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Délivré par :

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Calix[4]arènes chiraux contenant des groupes phosphine comme ligands pour la catalyse

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Calix[4]arènes chiraux contenant des groupes phosphine comme ligands pour la catalyse

Chiral phosphorus containing calix[4]arenes for asymmetric catalysis

Chimie Organométallique et de Coordination

THESE

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Résumé de thèse

Sujet : Calix[4]arènes chiraux contenant des groupes phosphine comme ligands pour la catalyse.

La thèse est consacrée à la développement de méthodes efficaces pour la synthèse d'une nouvelle classe d'intrinsèquement chiral calix[4]arènes contenant du phosphore, phosphines et acides phosphoriques avec une certaine disposition mutuelle des groupes fonctionnels sur le bord inférieur du macrocycle, avec un potentiel activité catalytique. La façon optimale fot la synthèse de calix[4]arènes contenant du phosphore par la substitution progressive des hydroxyles phénoliques a été développé afin de concevoir des intrinsèquement chiral calix[4]arènes avec des types de remplacement ABHH et ABCH au bord inférieur du macrocycle. En utilisant ces techniques, la synthèse de la six catalyseurs et efficaces avec chiralité planaire a été réalisée. En utilisant des études de diffraction des rayons X a permis d'étudier la localisation spatiale des groupes fonctionnels.

L'utilisation de la réaction de Mitsunobu autorisé à fournir une synthèse de la nouvelle "poche" -comme ligands - calix[4]arènes portant des fragments ferrocényle-phosphines chirales. L'efficacité des nouveaux ligands phosphine synthétisés a été confirmé par l'exemple du modèle de réaction Tsuji-Trost. intéressante dépendance du niveau de sélectivité de la taille du cation de métal de base ajoutée, en raison de l'effet de ligand de chélation du supramoléculaire a été observée.

Calix[4]arènes acides phosphoriques a d'abord été appliqués comme organocatalyseurs la série de réactions modèles: aza-Diels-Alder, aza-Mukayiama réaction asymétrique et réaction d'ouverture d’époxydes anneau.

Il a été constaté que la plupart des composés synthétisés présentent un degré notable de activitydue catalytique à des caractéristiques de chiralité interne.

Summary

Subject : Chiral phosphorus containing calix[4]arenes for asymmetric catalysis.

The thesis is devoted to the developing of effective methods for the synthesis of new class of inherently chiral phosphorus-containing calix[4]arenes, phosphines and phosphoric acids with a certain mutual arrangement of functional groups on the lower rim of the macrocycle, with potential catalytic activity. The optimal way fot the synthesis of phosphorus-containing calix[4]arenes by the stepwise substitution of the phenolic hydroxyls was developed in order to design inherently chiral calix[4]arenes with ABHH and ABCH replacement types at the lower rim of the macrocycle. By using these techniques, synthesis of six analogues of known and effective catalysts with planar chirality was performed. Using X-ray diffraction studies allowed to investigate spatial location of functional groups.

Using of Mitsunobu reaction allowed to provide synthesis of the new "pocket"-like ligands – calix[4]arenes bearing chiral ferrocenyl-phosphines moieties. The effectiveness of the synthesized new phosphine ligands was confirmed by the example of the model Tsuji–Trost reaction. Interesting dependence of the selectivity level on the metal cation size of added base, due to chelation effect of supramolecular ligand was observed.

Calix[4]arenes phosphoric acids was first applied as organocatalysts the series of model reactions: aza-Diels–Alder reaction, aza-Mukaiyama asymmetric reaction and epoxides ring opening reaction.

It was found that most of the synthesized compounds exhibit a noticeable level of catalytic activitydue to features of internal chirality.

Talbe of contents

ABBREVIATIONS

d	Doublet
DABCO	1,4-diazabicyclo[2.2.2]octane
dd.	Dublet of dublets
CDI	Carbonyldiimidazole
DCM	Dichloromethane
DMF	N,N-Dimethylformamide
DMSO	Dimethyl sulfoxide
IR	Infrared spectroscopy
q.	Quartet
LDA	Lithium diisopropylamide
m.	Multiplet
ppm	Parts Per Million
br. s.	Broaded singlet
s.	Singlet
t.	Triplet
THF	Tetrahydrofuran
TMS	Trimethylsilyl
m. p.	Melting point
TPP	Triphenyl phospine
TLC	Thin-layer chromatography
UV	Ultraviolet–visible spectroscopy
min.	Minute
NMR	Nuclear magnetic resonance spectroscopy
J	J-coupling constant
δ	Chemical shift

Introduction

Despite the large number of catalysts suitable for widespread use in industrial processes, searching for more effective and affordable materials is still an important task. Most of the currently existing catalysts have high selectivity only to a narrow range of substrates. Thus, the development of catalysis depends on research aimed at finding compounds with greater catalytic activity and selectivity to the widest possible range of substrates.

