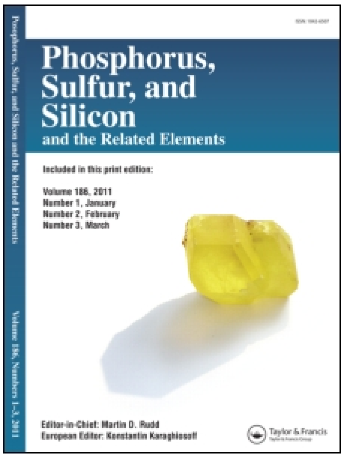

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CALIXARENE PHOSPHATES

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A SHORT REVIEW

CALIXARENE PHOSPHATES

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(Received 22 April 1997)

The syntheses of non-bridged and bridged calixarene phosphates and their structures were discussed.

Keywords: non-bridged and bridged calixarene derivatives; calixarene phosphates; P-bridged calixarenes; conformation of calixarenes

INTRODUCTION

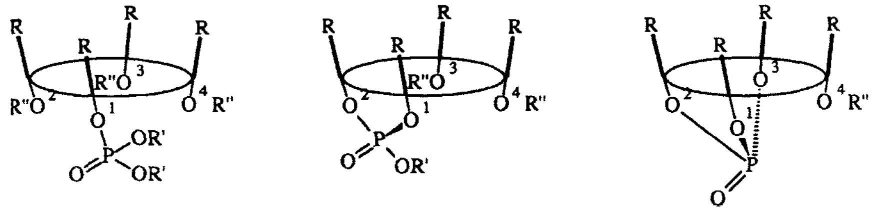
In the last years many phosphorus containing calixarenes have been synthesized.[1,2] They are good host molecules for selective separations of cations.[3–6]

This report concentrates on the syntheses of *O*-phosphorylated calixarenes. The phosphate group can be linked covalently to one, two or more points of the macrocyclic system. Therefore, two basic types of calixarene phosphates can be distinguished:

1. non-bridged calixarene phosphates (e.g. type **A**,[7] acyclic phosphates) and
2. bridged calixarene phosphates (e.g. type **B** or **C**, cyclic phosphates).

SYNTHESIS OF NON-BRIDGED CALIX[4]ARENE PHOSPHATES

Normally the phosphorylation of calix[4]arene derivatives **1** was carried out with diethyl chlorophosphate in the presence of a base (scheme 1). The grade of the phosphorylation and the conformation of the phosphorylated product depend on

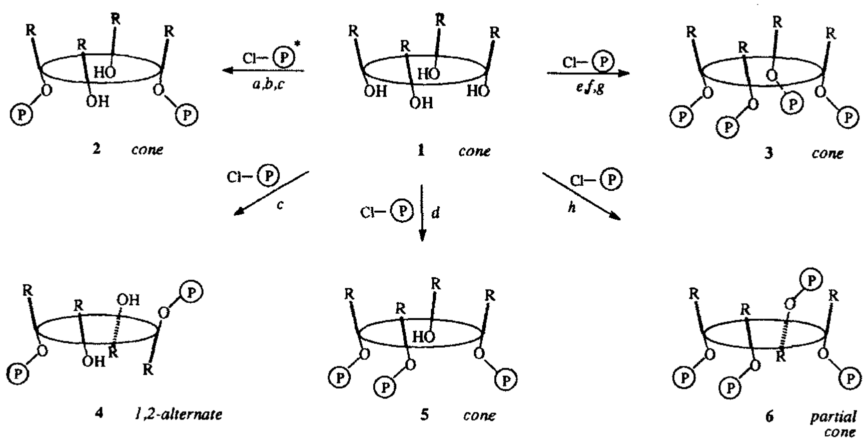


A B C

FIGURE 1 compounds **A**, **B**, **C**

the strength of the base, on the solvent and on the procedure used for the preparation.

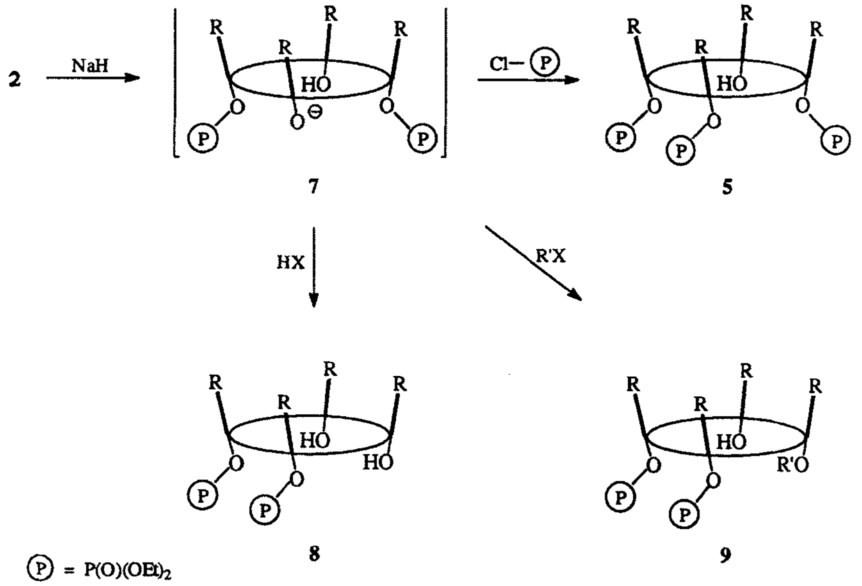
The reaction in acetonitrile or tetrahydrofuran in the presence of potassium carbonate gives the *cone* O^1,O^3-diphosphate[7] **2** (83% yield for R = H, 74% yield for R = tBu; reaction b)[8,9] and in the presence of triethylamine a mixture of **2** and **4** (85–90% *cone*, 10–15% *1,2-alternate*; reaction c).[10] The exchange of the chlorophosphate by diethyl phosphite/tetrachloromethane leads to **2** (65% yield for R = tBu; reaction a).[11] The phosphorylation with chlorophosphate in the presence of 20% sodium hydroxide in ether under phase-transfer catalysis (PTC) yields the *cone* triphosphate **5** (reaction d)[12] and in presence of 50%



