

Calixarenes with Nitrogen or Phosphorus Substituents on the Lower Rim*

D. M. ROUNDHILL**, E. GEORGIEV and A. YORDANOV
Department of Chemistry, Tulane University, New Orleans, LA 70118, U.S.A.

(Received: 3 March 1994; in final form: 27 July 1994)

Abstract. Calix[*n*]arenes (*n* = 4, 6) with diphenylphosphinite groups appended to their lower rim have been synthesized by reaction first with base, followed by chlorodiphenylphosphine. The reaction has also been carried out with the partially methoxylated calix[*n*]arenes. Calix[6]arenes with phosphate groups selectively bridging adjacent pairs of oxygens have been synthesized by reaction first with base, followed by ethyl dichlorophosphate. Calix[*n*]arenes (*n* = 4, 6) with 2-aminoethyloxy groups appended to the lower rim have been synthesized both by the reduction of an amide or nitrile group. Calixarenes with 2-hydroxyethyloxy and 2-bromoethyloxy groups appended to the lower rim have also been prepared. A route to preparing calixarene-functionalized polymers by the alkylation of polyethyleneimine is also described.

Key words: Calixarene, diphenylphosphinite, phosphate, amine, polymer.

1. Introduction

Although numerous examples exist of calixarenes with nitrogen or phosphorus substituents on the upper rim, relatively few such compounds have been prepared where these substituents are attached to the lower rim [1, 2]. Such compounds are, however, of importance because they can be potentially used as encapsulating ligands for metal ions. In order for these compounds to be useful as ligands, however, it is necessary that the nitrogen or phosphorus heteroatom either be in the tricoordinate form, or that an atom bonded to this heteroatom can act as a two-electron donor to a metal ion. In this article we describe some calixarenes that have nitrogen or phosphorus heteroatoms attached to their lower rim, and show how they can have applications to metal ion complexation chemistry.

2. Results and Discussion

Calixarenes with diphenylphosphinite groups appended to the lower rim can be synthesized by treating the *tert*-butylcalix[4]arene first with sodium hydride, then with chlorodiphenylphosphine (Equation 1) [3].

* This paper is dedicated to the commemorative issue on the 50th anniversary of calixarenes.

** Author for correspondence.

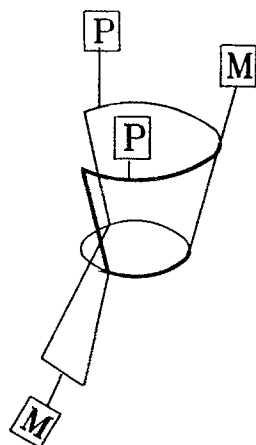
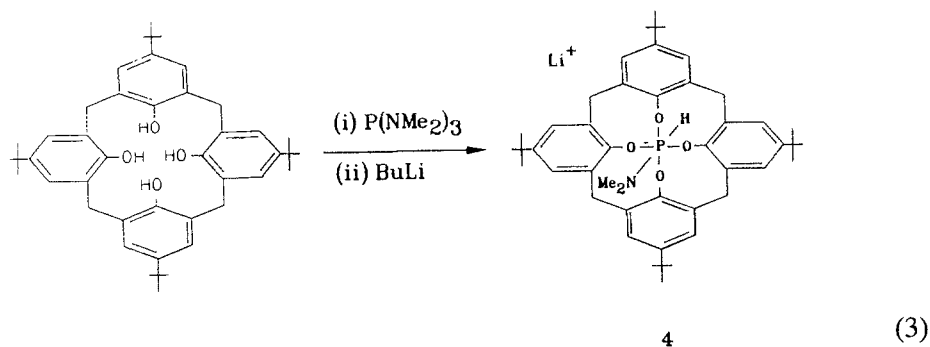


Fig. 1. Conformer of **2** where 'M' refers to OMe and 'P' refers to OPPh₂.

acetate [6]. In this synthetic procedure, however, LDA was used in place of sodium hydride as the base.

