Available online at www.sciencedirect.com
ScienceDirect
Mendeleev Commun., 2010, **20**, 359–360
Mendeleev Communications

Phosphorus-bridged calixarene phosphites: dramatic influence of a *tert*-butyl group at the upper rim of the macrocycle upon anion binding

**Ivan I. Stoikov,* Olga A. Mostovaya, Lyudmila S. Yakimova,
Alena A. Yantemirova, Igor S. Antipin and Alexander I. Konovalov**

*A. M. Butlerov Chemical Institute, Kazan University, 420008 Kazan, Russian Federation.
Fax: +7 8432 315 416; e-mail: Ivan.Stoikov@ksu.ru*

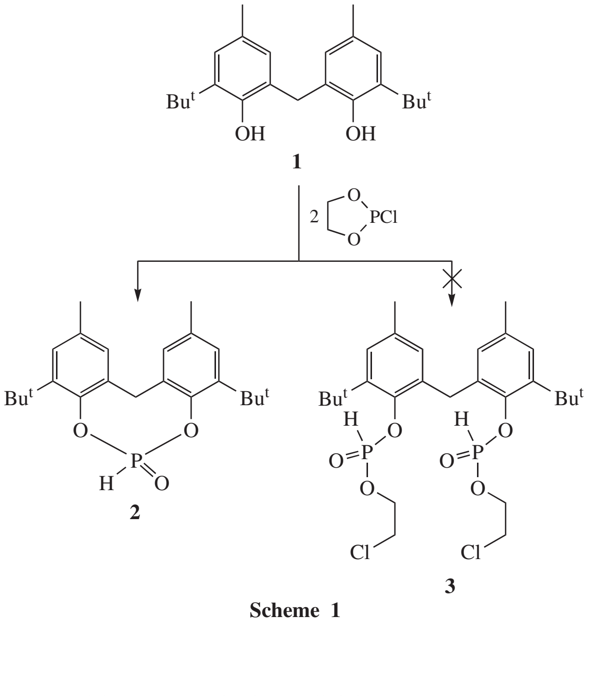
DOI: 10.1016/j.mencom.2010.11.021

New cyclic phosphite derivatives of calix[4]arenes in 1,2-*alternate* configuration were obtained by the interaction of calix[4]arenes with ethylene chlorophosphite; the influence of a *tert*-butyl group at the upper rim of the macrocycle upon anion binding was shown.

Calix[4]arenes are plenty favorable molecular platforms for the creation of three-dimensional structures with different sizes of intramolecular cavities, number, type and spatial orientation of binding sites, abilities to formation of asymmetric cavities and equilibrium change between receptor rigidity and flexibility.[1,2] Therefore, calix[4]arene derivatives are used for binding various small molecules and ions.[3–5]

Functionalization of phenol groups, aromatic and bridged fragments in calixarenes by corresponding organophosphorus reagents dramatically changes the effectiveness and selectivity of binding ions and neutral organic molecules.[6,7] The introduction of two α-aminophosphonate fragments in 1,3-positions at the upper and lower rims of a calix[4]arene platform was shown[8] to lead to a change in their complexing properties toward aromatic α-amino acids in comparison with their acyclic analogues.

The proton-donating ability of phosphonoyl groups and their reduced self-association ability make organophosphorus compounds the promising effective receptors and anion carriers.[7] Thus, it was interesting to prepare new substituted at the lower rim calix[4]arenes, containing phosphonoyl groups, and to study their complexing ability toward anions.



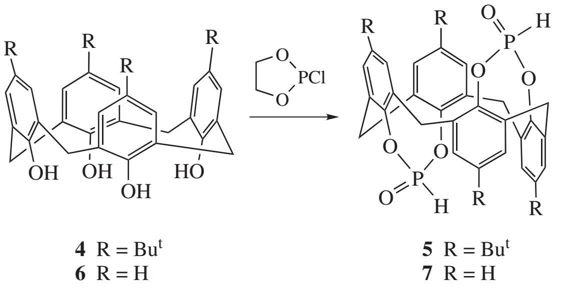
Scheme 1

We used the reaction of bis- and tetrakis-phenols with ethylene chlorophosphite (ECP). It is known that the reaction of this compound with phenol affords the phenyl ester of 2-chloroethylphosphorous acid.[9] We carried out the reaction of bisphenol with ECP in a 1:2 molar ratio. However, cyclic phosphite **2** was obtained instead of expected bis(hydrogenphosphite) **3** (Scheme 1). According to reported data,[10] a part of the phosphorylation reagent can be spent for secondary reaction – polymerization, so we employed a fourfold excess of ECP in reaction with bisphenol **1**. However, in this case, phosphite **2** was isolated in 96% yield.[†]

Apparently, formation of compound **2** results from intramolecular transesterification of the vicinal hydroxyl group in originally formed monophosphorylated derivative. Note that using ECP as phosphorylating reagent has advantages in comparison with the known synthesis of similar compounds by interaction with PCl_3.[11]

Treatment of *p*-*tert*-butylcalix[4]arene **4** with ECP (a 1:4 ratio) under similar conditions gave a high-melting crystalline compound after 6 h in 82% yield. To confirm the formation of compound **5** (Scheme 2), NMR and IR spectroscopy and mass spectrometry were used. ^{31}P NMR spectrum of **5** in $CDCl_3$ shows only one signal at –0.4 ppm ($^1J_{PH}$ 779.3 Hz).

