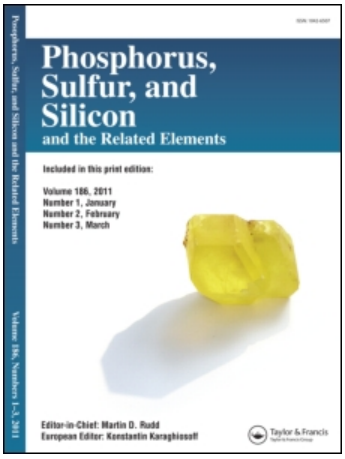


Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

Chiral Phosphorus-Contained Calixarenes

S. O. Cherenok[a]; V. I. Boyko[a]; A. V. Yakovenko[a]; V. I. Kalchenko[a]
[a] Institute of Organic Chemistry, National Academy of Sciences of Ukraine, Kyiv, Ukraine

To cite this Article Cherenok, S. O. , Boyko, V. I. , Yakovenko, A. V. and Kalchenko, V. I.(2008) 'Chiral Phosphorus-Contained Calixarenes', Phosphorus, Sulfur, and Silicon and the Related Elements, 183: 2, 431 — 434
To link to this Article: DOI: 10.1080/10426500701735510
URL: http://dx.doi.org/10.1080/10426500701735510

Phosphorus, Sulfur, and Silicon, 183:431–434, 2008

ISSN: 1042-6507 print / 1563-5325 online
DOI: 10.1080/10426500701735510

Taylor & Francis
Taylor & Francis Group

Chiral Phosphorus-Contained Calixarenes

S. O. Cherenok, V. I. Boyko, A. V. Yakovenko, and V. I. Kalchenko
Institute of Organic Chemistry, National Academy of Sciences of Ukraine, Kyiv, Ukraine

Synthesis and some properties of the three-dimensional calixarene molecules functionalized with chiral aminophosphonic or hydroxyphosphonic acid residues as well as inherently chiral calixarenes are discussed. The calixarene aminophosphonic acids show inhibitory activity toward porcine kidney alkaline phosphatase that strongly depends on the absolute configuration of the α-carbon atoms.

Keywords Aminophosphonic acids; calixarenes; chiral resolution; phosphatase inhibition; stereoselective synthesis

INTRODUCTION

Calixarnes are macrocyclic compounds for design of synthetic receptors in bioorganic and supramolecular chemistry. Incorporation of phosphorus-containing binding groups onto the macrocyclic platform enables supramolecular interactions to be defined a priori, having broad ramifications for chemistry, physics, biology, and material science. In this article, we present some recent achievements in design, synthesis, and properties of phosphorus-containing chiral calixarenes having three-dimensional molecular cavities, within the context of molecular recognition and bioactivity; as well as approaches to the synthesis and optical resolution of enantiomerically pure inherently chiral calixarenes.

Phosphorus-Containing Calixarenes with a Chiral Center

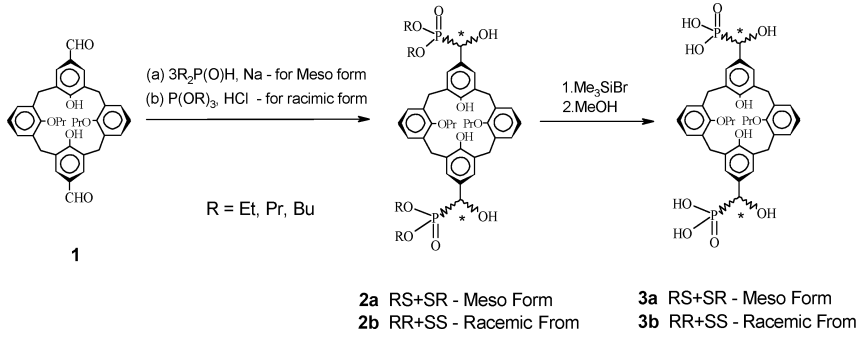
Two types of phosphorus-containing chiral calixarenes were discussed 1) compounds functionalized with chiral substituents;[1,2] and e2) calixarenes having chirality induced by the asymmetric arrangement

This work was partially supported by STCU (grant No 3594).

