Phosphorus Polybridged Calixarenes

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Vacuum pyrolysis of the dialkylphosphate esters of p-tert-butylcalix[4]arene and p-tert-butylcalix[6]arene results in phosphorus polybridged systems which display dynamic processes.

The synthetic hosts p-tert-butylcalix[4]arene 1 and p-tert-butylcalix[6]arene 2 are conformationally flexible cyclic condensation products of phenol and formaldehyde which are capable of including small molecules into their cavities.[1] In order to preorganize the host it is usually desirable to freeze the calixarene in a conformation suitable for complexation. This goal can be accomplished by derivatization of the OH groups to yield bulky ethers or esters[2] or by covalently linking ('bridging') the aryl rings at their extraannular or intraannular positions by a single atom or a chain of atoms.[3,4] Calix[4]arene systems covalently bonded to a single nonmetallic bridging atom (e.g. 3) were reported in the literature.[5] In this

communication we report the preparation and dynamic processes of *multiple* phosphorus-bridged calixarenes.

Poly(dialkylphosphate) ester derivatives of calixarenes are useful intermediates for the preparation of OH-depleted calixarenes[6] and aminocalixarenes.[7] Pyrolysis of these compounds results in multiple bridges. Heating the bis(diethyl-phosphate ester) calixarene derivative 4[6b] at 230 °C under vacuum for 35 min resulted in the formation of the pyrophosphate 5 (35% yield) in which two phosphorus atoms are each bridging two proximal phenoxy groups, and in the regeneration of 1, formed by cleavage of the phosphate ester groups. The yield of the reaction could be raised to 61% by using the