Ⓟ = $P(O)(OEt)_2$
(* from H–Ⓟ / CCl_4, reaction *a*)
R = H, tBu, TMB
(TMB = 1,1,3,3-Tetramethylbutyl)

Base / Solvent:
a: Et_3N / CCl_4; *b*: K_2CO_3 / MeCN; *c*: Et_3N / $CHCl_3$; *d*: 20% NaOH (Bu_4NBr) / Et_2O; *e*: 50% NaOH (Bu_4NBr) / CH_2Cl_2; *f*: 50% NaOH (Bu_4NBr) / CCl_4; *g*: NaH ; *h*: 50% NaOH (Et_4NBr) / CH_2Cl_2

SCHEME 1 syntheses of non-bridged calix[4]arene phosphates



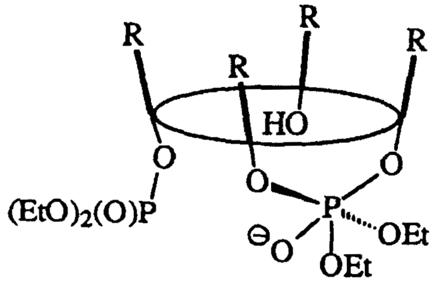
P = P(O)(OEt)$_2$
R = H, tBu
R' = MeOOCCH$_2$,PhCO

SCHEME 2 syntheses of substituted O^1,O^2-calix[4]arene diphosphates

sodium hydroxide in dichloromethane or tetrachloromethane yields the *cone* tetraphosphate **3** (57% yield for R = tBu, 55% yield for R = TMB; reaction e, f).[6,11] The reaction in the presence of sodium hydride gives **3**, too (reaction g).[10] A conversion of the conformation was observed, when the alkyl chain of the catalyst is smaller (Et instead of Bu). The *partial cone* tetraphosphate **6** (29% yield for R = tBu; reaction h)[13] was obtained and furthermore a bridged diphosphate was isolated (see also scheme 3). The reaction of phosphates **2** and **3** with trimethylsilyl bromide converts the ethyl esters into the silyl esters which react with methanol to give the corresponding acidic phosphates (93% and 80% yield, respectively).[14]

The further phosphorylation of **2** with chlorophosphate in the presence of sodium hydride leads to the *cone* triphosphate **5** (53% yield for R = H, 75% for R = tBu; scheme 2).[15]

The anion **7** was discussed as an intermediate. The O^1, O^2-diphosphates **8** (84% yield for R = H, 82% yield for R = tBu) were formed by addition of an acid to the solution of **7**. The alkylation and the acylation of **7** gave *O*-substituted O^1, O^2-diphosphates of the type **9** (32% yield for R = H, R' = MeOOCCH$_2$, 61% yield for R = H, R' = PhCO, 55% yield for R = tBu, R'

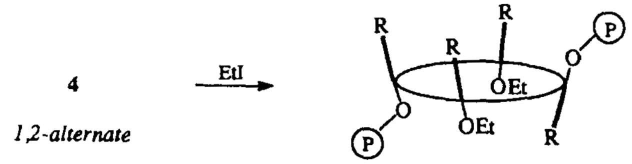


10

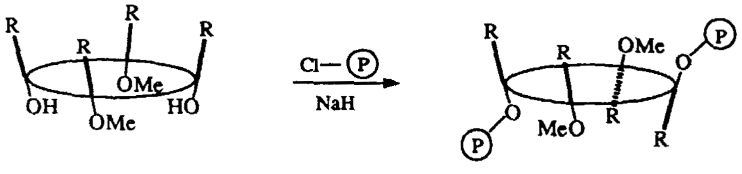
FIGURE 2 compound **10**

= PhCO), too.[15] The formation of **8** and **9** were explained with a phosphorotropic rearrangement.

The cyclic phoshorane **10** was discussed as an intermediate. Also the phosphorylation of **2** could proceed via **10**. Since the compounds of type **9** have a stereogenic plane (inherent chirality), racemic mixtures were obtained.[15]



4 *1,2-alternate* → **11** *partial cone* (1)



12 *cone* → **13** *1,2-alternate* (2)