Address correspondence to V. I. Kalchenko, Institute of Organic Chemistry, National Academy of Sciences of Ukraine 02094, Kyiv-94, Ukraine. E-mail: vik@bpci.kiev.ua

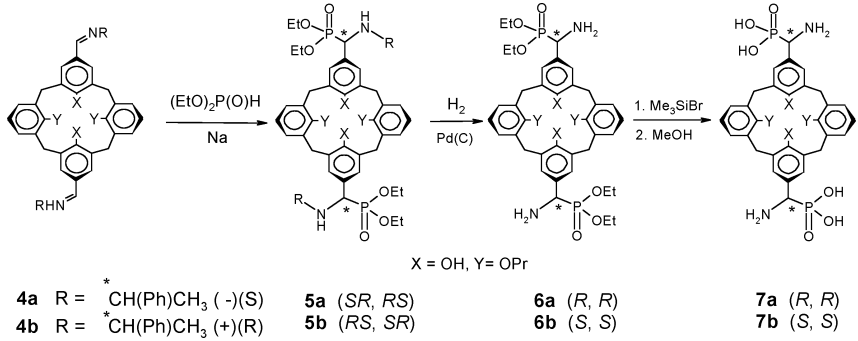
of achiral (or chiral) substituents at the wide/narrow rim of the macrocycle.[3,4]

Using the method developed, we synthesized calix[4]arene bis-α-hydroxyphosphonic acids as pure *Meso* **3a** and *Racemic* **3b** forms via the cleavage of appropriate esters **2a**, **b** obtained by the reactions of diformylcalixarene **1** with thrialkylphosphites or sodium dialkylphosphites.[1]



SCHEME 1

Chiral esters of calix[4]arene α-alkylaminophosphonic acids **5a**, **b** were obtained via the diastereoselective Pudovik-type addition of sodium diethylphosphites to the chiral calixarene imines **4a**, **b**. Further hydrogenolysis and hydrolysis resulted in α-aminophosphonic acids **7a**, **b** with high yields.[2]



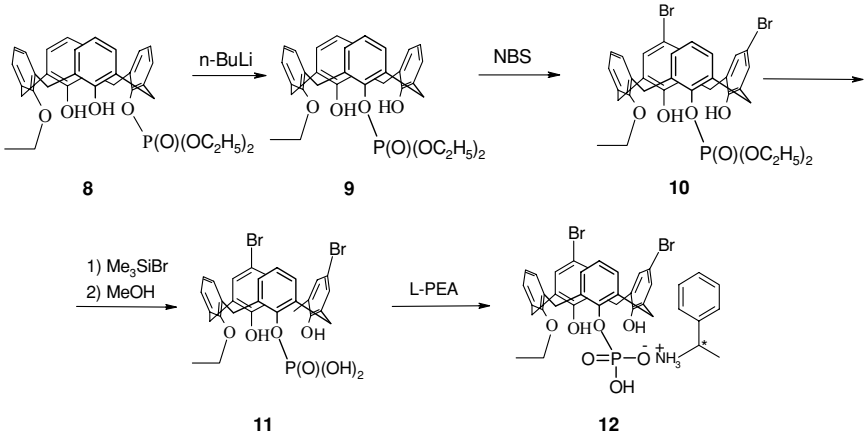
SCHEME 2

Pure *Racemic* form binds amino acids more strongly in methanol, compared with the *Meso* form.[1] The calixarene aminophosphonic acids show inhibitory activity toward porcine kidney alkaline phosphatase that strongly depends on the absolute configuration of the α-carbon atoms. In fact, *R*, *R* form of bis-aminophosphonic acid is the most effective inhibitor of alkaline phosphatase.[2]

Inherently Chiral Phosphorus-containing Calixarenes

Of particular interest, are inherently chiral calixarenes, which chirality originates from the asymmetric arrangements of functional groups attached to the wide and/or narrow rim of the macrocycle. Recently, the most of the inherently chiral calixarenes were obtained as racemic mixtures or mixture of diastereomers in 1:1 ratio. Amongst the substitution patterns of the calix[4]arene lower rim the simplest one is ABHH type, possessing two different substituents in proximal position.

