Threefold Bridged *p-tert*-Butylcalix[9]arene Triphosphate[‡]

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Dedicated to Prof. Dr. Hans Gross on the occasion of his 75th birthday

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p-tert-Butylcalix[9]arene **1** reacts with phosphorus pentachloride and then with water to give the *p-tert*-butylcalix[9]arene triphosphate **5**, representing the first bridged calix[9]arene derivative to be described in the literature.

Introduction

As part of an ongoing program directed towards the preparation of phosphorus-functionalized polyphenol derivatives, we have explored the reaction of PCl_5 with various calix[*n*]arenes. Most of these reactions resulted in the formation of chlorophosphonium salts and chlorophosphoranes that could be readily converted into the corresponding phosphates.

During the last decade many phosphorus-containing calixarenes have been described.[2] They are of particular interest for the complexation of cations, especially the cations of the f-block elements.[3] Recent work by our group includes the synthesis of calix[*n*]arene phosphates with n = 4, 6, and 8, as well as thiacalix[4]arene.[4−7] These compounds have phosphoryl units that act either as μ_2- or μ_3-bridges between phenolic oxygen atoms of the macrocyclic framework (cyclic and bicyclic phosphates) or simply behave as pendant $P(O)(OR)_2$ moieties (acyclic phosphates). Here we report on the synthesis of the first calix[9]arene that contains three bridged phosphoryl groups. Until now calix[9]arene phosphates and bridged calix[9]arene derivatives were unknown.

Results and Discussion

Reaction of *p-tert*-butylcalix[9]arene **1** (which is readily available[8,9]), with 6 equiv. of phosphorus pentachloride in dichloromethane yielded a reaction mixture for which the ^{31}P NMR spectrum showed several peaks. The main peaks at δ = 11.4, 10.6, and −298 ppm fell in the same region as those from the analogous products obtained from the smaller calixarenes. These are characteristic for the tris(aryloxy)chlorophosphonium unit,[4−6] indicating the presence of this kind of structure in the reaction solution.

The hydrolysis of the phosphonium salt was effected with concentrated hydrochloric acid on the unpurified intermediate, leading to a bridged calix[9]arene triphosphate in 63% yield.

The elemental analysis, molecular weight, and HPLC characteristics of the hydrolysis product were in accordance with those expected for a triphosphate. The ^{31}P NMR spectrum of this product in $CDCl_3$ solution shows a sharp peak at δ = −22.3 ppm and a broad peak at δ = −19.7 ppm (see Figure 1). The peaks for the methylene, *tert*-butyl and phe-

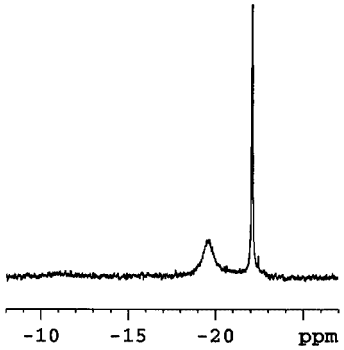

Figure 1. ^{31}P NMR spectrum of **5** in $CDCl_3$

[‡] Reaction of Phenols and Polyphenols with PCl_5, 14. Part 13: Ref.[1]

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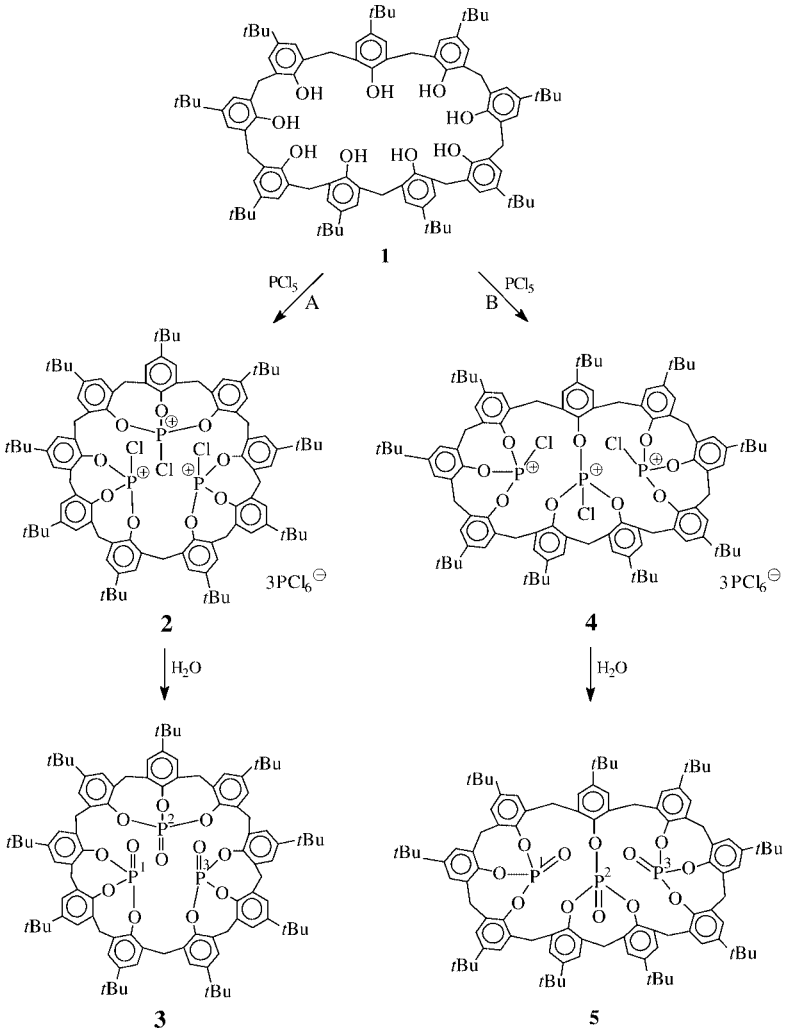