Ⓟ = P(O)(OEt)$_2$; R = tBu

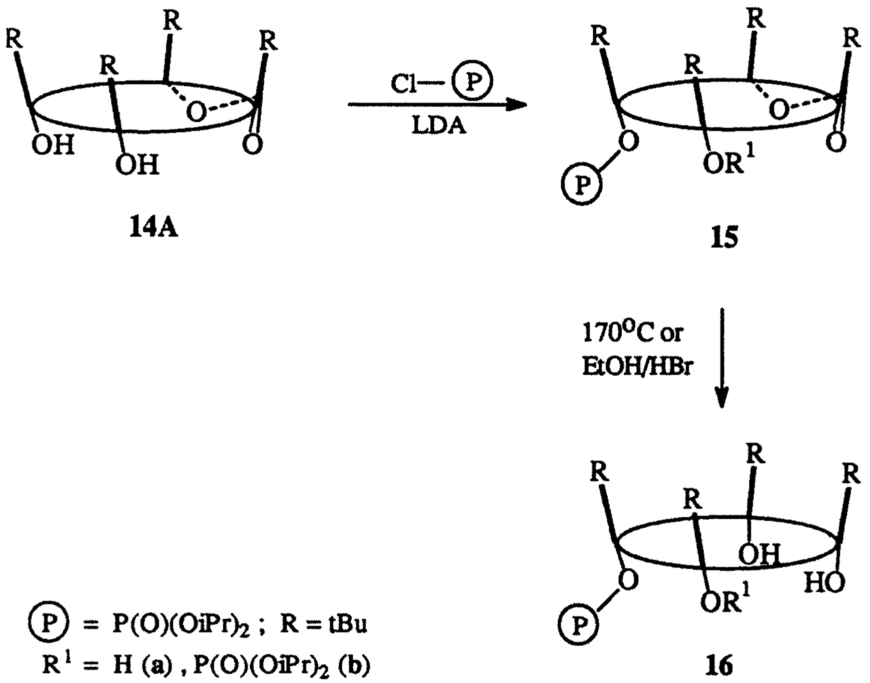


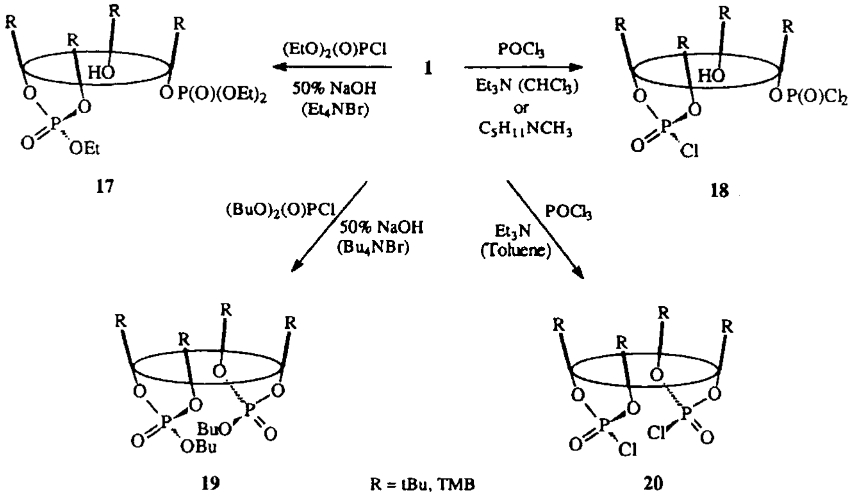
FIGURE 4 synthesis via **14**

The alkylation of the *1,2-alternate* diphosphate **4** with ethyl iodide leads to the *partial cone* diphosphate **11** (equation 1). A migration of a phosphate group was not observed.[10b]

The phosphorylation of the methylated *cone* derivative **12** in the presence of sodium hydride occurs by change of conformation, too. The *1,2-alternate* O^1, O^3-diphosphate **13** was obtained (equation 2).[9] The dibenzyl derivative was synthesized analogously (44% yield). The conformation was not studied.[6]

It is not possible to obtain a monophosphate by the phosphorylation of **1**. Recently, it was reported that the monophosphate can be synthesized with a technique which uses a protection of the OH-groups.

The first step is the oxidation of **1** to the monospirodienone **14** (short form **14A**),[16] in the second step **14** was phosphorylated to the monophosphate **15a** (47% yield) or diphosphate **15b** (55% yield), and in the third step the dihydrobenzofuran system was split off by reduction or heating. The product of this reaction sequence is the monophosphate **16a** or the O^1,O^2-diphosphate **16b** (85% yield). The chiral phosphates **15** exist as racemic mixtures.[17–19]



SCHEME 3 syntheses of 1,2-bridged calix[4]arene phosphates

SYNTHESIS OF BRIDGED CALIX[4]ARENE PHOSPHATES

1,2-Bridged Calix[4]arene Phosphates

The phosphorylation of **1** with diethyl chlorophosphate under PTC conditions with the catalyst Et_4NBr gives the non-bridged derivative **6** and the bridged diphosphate **17** (scheme 3 and 1).[13] The connection of the phosphorus atom to the proximate OH-groups (1,2-bridge) was derived from X-ray crystallography.[13]

If the phosphorylating reagent and the catalyst were changed, the bis-bridged $O^1,O^2;O^3,O^4$-diphosphate **19** was obtained (scheme 3).[6] The phosphorylation with phosphorus oxychloride in the presence of triethylamine and toluene (80°) gives the bis-bridged dichloro-diphosphate **20** (18% yield) and in boiling chloroform the 1,2-bridged trichloro-diphosphate **18** (30% yield).[19] If triethylamine was substituted by *N*-methylmorpholine, an increase of the yield of **18** was observed (94% yield).[1]

The hydrolysis of **18** with water leads to the bridged monochloro-diphosphate **21** (85% yield). The exchange of the last chlorine atom is possible by boiling with concentrated hydrochloric acid. The diphosphate **22** was obtained in good yield (87%).

The alkylation of **22** with triethyl orthoformate gives the triethyl ester **17** (74% yield) and with diazomethane the corresponding trimethyl ester (79% yield).[1]