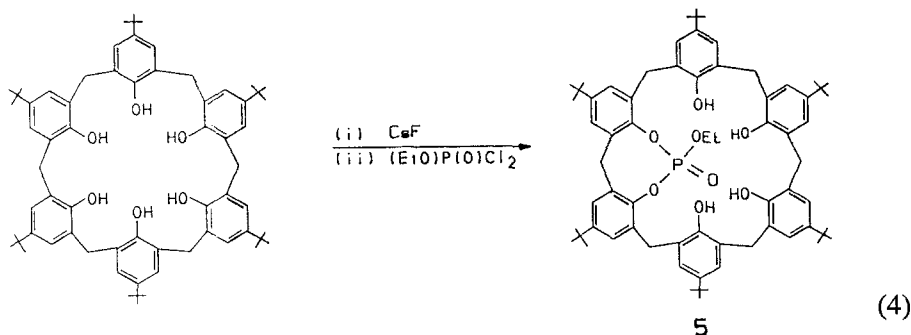
Phosphate groups can also be appended to the lower rim of *tert*-butylcalix[4]-arene and -calix[4]arene. The method of choice involves treating the calixarene with diethoxyphosphoryl chloride in basic solution. By changing the reaction conditions that are used it is possible to prepare compounds having different numbers of phosphate groups appended to the lower rim [7–10].

Phosphate groups can also be used to bridge and cap the oxygen atoms on the lower calix[4]arene rim. An example of a capped calix[4]arene where all four oxygens on the lower rim bind to a single phosphorus heteroatom is found in the reaction of *tert*-butylcalix[4]arene with P(NMe₂)₃ (Equation 3). The product **4** has a hypervalent phosphorus capping the lower rim of the calix[4]arene [11].

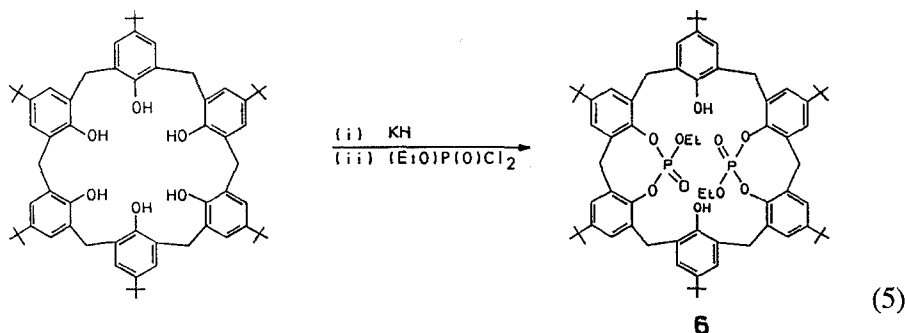


Phosphorus heteroatoms can also be incorporated onto the lower rim of a calixarene in a pairwise manner. Such bridged compounds have been prepared by treating *tert*-butylcalix[6]arene with base followed by ethyl dichlorophosphate [12]. Thus the addition of cesium fluoride followed by 1 equivalent of ethyl

dichlorophosphate results in the incorporation of a single ethyl phosphate group into the compound, in a manner where it spans two adjacent positions on the lower calix[6]arene rim (Equation 4).

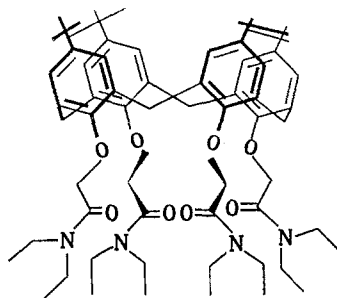


The $^{13}\text{C}\{^1\text{H}\}$ -NMR spectrum of this compound **5** shows three resonances for the *tert*-butyl groups at δ 31.26, 31.57 and 31.62. The presence of these resonances supports the structure shown for the compound. When potassium hydride is used as base in place of cesium fluoride, *tert*-butylcalix[6]arene can be reacted with 2 equivalents of ethyl dichlorophosphate to give the compound **6**, where now two sets of adjacent lower rim oxygens are spanned by ethyl groups (Equation 5).



The ^1H -NMR spectrum of **6** shows resonances at δ 1.03 and 1.38 for the *tert*-butyl groups in the ratio of 2 : 1, and a single multiplet for the methylenes at δ 4.64. These data support the structure shown where pairs of oxygens across the lower rim are bridged, and do not support a structure where adjacent pairs of phenolic groups around the lower calix[6]arene rim are sequentially spanned by ethyl phosphate groups.

