s.d.'s have been deposited at the Cambridge Crystallographic Data Centre.
14. Kanamatareddy,S.; Gutsche,C.D. *J.Am.Chem.Soc.*, **1993**, *115*, 6572-6579.
15. Corbridge, D.E.C. The structural chemistry of phosphorus. Amsterdam – London – N.Y.: Elsevier , 1974, 518p.
16. (a) Prakasha, T.K.; Day, O.R.; Holmes, R.R. *Inorg.Chem.*, **1994**, *33*, 93-98; (b) Holmes, R.R. *Chem.Rev*, **1996**, *96*, 927-950.
17. Bondi, A. *J.Chem.Phys.*, **1964**, *68*, 441-458.