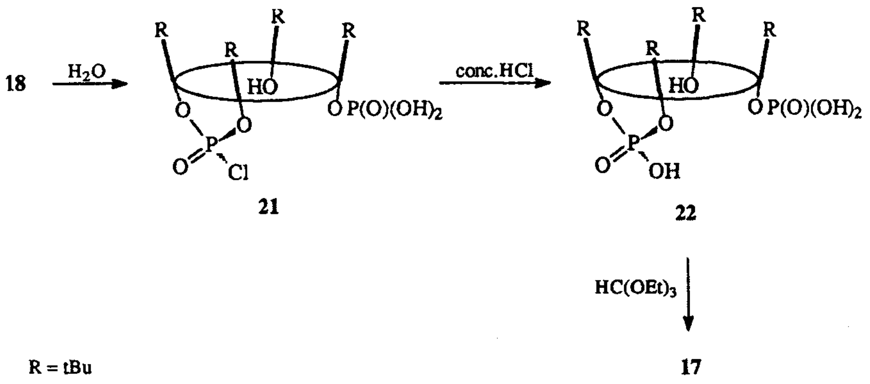


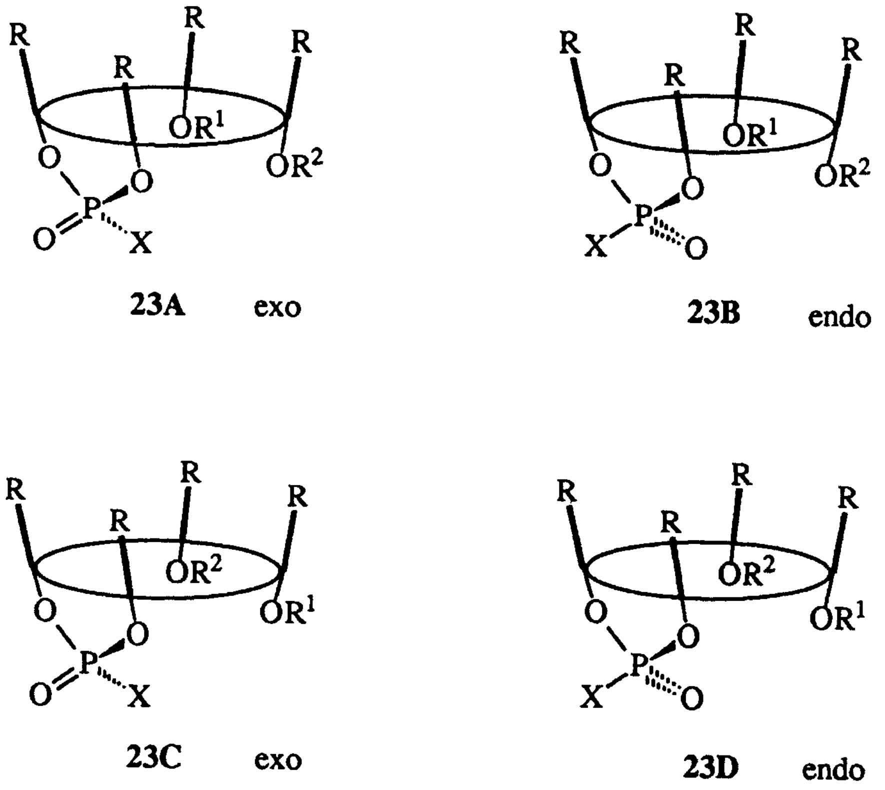
FIGURE 5 hydrolysis of **18**

Some stereochemical aspects of the 1,2-bridged calix[4]arene phosphates should be considered. The free rotation of the bridged phosphoryl group is reduced. There exist mainly two directions of orientation. Either the oxygen of the phosphoryl group is directed to the periphery of the macrocyclic system (e.g. **23A**), -it is an *exo-* or *outward*-standing PO-group -, or the oxygen is directed to the centre of the macrocyclic system (e.g. **23B**), -it is an *endo-* or *inward-*standing PO-group (figure 6).[1,6,19,20] The structure of the *exo* and the *endo* compound of **17** was proved by means of X-ray studies.[1] The derivative **19** could exist in three isomers: *exo-exo endo-endo*, and *exo-endo*. Structural data were already published for two isomers (*exo-exo* and *exo-endo*).[6]

Furthermore, it is important to consider the substituents on the O-atoms 3 and 4. If the residues R^1 and R^2 are identical, there exist the isomers **23A** and **23B**. If the residues R^1 and R^2 are different, the molecule has a stereogenic plane (inherent chirality). Often these molecules contain in addition a stereogenic centre. In this case the four isomers **23A–D** exist. All four stereoisomers were found in the diphosphate **17**, synthesized by alkylation of **22** (chiral HPLC, chiral NMR shift reagents, X-ray crystallography).[1] These studies reveal that the *exo* compounds **23A** and **23C** and the *endo* compounds **23B** and **23D** are enantiomeric pairs.[1]

The isolated derivatives **17** and **18** (scheme 3), obtained on direct phosphorylation of **1**, contain only the *exo* enantiomers. Hence these reactions are stereoselective.[13,19] The compound **22** has no stereogenic centre, therefore only two isomers were detected.[1]

The pyrolysis of the phosphates **2**, **6**, **15a**, **16a**, **16b**, and **18** leads to the bridged anhydride **24**.[19] In the solid state the compound has a *flattened cone* conformation. In the liquid state (**24** solved) a dynamic change of two *flattened*



23A exo **23B** endo

23C exo **23D** endo

FIGURE 6 isomers of **23**

cone conformations (**24A** and **24B**) was observed by means of NMR investigations.[19]

1,2,3-bridged Calixarene Phosphates

The phosphorylation of *tert*-butylcalix[4]arene with phosphorus pentachloride gives the phosphonium salt **25** (quantitative yield; (scheme 4),[1,21] which exists in a *partial cone* conformation.[22]

25 reacts with *O*-containing compounds to give the stable bridged diphosphates **26**, **27**, and **28**[23] (50%, 95%, and 86% yield).[21,24] With S-containing compounds 1,2,3-bridged calix[4]-arene thiophosphates were obtained.[24]

One heterocyclic bond of the 1,2,3-bridged derivatives **25** and **28** was broken by alcaline hydrolysis under drastic conditions. The chiral 1,2-bridged calixarene