The presence of two doublets (3.59 and 4.47 ppm, AB spin system, $^2J_{HH}$ 14.9 Hz) and a singlet at 4.12 ppm, which correspond to the methylene bridge protons of calix[4]arene in ^{1}H NMR spectrum, clearly indicate the 1,2-*alternate* conformation of calix[4]arene **5**. That was also confirmed by the appearance of two signals at 31.4 ppm in its ^{13}C NMR spectrum.[12]



Scheme 2

[†] For preparation procedure and characteristics of 2-*H*-5,15-di(*tert*-butyl)-7,13-dimethyl-2-oxodibenzo[*d*,*g*]-1,3,2-dioxaphosphocin **2**, see Online Supplementary Materials.

The reaction of *p-tert*-butylcalix[4]arene **4** with a tenfold excess of a phosphorylating reagent, as in the case of model bisphenol **1**, did not lead to the formation of other products or yield change. Obviously, in the synthesis of compound **5**, one molecule of ECP interacts with two phenolic groups. When we used a **4**:ECP molar ratio of 1:2, the yield of **5** was 100%. Apparently, if an excess of ethylene chlorophosphite is applied, part of the product is lost during recrystallization.

Published data show that phosphorylated calix[4]arenes usually have *cone* and *partial cone* conformations.[13–17] Evidently, the formation of 1,2-*alternate* conformation in the case of cyclic phosphate derivative **5** results from both less steric hindrance between the phosphoryl groups and its greater thermodynamic stability, taking into account that the interaction occurs at a high temperature (150 °C). The formation of cyclic phosphites apparently proceeds through an intramolecular transesterification with β-chloroethanol elimination, that was confirmed by gas chromatography–mass spectrometry. Analysis of the chromatogram of the reaction mixture resulting in the typical total ion current plot showed that the amount of this compound ($M^{+\cdot}$ 80) is twice as much that of initial calixarene. Distance between the reaction centres (phenolic groups) and conformational flexibility or geometric preorganization of the macrocyclic structure play a central role in the transesterification reaction. Therefore, we studied the reaction of ECP with calix[4]arenes **6** without *tert*-butyl groups at the upper rim. Under similar reaction conditions with a reagent ratio of 1:2, initial macrocycle **6** was isolated quantitatively from the reaction mixture. However, using a fourfold excess of ECP led to compound **7** in 62% yield (Scheme 2).[‡]

Characteristic signals of methylene protons as AB spin system ($^2J_{\mathrm{HH}}$ 15.4 Hz) and singlet in the ^{1}H NMR spectrum evidence the 1,2-*alternate* conformation of calixarene **7**. This structure is also confirmed by ^{13}C NMR data (the methylene bridge atoms of calixarene appear as two signals at 31.7 and 34.8 ppm).

The lower yield of product **7**, in comparison with that of calix[4]arene **5**, is most likely due to increase in the conformational lability of the macrocycle and reduction of spatial preorganization of the structure[18] reacting with ECP. The presence of bulky *tert*-butyl substituents at the upper rim of a calixarene platform in compound **4**, due to mutual steric hindrance, leads to a conformationally more rigid structure, thus creating a geometric preorganization to interact with ECP.

The receptor ability of the 1,2-*alternate* stereoisomers toward various anions [spherical (F^-, Cl^-, Br^-, I^-), Y-shaped (AcO^-), trigonal (NO_3^-) and tetrahedral ($H_2PO_4^-$)] was evaluated by ^{1}H and ^{31}P NMR and UV spectroscopies for studying the influence of structural factors (the presence of cyclic phosphite fragment and *tert*-butyl group at the upper rim of the macrocycle) on the complexation properties of synthesized macrocycles **5** and **7**.

The absorption spectra of compounds **5** and **7** in the presence of a 100-fold excess of tetrabutylammonium salts in chloroform were recorded. The significant changes in ^{1}H, ^{31}P NMR and UV spectra of macrocycle **7** were observed only in the presence of Bu_4NF, Bu_4NOAc and $Bu_4NH_2PO_4$. Thus, the hyperchromic effect and bathochromic shift were detected in the UV spectra of host **7** (Figure 1). The downfield shift of signals due to phosphorus atoms by 1–2 ppm occurred in the ^{31}P NMR spectra for complexes of macrocycle **7** with Bu_4NX ($X = F^-$, AcO^-, $H_2PO_4^-$), whereas the chemical shifts of tetrabutylammonium protons in the ^{1}H NMR spectra do not change. There were no changes in the spectra of *p-tert*-butylcalix[4]arene **5** recorded in the presence of these tetrabutylammonium salts. This fact indicates that interaction does not take place. Obviously, the *tert*-butyl substituent at the upper rim of calix[4]arene shields the phosphoryl group, that prevents from the binding between macrocycle **5** and anions.