1; R¹ = R² = OH
4; R¹ = OPO(OEt)₂, R² = OH
6; R¹ = OPO(OPrⁱ)₂, R² = OH

2

X = P(H)NHMe₂

3

5

7

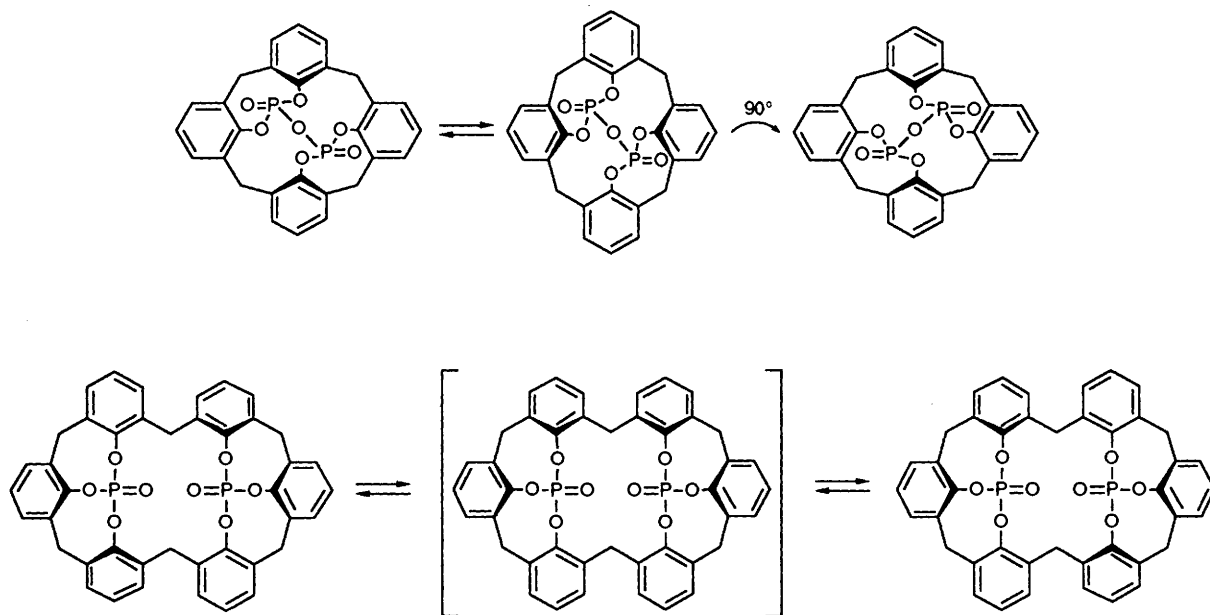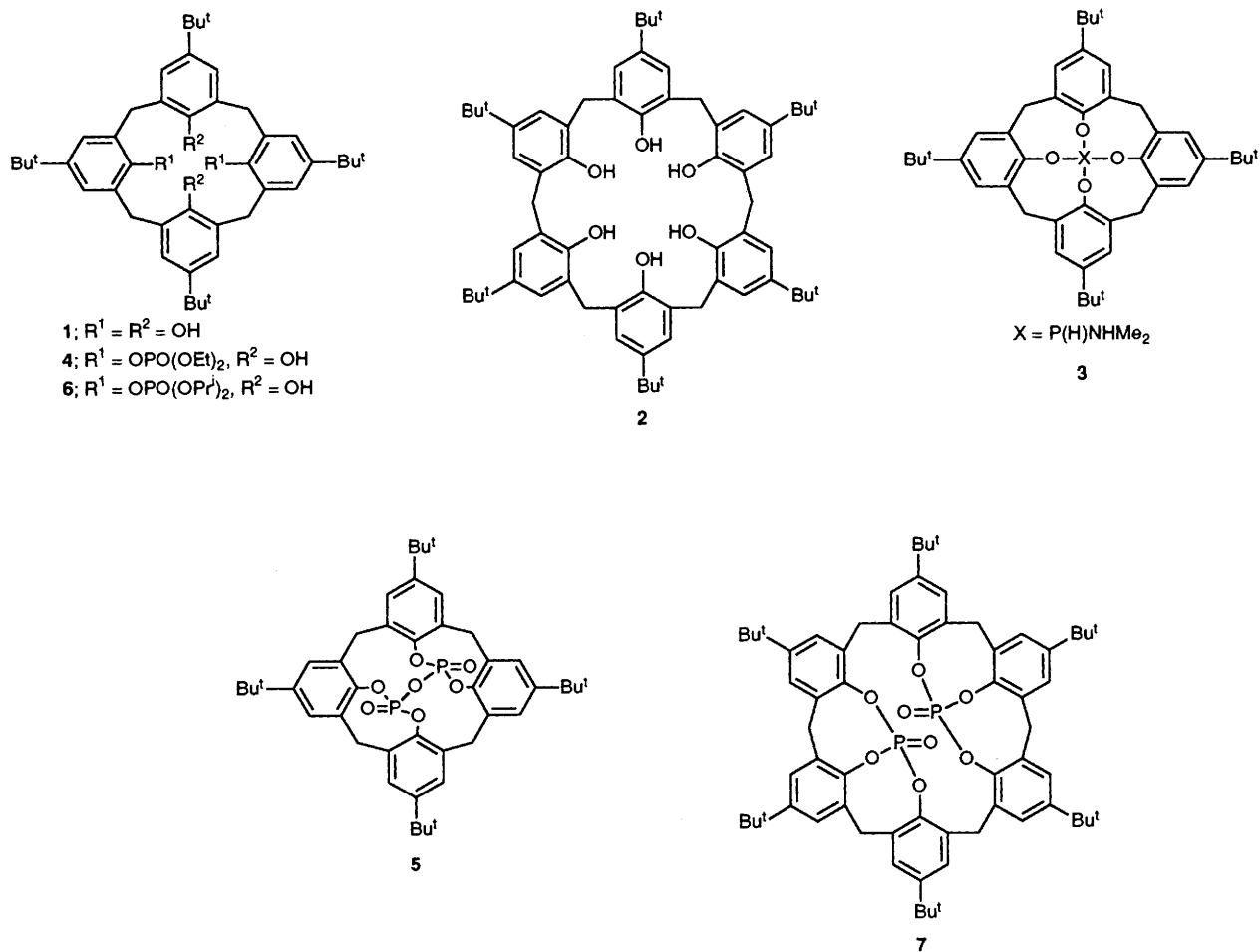**Fig. 1** The dynamic process (flattened cone ⇌ flattened cone interconversion) present in **5** (top) and **7** (bottom). *tert*-Butyl groups are ommited for clarity. Both processes result in enantiomerization. In the case of **5** (top) the structure resulting from the interconversion is rotated by 90° in order to show the enantiomeric relationship with the starting conformation.
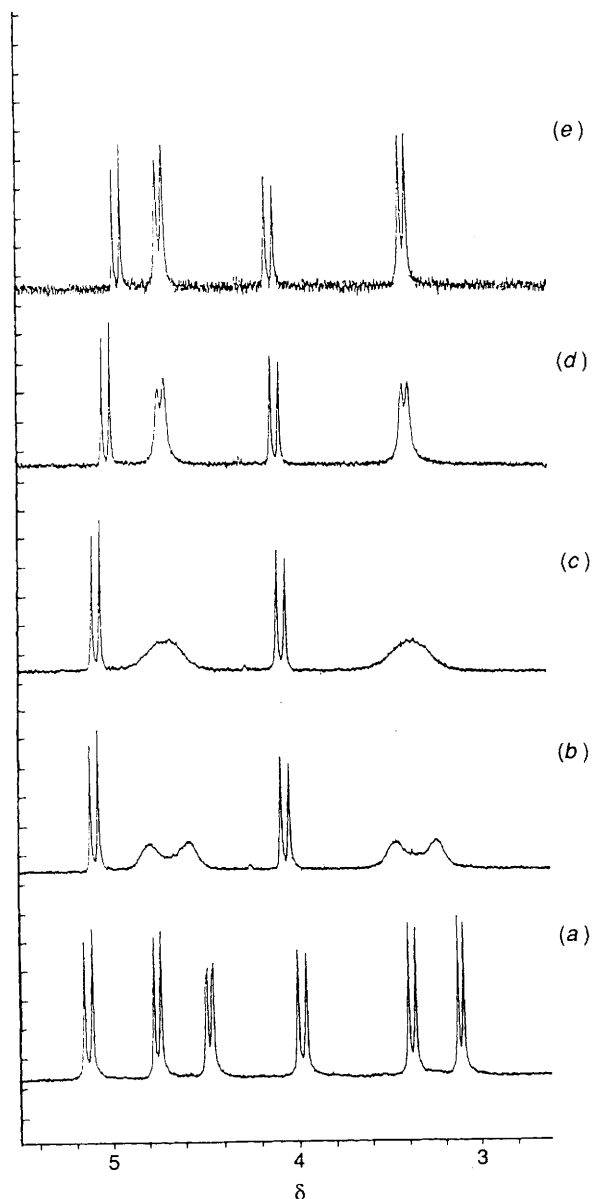
Fig. 2 400 MHz ^{1}H NMR spectrum of the methylene region of **7** in CD$_3$C$_6$D$_5$ at (a) 250; (b) 295; (c) 303; (d) 330; (e) 350 K.