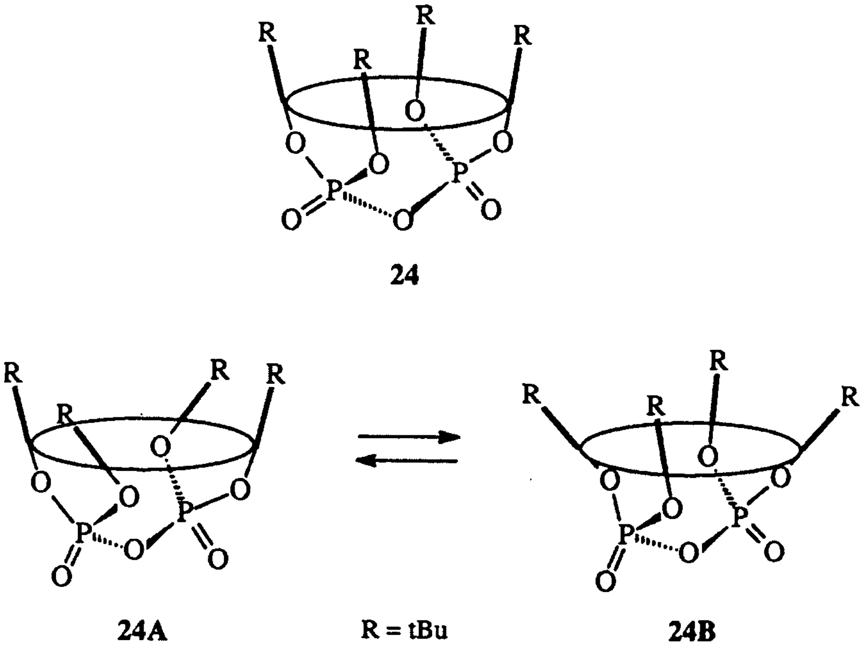
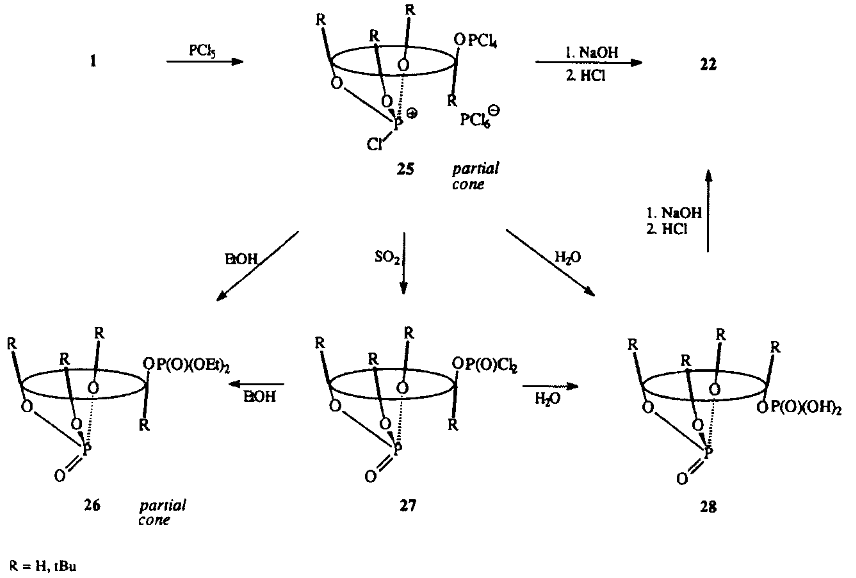


FIGURE 7 compound 24



SCHEME 4 syntheses of 1,2,3-bridged calix[4]arene phosphates

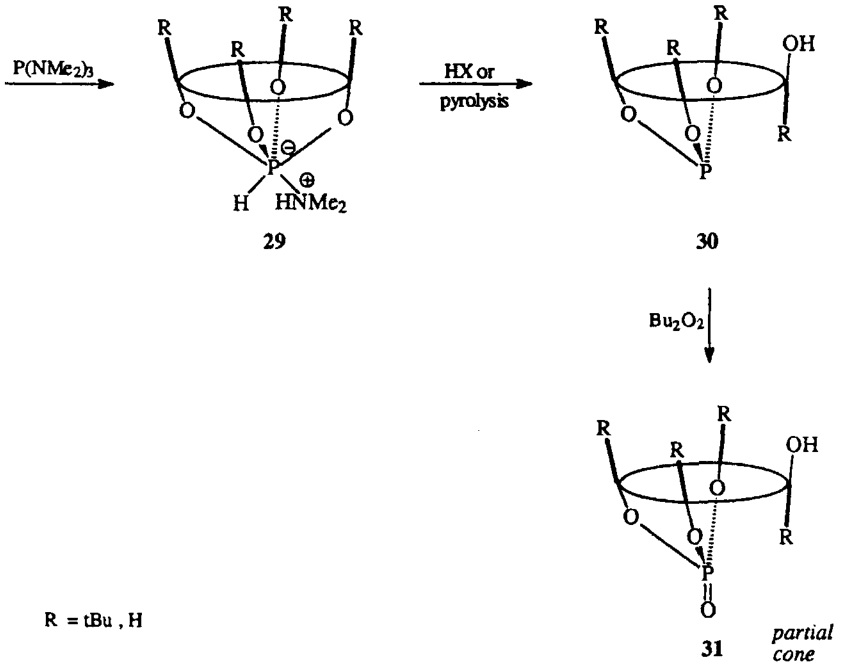


FIGURE 8 synthesis of 31

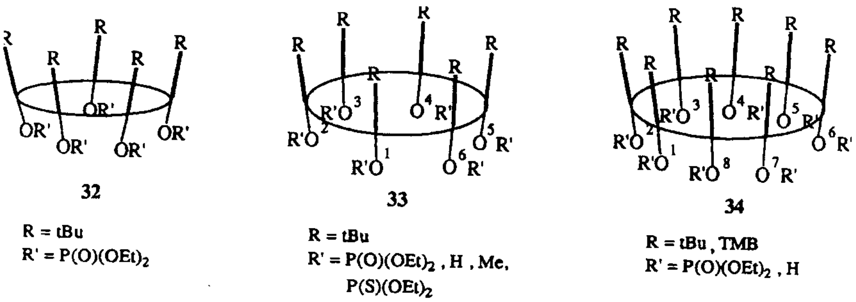
derivative **22** was formed (38 and 46% yield, respectively).[1] It is a new method of synthesizing chiral calixarenes from achiral derivatives.