Scheme 1

nyl groups in the ^{1}H and ^{13}C NMR spectra (taken in $CDCl_3$) are very broad; therefore an accurate assignment was impossible.

This reaction can lead to two different *p-tert*-butylcalix[9]-arene triphosphates **3** and **5**. In the first case (Scheme 1, Route A), PCl_5 attacks the three neighbouring OH groups in **1** in a stepwise fashion, yielding the tris(phosphonium) salt **2**, which upon hydrolysis gives the phosphate **3**. Alternatively (Scheme 1, Route B), PCl_5 attacks the two triads of OH groups on the sides of the molecule first, and then the central OH groups, yielding the tris(phosphonium) salt **4**, which upon hydrolysis gives the phosphate **5**.

There should be only one peak in the ^{31}P NMR spectrum of **3** because the three P atoms are identical. In contrast, two peaks should be observed in the ^{31}P NMR spectrum for **5** because the central P atom (P^2) is in a different environment from the other two P atoms (P^1 and P^3). This led us to the conclusion that the product we had isolated was **5**, confirming that Route B must be favoured over Route A, and that the starting compound **1** prefers the "pleated loop" conformation.[10]

It is known that cyclic calixarene phosphates are dynamic systems.[11,12] The aromatic rings can exchange their positions from the "up" position to the "in" position and from the "down" position to the "in" position and vice versa.[13] This dynamic behaviour for the phosphate **5** should lead to an equilibrium between **5′**, **5′′**, and **5′′′** (Figure 2).[14]

The exchange of the residues which are connected to the central P atom (P^2) is probably faster than the corresponding exchange for the residues bonded to the other P atoms.

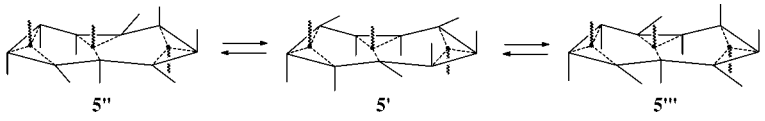

Figure 2. Dynamic behaviour of **5**

This behaviour could explain why, in the ^{31}P NMR spectrum, the peaks for the P^1 and P^3 atoms are broad, whereas the peak for the P^2 atom is sharp.

The triphosphate **5** can also exist in three conformations (**5A**, **5B**, and **5C**), as shown in Figure 3.[14]

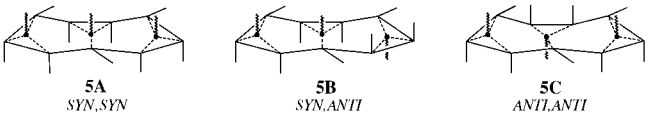

Figure 3. Conformers of **5**

The terms *SYN* and *ANTI* correspond to the position of the P=O groups in the molecule; the pivot group is the P^1=O group. This nomenclature was first introduced for the conformers of *p-tert*-butylcalix[8]arene triphosphate.[6]

A precise structure for **5** cannot be given, because it was not possible to obtain single crystals for X-ray studies from the white powder. It might, however, be possible to obtain a crystal structure on complexation of the phosphate groups with a cation.