bis(diisopropylphosphate ester) derivative **6**.† When **5** was dissolved in MeOH or EtOH, peaks at m/z 785.9 ([M − H + MeOH]$^-$) and 799.8 ([M − H + EtOH]$^-$) were observed in the fast atom bombardment (FAB) mass spectra, probably resulting from the addition of the alcohols to the central P–O bond. Compound **5** displays a ^{31}P NMR signal (δ −22.3) which is shifted ca. 16 ppm with regard to the starting material **4** with nonbridging phosphate ester groups (δ −6.4). The bridged calixarene **5** displays in the NMR spectrum at room temperature (400 MHz, CD$_2$Cl$_2$) one tert-butyl signal, two AB systems for the methylene protons and two mutually coupled signals for the aromatic protons. Lowering the temperature of the

NMR sample resulted in broadening and decoalescence of the tert-butyl and aromatic signals while the methylene protons remained unchanged and at 203 K two Bu^t and four aromatic signals are observed. The low temperature NMR is in agreement with a chiral 'flattened cone' (fc) conformation of C_2 symmetry (also called 'boat' or 'pinched cone' form)[1,8] where two distal rings are nearly coplanar with the main macrocyclic plane and the other two rings are twisted with regard to that plane (Fig. 1). From the frequency difference under slow exchange and the coalescence temperatures for the tert-butyl ($\Delta v = 68.5$ Hz, $T_c = 212$ K) and the two pairs of aromatic signals ($\Delta v = 56.1$ Hz, $T_c = 209$ K; $\Delta v = 109.7$ Hz, $T_c = 217$ K) a barrier of 10.1 ± 0.1 kcal mol^{-1} (1 cal = 4.184 J) was calculated for the dynamic process.‡ The process followed by NMR is most likely a fc $\rightleftharpoons$ fc interconversion[8] which can be achieved by rotating the rings about the Ar–CH$_2$ bonds and exchanges the 'twisted' and 'coplanar' rings but without concomitant ring inversion, since the pyrophosphate moiety does not pass through the ring cavity. This fc $\rightleftharpoons$ fc interconversion results in enantiomerization of the system (Fig. 1).