A further method for the synthesis of 1,2,3-bridged phosphates uses a tricoordinated phosphorus compound as phosphorylating reagent:

1 reacts with tris(dimethylamino)phosphane to give the 1,2,3,4-bridged derivative **29**. The acidolysis or pyrolysis of **29** leads to the phosphite **30** and the following oxidation gives the *partial cone* phosphate **31**.[25]

SYNTHESIS OF NON-BRIDGED PHOSPHATES OF CALIX[5]ARENE, CALIX[6]ARENE AND CALIX[8]ARENE

The phosphorylation of *tert*-butylcalix[5]arene, *tert*-butylcalix[6]arene, *tert*-butylcalix[8]arene and 1,1,3,3-tetramethylbutyl-calix[8]arene with diethyl chlorophosphate under PTC conditions leads to the pentaphosphate **32** (73% yield),[19] hexaphosphate **33** (36% yield for R' = $P(O)(OEt)_2$)[26] and octaphosphate **34** (29% yield for R = tBu,[11] 64% yield for R = TMB[6]).



32

R = tBu
R' = P(O)(OEt)$_2$

33

R = tBu
R' = P(O)(OEt)$_2$, H , Me,
P(S)(OEt)$_2$

34

R = tBu , TMB
R' = P(O)(OEt)$_2$, H

FIGURE 9 non-bridged phosphates of calix[5]-, calix[6]-, and calix[8]arene

The phosphorylation in the presence of triethylamine gives a mixture of partially phosphorylated calixarenes, which were separated by flash chromatography. The following derivatives of type **33** (R' = P(O)(OEt)$_2$ and H) and **34** (R = tBu, R' = P(O)(OEt)$_2$ and H) were isolated: **33** - monophosphate (37% yield), *O^1,O^3*-diphosphate (31% yield), *O^1,O^4*-diphosphate (28% yield), *O^1,O^2,O^4*-triphosphate (56% yield)[6,26,27] and *O^1,O^3,O^5*-triphosphate (60% yield; without flash chromatography);[10a,31] **34**—monophosphate (31% yield), *O^1,O^3*-diphosphate (15% yield) and *O^1,O^5*-diphosphate (12% yield).[6]

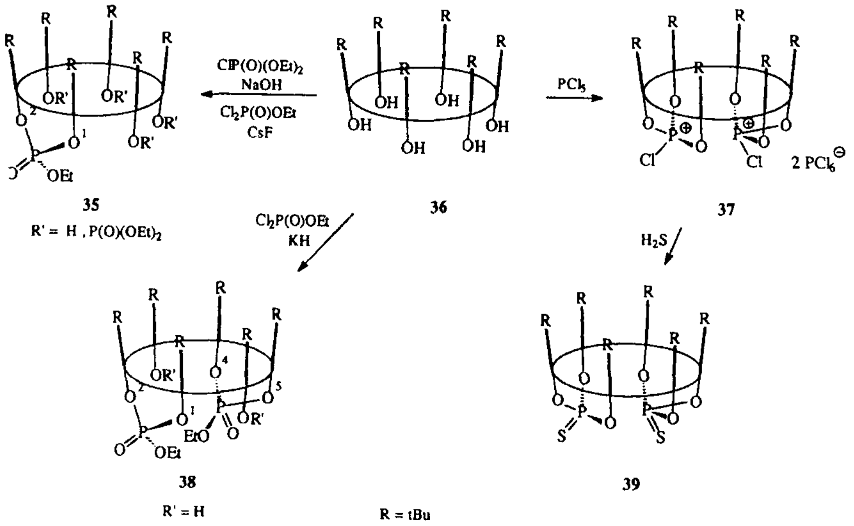
By means of the same method thiophosphate **33** (R' = P(S)(OEt)$_2$ and H) were synthesized: monothiophosphate (25% yield), *O^1,O^3*-bis(thiophosphate) (25% yield), *O^1,O^4*-bis(thiophosphate) (68% yield) and pentakis(thiophosphate) (32% yield).[4,26] The *O*-methylated derivatives **33** (R' = P(O)(OEt)$_2$ and Me, R' = P(S)(EtO)$_2$ and Me) were obtained by phosphorylation of methylated calixarenes or by methylation of phosphorylated calixarenes.[4,26]

SYNTHESIS OF BRIDGED PHOSPHATES OF CALIX[6]ARENE AND CALIX[8]ARENE

The phosphorylation of *tert*-butylcalix[6] arene **36** with diethyl chlorophosphate under PTC conditions gives besides the hexaphosphate also the 1,2-bridged pentaphosphate **35** (17% yield for R' = P(O)(OEt)$_2$; (scheme 5).[28]

The phosphorylation in the presence of cesium fluoride leads to the 1,2-bridged monophosphate **35** (25% yield for R' = H) and in the presence of potassium hydride to the bis-bridged *O^1,O^2;O^4,O^5*-diphosphate **38** (9% yield for R' = H).[29]