It has been reported that the δ values for the P atoms in the ^{31}P NMR spectra of calixarene phosphates are shifted differently when a shift reagent is added.[15] The magnitude of the shift (dependent on the attack of the europium ion on the P=O group), has a range of about 100 ppm. No shift is observed when the attack of the europium ion is hindered by bulky residues.

When [Eu(FOD)$_3$] was added to the solution of triphosphate **5**, we observed in the ^{31}P NMR spectrum three broad peaks (at δ = −17.8, −38.3, and −55.4 ppm), in a ratio of 1:1:1 (see Figure 4).

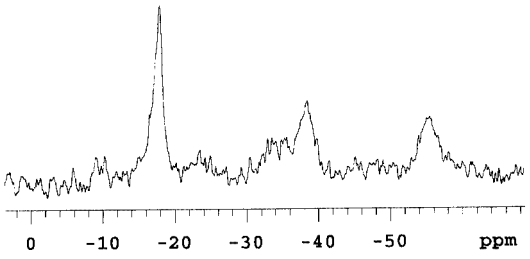

Figure 4. ^{31}P NMR spectrum of **5** in $CDCl_3$ with Eu(FOD)$_3$

We postulate that only the P^1=O and P^3=O groups interact with the shift reagent, resulting in the peaks at δ = −38.3 and −55.4 ppm. The peak at δ = −17.8 ppm would therefore correspond to the P^2 atom. It is probable that the europium ion attacks the P=O groups on the top and bottom faces, but is prevented from attacking the P^2=O group because it is blocked by the aromatic residues and by the already complexed Eu species, as shown in Figure 5.

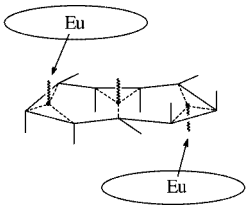

Figure 5. Possible structure of the complex from **5** with Eu(FOD)$_3$

If this is the case, the preferred conformation of the *p-tert*-butylcalix[9]arene triphosphate **5** ought to be the *SYN,ANTI* conformation (**5B**).

Conclusion

Compound **5** is the first calix[9]arene derivative with three intramolecular bridges involving all nine oxygen atoms of the macrocyclic system.

Experimental Section

General: The ^{31}P NMR spectra were recorded with a Varian Mercury 200 spectrometer (81.014 MHz). The ^1H and ^{13}C NMR spectra were recorded with a Bruker DRX 400 spectrometer. The mass spectrum was recorded with a Micromass Autospec instrument. Solvents were dried with activated molecular sieves (4 Å).

***p-tert*-Butylcalix[9]arene Triphosphate 5:** A solution of **1** (438 mg, 0.3 mmol) and phosphorus pentachloride (375 mg, 1.8 mmol) in dry dichloromethane (15 mL) was heated under reflux for 30 min. The solvent was removed by evaporation, and the residue was treated with concentrated HCl (15 mL) and dioxane (5 mL). The resulting solution was heated under reflux for 2 h. The precipitated solid was removed by filtration, washed with hexane (15 mL), purified by column chromatography (silica; $CHCl_3$/MeOH, 100:1), and recrystallized from $CHCl_3$/MeOH to yield **5** (300 mg, 63%). M.p. > 450 °C (dec.). $C_{99}H_{117}O_{12}P_3$ (1591.93): C 74.69, H 7.41, P 5.84, found C 74.67, H 7.39, P 5.78; HPLC (Lichrospher, Si 60; $CHCl_3$/hexane, 6:4); flow rate: 1 mL/min, retention time: 2.6 min. MS (FAB): *m/z* = 1591 $[M + 1]^+$. ^{31}P NMR ($CHCl_3$, 23 °C): δ = −19.7 (broad), −22.3 (sharp) ppm.

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[14] Conversion of the full formula of **5′** to a short form, see Figure 6.

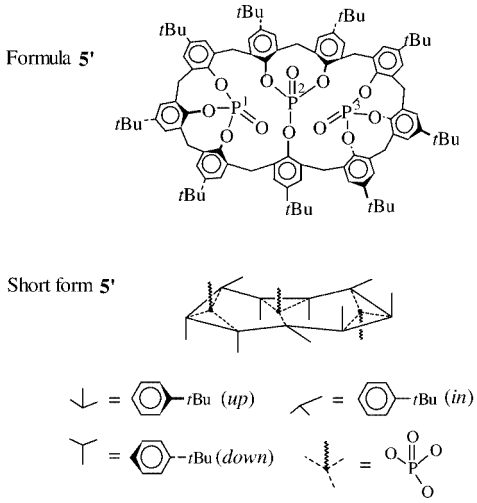

Figure 6. Conversion of the full formula of **5′** to a short form

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