Just as phosphorus heteroatoms can be appended to the lower calixarene rim, so can functional groups that contain a nitrogen atom. Among the nitrogen containing substituents that can be introduced onto the lower rim of a calixarene are the amide and amine moieties. Compounds having an amide substituent can be prepared by the sequence of reactions shown in Scheme 1 [13]. A similar calix[4]arene with amide substituents on the lower rim has been used as a ligand for the encapsulation of



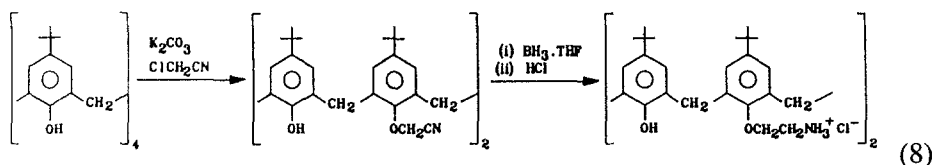
Eu^{3+} , Tb^{3+} and Gd^{3+} are encapsulated

Lifetime of LMCT (nsec)

Complex	300K (H_2O)	300K (D_2O)	77K (D_2O)	ϕ 300K (H_2O)
Eu^{3+}	0.65	1.9	1.8	2×10^{-4}
Tb^{3+}	1.5	2.6	1.6	2×10^{-1}

Fig. 2. Lifetime and quantum yield data for encapsulated lanthanide ions.

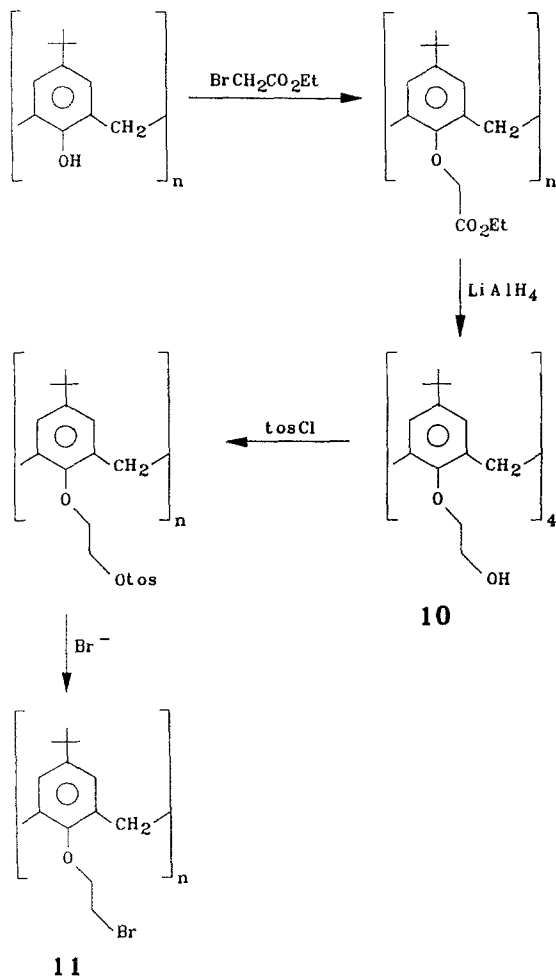
The intermediate compound **7** is identified in the $^1\text{H-NMR}$ spectrum by resonances at δ 4.18 (CH_2) and 7.35 (NH_2). Compound **8** has the amine resonance at δ 8.43, which is identifiable by its exchange reaction with D_2O . The latter method via the cyanomethoxy intermediate can be used to prepare partially substituted calixarenes, since the addition of chloroacetonitrile to calix[4]arene can be used to selectively substitute the two alternate positions on the lower rim (Equation 8).



9

Subsequent reduction with $\text{BH}_3 \cdot \text{THF}$, followed by quaternization of the amine with HCl , can be used to obtain the alkylammonium salt **9**. The compound shows a resonance at δ 8.57 (8H) due to the OH and NH groups which undergoes exchange with added D_2O .