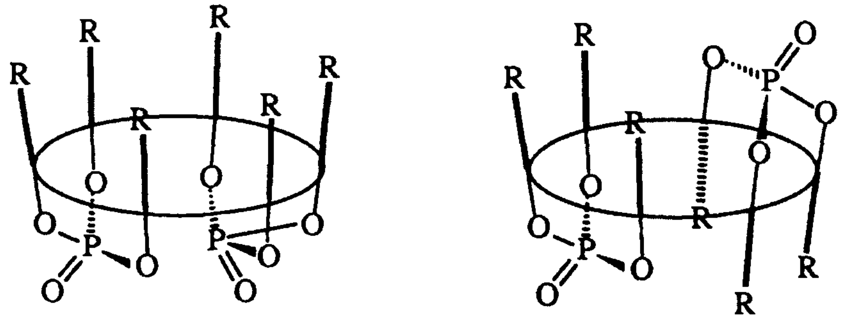
The bisphosphonium salt **37** was formed by the reaction of **36** with phosphorus pentachloride (scheme 5).[24] The thiolysis of **37** with hydrogen sulphide



SCHEME 5 syntheses of bridged calix[6]arene phosphates

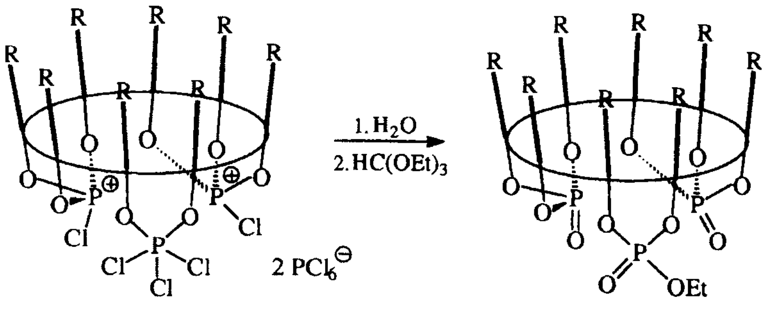
provides the bis-bridged thiophosphate **39** (33% yield) and the hydrolysis the corresponding diphosphate **40** (74% yield).[24] This diphosphate can exist in a *syn* and *anti* conformation **40A** and **40B**.

The hydrolysis of **37** gives only *syn* **40A** and the pyrolysis of a non-bridged *tert*-butylcalix[6]-arene triphosphate gives a mixture of *syn* **40A** (43% yield) and *anti* **40B** (9% yield).[17,19] A dynamic change in the molecule was observed for


40A *syn* **40B** *anti*

R= tBu

FIGURE 10 compounds **40A**, **40B**



41

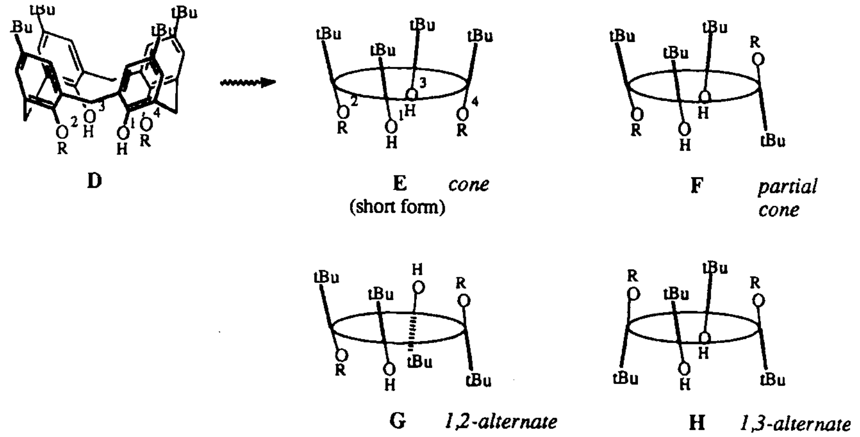
42

(3)

R = tBu

40A. A comparable transistion was described for the calix[4]arene derivative **24** (see figure 7). Hence **40A** is a racemic mixture.[19]

The phosphorylation of *tert*-butylcalix[8]arene with phosphorus pentachloride leads to a mixture, in which the phosphoranyl-bisphosphonium salt **41** was detected.[30] The hydrolysis of this mixture and the following alkylation give the tris-bridged triphosphate **42** (equation 3).[30] It is a calixarene phosphate with two 1,2,3-bridges and one 1,2-bridge.



D

E *cone* (short form)

F *partial cone*

G *1,2-alternate*

H *1,3-alternate*

FIGURE 1A compounds **D**, **E**, **F**, **G**, **H**

CONCLUSION

The *O*-phosphorylation of calixarene derivatives leads in dependence on base, solvent, phosphorylating reagent and procedure used for the preparation to non-bridged and bridged calixarene phosphates. The analytical and physical investigations with these phosphates afforded new insights into the structure of calixarenes.

Acknowledgements

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References

[1] See for example: J. Gloede, B. Costisella, A. Kunath and M. Schneider, *Phosphorus, Sulfur, and Silicon*, **117**, 67 (1996).

[2] See for example: S. Ozegowski, B. Costisella and J. Gloede, *Phosphorus, Sulfur, and Silicon*, **119**, 209 (1996).

[3] J.-C. G. Bünzli and J. M. Harrowfield, *Calixarenes. A versatile Class of Macrocyclic Compounds*, (eds. J. Vicens and V . Böhmer, Kluwer Academic Publishers, Dordrecht, 1991) pp. 211–231.

[4] W. Wroblewski, Z. Brzozka, R. G. Janssen, W. Verboom and D. N. Reinhoudt, *New J. Chem.*, **20**, 419 (1996).