In order to attempt the multiple bridging of a calix[6]arene we treated **2** with ClPO(OEt)$_2$ according to the procedure of Markovsky et al.[9] and heated the isolated product under vacuum to 330 °C for 1.5 h yielding **7** in 47% yield. The multiple bridged system **7** can be viewed as having two subunits, each formed by three proximal phenolic oxygens bridged by a phosphorus atom. The compound displays a single singlet in the ^{31}P NMR spectrum at δ − 22.4. The 400 MHz ^{1}H NMR spectrum of the compound in CD$_3$C$_6$D$_5$ at 295 K displays one sharp and two broad tert-butyl signals and two sharp and four broad doublets in the methylene region (Fig. 2). Lowering the temperature resulted in sharpening of the broad signals and six sharp doublets and three sharp singlets were observed at 250 K for the methylene and tert-butyl groups, respectively. In principle several stereoisomers are possible for the molecule depending on the conformation adopted by the three rings attached to the phosphorus, on the orientation of the PO moieties [towards the cavity (endo) **8** or away from it (exo) **9**] and on the mutual orientation of the two subunits (syn **10** or anti **11**). The low temperature NMR pattern is compatible only with a structure of C_2 symmetry in which the C_2 axis is perpendicular to the main macrocyclic plane, and therefore both subunits must be syn and the two P–O moieties must be both endo or exo. X-Ray diffraction data of a single crystal of **7** grown in MeCN shows that the calixarene crystallizes in a conformation of approximate C_2 symmetry with five MeCN molecules.§ Both subunits exist in a conformation in which two rings are twisted with regards to the macrocyclic plane while the third ring is nearly coplanar to it (a 'flattened cone') (Figs. 3 and 4). The two 'flattened cone' subunits of the macrocycle are syn to each other with the PO bonds exo oriented. Interestingly, for the titanium bridging complex of **2** the conformation of the subunits is more markedly cone-like.[10]

Raising the temperature resulted in coalescence of the two pairs of broad doublets and at 350 K four doublets (in a 1:2:1:2 ratio) were observed (Fig. 2). A barrier of 14.4 kcal mol^{-1} was calculated for the dynamic process.‡ The

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† The phosphate ester **5** was prepared in 25% yield by bubbling NH$_3$ through a toluene solution of **1** and ClPO(OPr^i)$_2$. The chlorophosphate was prepared according to the literature procedure (H. McCombie. B. C. Saunders and G. J. Stacey, *J. Chem. Soc.*, 1945, 380).

‡ The exchange rates at the coalescence temperatures were calculated using the Gutowsky–Holm approximation (H. S. Gutowsky and C. H. Holm, *J. Chem. Phys.*, 1956, **25**, 1228).

§ *Crystal data*: C$_{66}$H$_{78}$P$_2$O$_8$·5MeCN, space group P$\bar{1}$, $a = 15.110(7)$, $b = 19.435(10)$, $c = 14.192(2)$ Å, $\alpha = 102.11(4)$, $\beta = 106.35(3)$, $\gamma = 89.84(5)$°; $V = 3903(1)$ Å^3, $Z = 2$, $D_c = 1.08$ g cm^{-3}, μ(Cu-Kα) = 9.01 cm^{-1}, no. of unique reflections: 9632, no of reflections with $I > 3\sigma(I)$: 6931, $R = 0.073$, $R_w = 0.104$. Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See Notice to Authors, Issue No. 1.

Fig. 3 Top view and numbering scheme of the molecular structure of **7**. The acetonitrile molecules are omitted for clarity. The torsional angles (°) between the planes of the phenyl rings and the least-squares plane of the four methylene carbons C(42), C(7), C(14) and C(21) are for C(1)–C(6): 4.5, C(8)–C(13): 64.4, C(15)–C(20): 52.8. The torsional angles (°) with the plane defined by C(21), C(28), C(35) and C(42) are C(22)–C(27): 2.7, C(29)–C(34): 60.2, C(36)–C(41): 54.5°.

Fig. 4 Stereoscopic representation of the side view of **7**

dynamic process which exchanges the two sets of methylene groups can be ascribed to a fc ⇌ fc interconversion, which as in the case of **5**, leads to enantiomerization of the molecule (Fig. 1, bottom). In each subunit the 'twisted' and 'coplanar' rings vicinal to the methylene groups which join the two subunits rotate and exchange their identities, the 'coplanar' ring becoming 'twisted' and *vice versa*. In order to enantiomerize the molecule the two subunits must undergo the fc ⇌ fc interconversion, but it seems likely that the process is a stepwise and not a simultaneous interconversion of the two subunits. Since the dynamic processes present in **5** and **7** do not involve ring inversion, the methylene protons of a given methylene unit remain diastereotopic even under fast exchange conditions.

We thank Dr Shmuel Cohen for the X-ray structural determination and the Mass Spectrometry Center at the

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