We have also prepared a calix[4]arene with a 2-bromoethoxy substituent appended onto the lower rim. The compound has been prepared by the sequence of reactions shown in Scheme 2. The sequence involves first converting the calixarene into the acetate derivative by reaction with ethyl bromoacetate, followed by reduction of this intermediate ester to the 2-hydroxyethyloxy derivative **10**. This com-



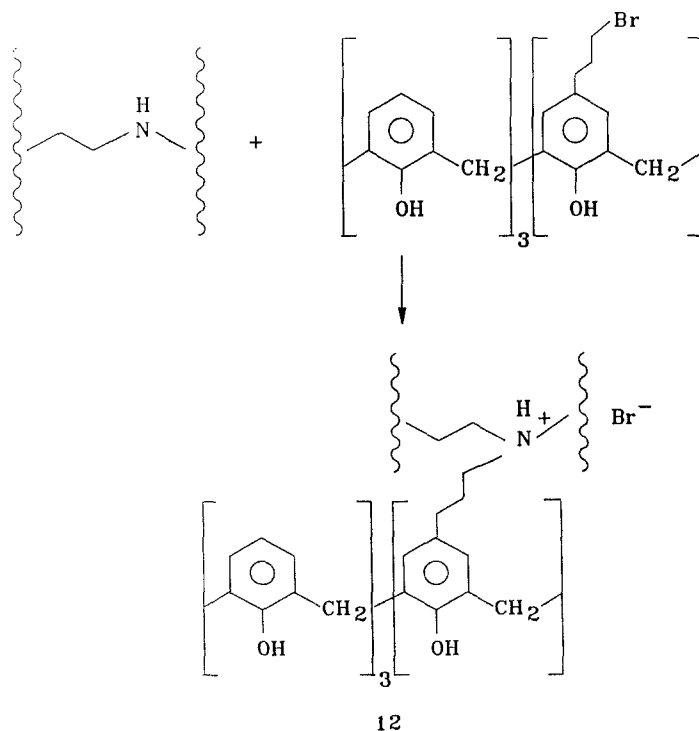
Scheme 2.

Compound **11** is characterized by resonances in the $^1\text{H-NMR}$ spectrum at δ 4.03 (OCH_2) and δ 5.6 (OH). This intermediate **10** can be converted into the 2-bromoethoxy compound **11** by replacement of the tosylate group with bromide ion. Compound **11** shows characteristic resonances in the $^1\text{H-NMR}$ spectrum for the OCH_2 and CH_2Br groups at δ 4.24 and 3.86, respectively. This new 2-bromoethoxy calix[4]arene is a potentially useful synthon for the introduction of a wide range of heteroatom substituents onto the lower rim.

A relatively new development in calixarene chemistry is their immobilization on polymeric supports. For certain applications such as the separation of heavy metal ions from aqueous media, it is advantageous for these calixarene-impregnated polymers to be available in an insoluble form. This goal is relatively easy to achieve since insoluble materials can be obtained by cross-linking the calixarene to the polymer via several attachment points. Since reactions leading to the chemical modification

of calixarenes usually lead to functionalization at multiple sites, precursor calixarenes for such uses are readily available. Several examples of such cross-linked calixarene modified polymers are reported in the literature. An example by Harris involves the synthesis of silicone bound calixarenes where the attachment is via multiple ester functionalities between the polymer and the calixarene [15, 16]. A further cross-linked calixarene modified polymer has been prepared by Shinkai from treating polyethyleneimine with a chloro-sulfonated calixarene [17]. These insoluble modified polymers have been used by Shinkai for the extraction of uranium ion from seawater [18, 19]. Recently Harris has reported the synthesis of a new calixarene bearing a single methacrylate functionality that is potentially suitable for use as a reagent to give living polymers and copolymers. Attempted homopolymerization of this compound, however, yielded an oligomer that had only approximately six calixarene units in the chain [20]. More recently we have prepared a cross-linked material by treating a 50% aqueous solution of polyethyleneimine with 5,11,17,23-tetrachloromethyl-25,26,27,28-tetrahydroxycalix[4]arene [21].