[5] F. Arnaud-Neu, V . Böhmer, J.-F. Dozol, C. Grüttner, R. A. Jakobi, D. Kraft, O. Mauprivez, H. Rouchette, M.-J. Schwing-Weill, N. Simon and W. V oigt, *J. Chem. Soc., Perkin Trans. 2*, **1996**, 1175.

[6] J. M. Harrowfield, M. Mocerino, B. J. Peachey, B. W. Skelton and A. H. White, *J. Chem. Soc., Dalton Trans.*, **1996**, 1687.

[7] In this report all calixarene derivatives were described in a short form, e.g. the p-*tert*-butylcalix[4]arene derivative **D** in the short form **E**. The different conformers of the calix[4]arenes were characterized by the corresponding short forms **E–H**. The conformation of all compounds, which were marked with a conformation under the formula (see schemes and figures), is proved. The oxygen atoms of the phenol units were numbered in the sequence, shown for compounds **D** and **E**, in order to achieve an unambiguous assignment of the different *O*-substituted calixarene derivatives.

[8] P. L. H. M. Cobben, R. J. M. Egberink, J. G. Bomer, P. Bergveld, W. Verboom and D. N. Reinhoudt, *J. Amer. Chem. Soc.*, **114**, 10573 (1992).

[9] Y . Ting, W. Verboom, L. C. Groenen, J.-D. van Loon and D. N. Reinhoudt, *J. Chem. Soc., Chem. Commun.*, **1990**, 1432.

[10] a) L. N. Markovsky, V . I. Kalchenko and N. A. Parchomenko, *Zhur. Obshch. Khim.*, **60**, 2811 (1990); b) V . I. Kalchenko, J. Lipkowski, Y . A. Simonov, M. A. Visotsky, K. Suwinska, A. A. Dvorkin, V . V . Pirozhenko, I. F. Zimbal and L. N. Markovsky, *Zhur. Obshch. Khim.*, **65**, 1311 (1995).

[11] Z. Goren and S. E. Biali, *J. Chem. Soc., Perkin Trans. 1*, 1484 (1990).

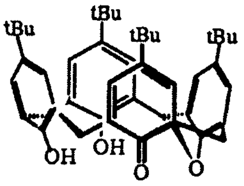
[12] T. Harada, F. Ohseto and S. Shinkai, *Tetrahedron*, **50**, 13377 (1994).

[13] L. T. Byrne, J. M. Harrowfield, D. C. R. Hockless, B. J. Peachey, B. W. Skelton and A. H. White, *Aust. J. Chem.*, **46**, 1673 (1993).

[14] V . I. Kalchenko, M. A. Visotsky, V . V . Pirozhenko, A. N. Shivenyuk and L. N. Markovsky, *Zhur. Obshch. Khim.*, **64**, 1560 (1994).

[15] L. N. Markovsky, M. A. Visotsky, V . V . Pirozhenko, V . I. Kalchenko, J. Lipkowski and Y . A. Simonov, *J. Chem. Soc., Chem. Commun.*, **1996**, 69.

[16]



14

[17] O. Aleksiuk, F. Grynszpan and S. E. Biali, *J. Chem. Soc., Chem. Commun.*, **1993**, 11.

[18] F. Grynszpan, O. Aleksiuk and S. E. Biali, *J. Org. Chem.*, **59**, 2070 (1994).

[19] O. Aleksiuk, F. Grynszpan and S. E. Biali, *J. Incl. Phenom. Mol. Recogn.*, **19**, 237 (1994).

[20] T. Lippmann, E. Dalcanale and G. Mann, *Tetrahedron Letters*, **35**, 1685 (1994).

[21] J. Gloede, B. Costisella, M. Ramm and R. Bienert, *Phosphorus, Sulfur, and Silicon*, **84**, 217 (1993).

[22] H. Thönnessen, P. G. Jones, R. Schmutzler and J. Gloede, *Acta Crystallogr.*, **C53**, 1310 (1997).

[23] The exact conformation of **28** is not clear. The NMR data correspond to the *cone* conformation.

[24] J. Gloede and I. Keitel, *Phosphorus, Sulfur, and Silicon*, **104**, 103 (1995).

[25] a) D. V . Khasnis, J. M. Burton, J. D. McNeil, H. Zhang and M. Lattman, *Phosphorus, Sulfur, and Silicon*, **75**, 253 (1993); b) D. V . Khasnis, J. M. Burton, D. J. McNeil, C. J. Santini, H. Zhang and M. Lattman, *Inorg. Chem.*, **33**, 2657 (1994).

[26] 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.*, **1993**, 506.

[27] J. P. M. van Duynhoven, R. G. Janssen, W. Verboom, S. M. Fanken, A. Casnati, A. Pochini, R. Ungaro, J. de Mendoza, P. M. Nieto, P. Prados and D. N. Reinhoudt, *J. Amer. Chem. Soc.*, **116**, 5814 (1994).

[28] J.-B. Regnouf de Vains, S. Pellet-Rostaing and R. Lamartine, *Tetrahedron Letters*, **35**, 8147 (1994).

[29] J. K. Moran and D. M. Roundhill, *Phosphorus, Sulfur, and Silicon*, **71**, 7 (1992).

[30] J. Gloede, Lecture on the XIth. International Conference on Chemistry of Phosphorus Coumpounds (ICCPC-XI), Kazan (Russia), 1996, Sept. 12th., publication in preparation.

[31] Studies on the dynamics of phosphorylated p-tert-butylcalix[6]arenes see [32].

[32] R. G. Janssen, J. P. M. van Duynhoven, W. Verboom, G. J. van Hummel, S. Harkema and D. N. Reinhoudt, *J. Amer. Chem. Soc.*, **118**, 3666 (1996).