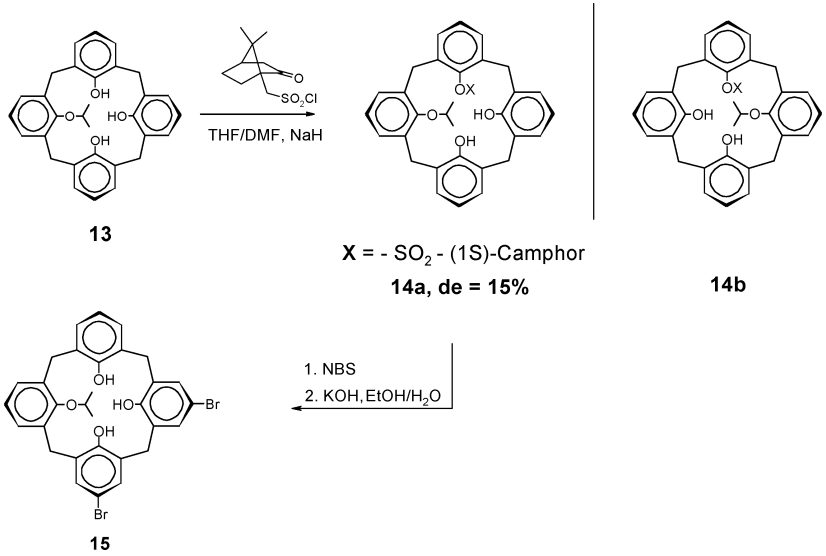
In our recent research, we have developed an approach based on phosphorotropic isomerization of symmetrically *1,3-disubstituted* calix[4]arenes into asymmetrical *1,2-regioisomers* promoted by strong bases.[3] For example, enantiomeric mixture of inherently chiral 25-ethoxy-26(28)-diethoxyphosphoryloxycalix[4]arenes **9** was synthesized by the reaction of C_s-symmetric 25-ethoxy-27-diethoxyphosphoryloxycalix[4]arene **8** with one equivalent of *n*-butyl lithium. Chiral calixarene dibromides **10** were synthesized by regioselectively brominating the esters **9** with bromosuccinimide. By treatment with trimethylbromosilane and methanol, phosphonic esters **10** then have been transformed into chiral calix[4]arene phosphoric acids **11.** The further interaction of the acids **11** with L-(-)-α-phenylethylamine (PEA) leads to diastereomeric salts **12**.[3]



SCHEME 3

A HPLC method allowed to separate in semi-preparative scale the diastereomeric salts **12** of the inherently chiral calixarene phosphoric acids with L-(-)-α-phenylethyl amine into individual diastereomers.

By another approach, selective sulfonylation of **13** with 1.08 equiv of 1(S)-(+)-camphor-10-sulfonyl chloride in THF/DMF (10/0.5) solution at room temperature at the presence of 1.1 equiv. of NaH leads to the diasteremeric sulfoesters **14a**, **b** with 85% total yield.



13 15

SCHEME 4

At the first time, separation of the diasteremers **14a**, **b** has been performed by means of simple crystallization. Calixarene **14a** was obtained with 98% purity and 41% yield. Another one—**14b**—was obtained with 92% purity and 35% yield. We found evidence of absolute configuration of the diastereomers from the X-ray analysis data.

Inherently chiral 5,11-dibromo-28-isopropoxycalix[4]arene **15** was obtained with a high yield via dibromination of the diastereomer **14a** with bromosuccineimide and further removal of camphorsulfonyl group under basic conditions. The calixarene **15** possessing the reactive OH groups and bromine atoms could be used as a versatile platform in design of chiral receptors or chiral advanced materials.

REFERENCES

[1] W. Zielenkiewicz, A. Marcinowicz, S. Cherenok, V. Kalchenko, and J. Poznański, *Supramolecular Chemistry*, **18,** 167 (2006).

[2] S. Cherenok, A. Vovk, I. Muravyova, A. Shivanyuk, V. Kukhar, J. Lipkowski, and V. Kalchenko, *Organic Letters*, **8,** 549 (2006).

[3] (a) L. N. Markovsky, M. A. Visotsky, V. V. Pirozhenko, V. I. Kalchenko, J. Lipkowski, and Yu. A. Simonov, *Chem. Commun*., 69 (1996); (b) M. O. Vysotsky, M. O.Tairov, V. V. Pirozhenko, and V. I. Kalchenko, *Tetrahedron Lett.*, **39,** 6057 (1998); (c) M. A. Tairov, M. O. Vysotsky, O. I. Kalchenko, V. V. Pirozhenko, and V. I. Kalchenko, *J. Chem. Soc. Perkin Trans.*, **1,** 1405 (2002).

[4] A. V. Yakovenko, V. I. Boyko, O. Danylyuk, K. Suwinska, J. Lipkowski, and V. I. Kalchenko, *Organic Letters*, **9,** 1183 (2007).