For other applications such as in electrokinetics or the synthesis of radiopharmaceuticals it is desirable that the calixarene-functionalized polymer be soluble in aqueous media. In order to achieve such a goal it is necessary to avoid the formation of cross-linking within the polymer. Such a polymer **12** that is soluble in aqueous or organic solvents is formed when a calixarene with a single haloalkyl substituent on the upper rim is reacted with the polyethyleneimine solution (Equation 9).



(9)

This availability of two separate rims that can be independently modified for either selective ligation or for the attachment to polymers makes the calixarenes an attractive class of compounds for a wide range of applications involving metal ions.

Acknowledgment

We thank the Center for Bioenvironmental Research at Tulane University for financial support.

References

1. C. D. Gutsche: *Calixarenes*, Royal Society of Chemistry, Cambridge, U.K. (1989).
2. J. Vicens and V. Böhmer: *Calixarenes: A Versatile Class of Macrocyclic Compounds*, Kluwer, Dordrecht, the Netherlands (1991).
3. C. Floriani, D. Jacoby, A. Chiesi-Villa, and C. Guastini: *Angew. Chem., Int. Ed. Engl.* **28**, 1376 (1989).
4. D. Jacoby, C. Floriani, A. Chiesi-Villa, and C. Rizzoli: *J. Chem. Soc. Dalton Trans.* 813 (1993).
5. J. K. Moran and D. M. Roundhill: *Inorg. Chem.* **31**, 4213 (1992).
6. D. Matt, C. Loeber, J. Vicens, and Z. Asfari: *J. Chem. Soc., Chem. Commun.* 604 (1993).
7. L. N. Markovskii, V. I. Kal'chenko, and N. A. Parkhomenko: *Zh. Obshch. Khim.* **60**, 2811 (1990).
8. Y. Ting, W. Verboom, L. C. Groenen, J.-D. van Loon, and D. N. Reinhoudt: *J. Chem. Soc., Chem. Commun.* 1432 (1990).
9. F. Grynszpan, Z. Goren, and S. E. Biali: *J. Org. Chem.* **56**, 532 (1991).
10. R. G. Janssen, W. Verboom, S. Harkema, G. J. van Hummel, D. N. Reinhoudt, A. Pochini, R. Ungaro, P. Prados, and J. de Mendoza: *J. Chem. Soc., Chem. Commun.* 506 (1993).
11. D. V. Khasnis, M. Lattman, and C. D. Gutsche: *J. Am. Chem. Soc.* **112**, 9422 (1990).
12. J. K. Moran and D. M. Roundhill: *Phosphorus, Sulfur, and Silicon* **71**, 7 (1992).
13. S.-K. Chang, S.-K. Kwan, and I. Cho: *Chem. Lett.* 947 (1987).
14. N. Sabbatini, M. Guardigli, A. Mecati, V. Balzani, R. Ungaro, E. Ghidini, A. Casnati, and A. Pochini: *J. Chem. Soc., Chem. Commun.* 878 (1990).
15. S. J. Harris, M. A. McKervey, D. P. Melody, J. G. Woods, and J. M. Rooney: *Eur. Patent Appl.*, 151, 527 (1985); *Chem. Abstr.* **103**, 216, 392x (1985).
16. B. Kneafsey, J. M. Rooney, and S. J. Harris: *U.S. Patent*, 4,912,183 (1990); *Chem. Abstr.* **114**, 123, 273 (1991).
17. S. Shinkai, H. Kawaguchi, and O. Manabe: *J. Polym. Sci.* **C26**, 391 (1988).
18. Y. Kondo, T. Yamamoto, O. Manabe, and S. Shinkai: *Jpn. Kokai Tokkyo Koho JP 62/210055 A2* [87/210055] (1987); *Chem. Abstr.* **108**, 116, 380b (1988).
19. Y. Kondo, T. Yamamoto, O. Manabe, and S. Shinkai: *Jpn. Kokai Tokkyo Koho JP 63/7837 A2* [88/7837] (1988); *Chem. Abstr.* **109**, 137, 280b (1988).
20. S. J. Harris, G. Barrett, and M. A. McKervey: *J. Chem. Soc., Chem. Commun.* 1224 (1991).
21. E. M. Georgiev, K. Troev, and D. M. Roundhill: *Supramol. Chem.* **2**, 61 (1993).