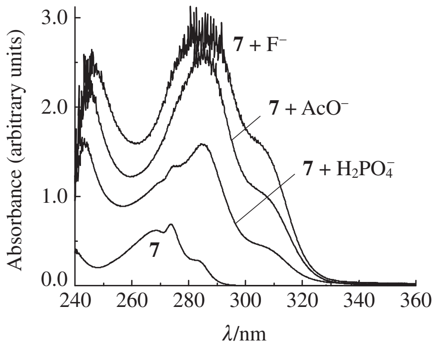


Figure 1 Changes in the UV absorption spectra of compound **7** upon addition of Bu_4NX ($X = F^-$, AcO^-, $H_2PO_4^-$) salts ($CHCl_3$, [**7**] = 2.5×10^{-4} mol dm^{-3}, [Bu_4NX] = 2.5×10^{-2} mol dm^{-3}).

Thus, the study of the reaction of ECP with calix[4]arenes unsubstituted at the lower rim showed that high temperature (≥ 150 °C) conditions favor the formation of organophosphorus derivatives in the 1,2-*alternate* conformations. The dramatic influence of the *tert*-butyl group at the upper rim of the synthesized macrocycles upon anion (F^-, AcO^-, $H_2PO_4^-$) binding was demonstrated.

This study was supported by the Russian Foundation for Basic Research (project no. 09-03-00426) and a programme of the Russian Federation President grants for the State Support of Young Russian Scientists (MD-2747.2010.3).

Online Supplementary Materials

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.mencom.2010.11.021.

References

1 Z. Asfari, V. Bohmer, J. Harrowfield, J. Vicens and M. Saadioui, *Calixarenes 2001*, Kluwer Academic Publishers, Dordrecht, Boston, London, 2001.
2 A. I. Konovalov and I. S. Antipin, *Mendeleev Commun.*, 2008, **18**, 229.
3 C. Seel, A. Galan and J. deMendoza, *Top. Curr. Chem.*, 1995, **175**, 101.
4 J. Scheerder, J. F. J. Engbersen, A. Casnati, R. Ungaro and D. N. Reinhoudt, *J. Org. Chem.*, 1995, **60**, 6448.
5 A. Casnati, *Gazz. Chim. Ital.*, 1997, **127**, 637.
6 *Analogue-based Drug Discovery*, eds. J. Fischer and C. R. Ganellin, Wiley-VCH, 2006.
7 I. I. Stoikov, S. A. Repejkov, I. S. Antipin and A. I. Konovalov, *Heteroat. Chem.*, 2000, **11**, 7, 518.
8 I. S. Antipin, I. I. Stoikov, E. M. Pinkhassik, N. A. Fitseva, I. Stibor and A. I. Konovalov, *Tetrahedron Lett.*, 1997, **38**, 5865.
9 V. V. Kormachev and M. S. Fedoseev, *Preparativnaya khimiya phosphora* (*Preparative Chemistry of Phosphorus*), UrO RAN, Perm, 1992 (in Russian).
10 E. E. Nifantiev, *Khimiya hydrophosphoril'nykh soedinenii* (*Chemistry of Hydrophosphoryl Compounds*), Nauka, Moscow, 1983 (in Russian).
11 R. R. Holmes, D. J. Sherlock, A. Chandrasekaran and R. O. Day, *Inorg. Chem.*, 1997, **36**, 5082.
12 C. Jaime, J. de Mendoza, P. Prados, P. M. Nieto and C. Sanchez, *J. Org. Chem.*, 1991, **56**, 3372.
13 I. Neda, T. Kaukorat and R. Schmutzler, *Main Groups Chem. News*, 1998, **6**, 4.
14 C. Wieser-Jeunesse, D. Matt, M. R. Yaftian, M. Burgard and J. M. Harrowfield, *C. R. Acad. Sci. Paris, Ser. II*, 1998, 479.
15 I. S. Antipin, E. Kh. Kazakova, W. D. Habicher and A. I. Konovalov, *Usp. Khim.*, 1998, **67**, 995 (*Russ. Chem. Rev.*, 1998, **67**, 905).
16 J. Gloede, *Phosphorus Sulfur Silicon Relat. Elem.*, 1997, **127**, 97.
17 S. Cherenok and V. Kalchenko, *Top Heterocycl. Chem.*, 2009, **20**, 229.
18 V. Bohmer, *Angew. Chem., Int. Ed. Engl.*, 1995, **34**, 713.

Received: 30th April 2010; Com. 10/3517

[‡] For preparation procedure and characteristics of compounds **5** and **7**, see Online Supplementary Materials.