Several ferrocenylphosphines have already be well established as effective ligands for a wide range of homogeneous catalysis reactions (hydrogenation of unsaturated compounds of different classes, cross-coupling, carbonylation, metathesis). Grafting of these kind of molecules to substrates with potential "host"-properties is a key aspect of modern research supramolecular chemistry.

In another hand, calix[4]arenes are a well-known family of polyphenolic compounds which found application in various fields of modern chemistry [1-5]. Interest in these macrocycles is growing, despite the fact that rational methods of their obtaining became available about 35 years ago. Their success as molecular synthon to build sophisticated functional molecules, essentially depends on two main factors: their ability to control the orientation and sequence of substituents attached to one of the macrocycle crowns; their special three-dimensional structure that defines a molecular cavity with potential receptor properties. It is worth to note that macrocycle skeleton can take many flexible conformations depending on the chemical modification. Initial studies of P(III)-modified calix[4]arenes were focused on the synthesis tetraphosphinites through the lower rim of calix[4]arene. These compounds have their P(III) binding sites in close proximity, and therefore had to assist the cooperative interaction effects between centers of coordinated metals. Many further studies on coordination chemistry of P(III)-modified calix[4]arenes

exploit some specific structural and functional characteristics of polyphenolic macrocyclic backbone. Among them, more than 50 papers reporting attempts to use of such catalytic ligands, some of which are of scientific interest in supramolecular chemistry.

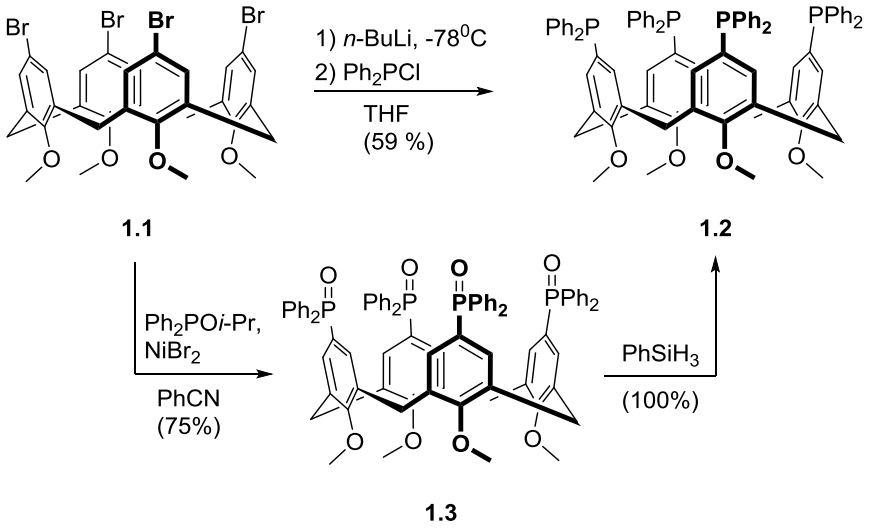
CHAPTER 1
SYNTHESIS AND CATALYTIC PROPERTIES OF P (III) AND P(V)-FUNCTIONALYSED CALIX[4]ARENES
(Literary Review)

This study concerns P(III) (phosphines) and P(V)-containing calix[4]arene derivatives (including phosphoric acids). Some aspects of the chemistry described in this section were discussed in various reviews and books published in recent years [6-11].

1.1. Synthesis of P (III) and P (IV)-containing calix[4]arenes

1.1.1. Phosphines

The first calix[4]arenes containing trivalent phosphorus atoms in the upper rim of macrocycle were synthesized by Hamad and others. [12]. Tetraphosphine **1.2** was obtained from tetrabromo calix[4]arene **1.1** [13] by reaction with *n*BuLi followed by reaction with Ph_2PCl (Scheme 1.1). In solution, compound **1.2** exists as a mixture of conformers in interconversion.

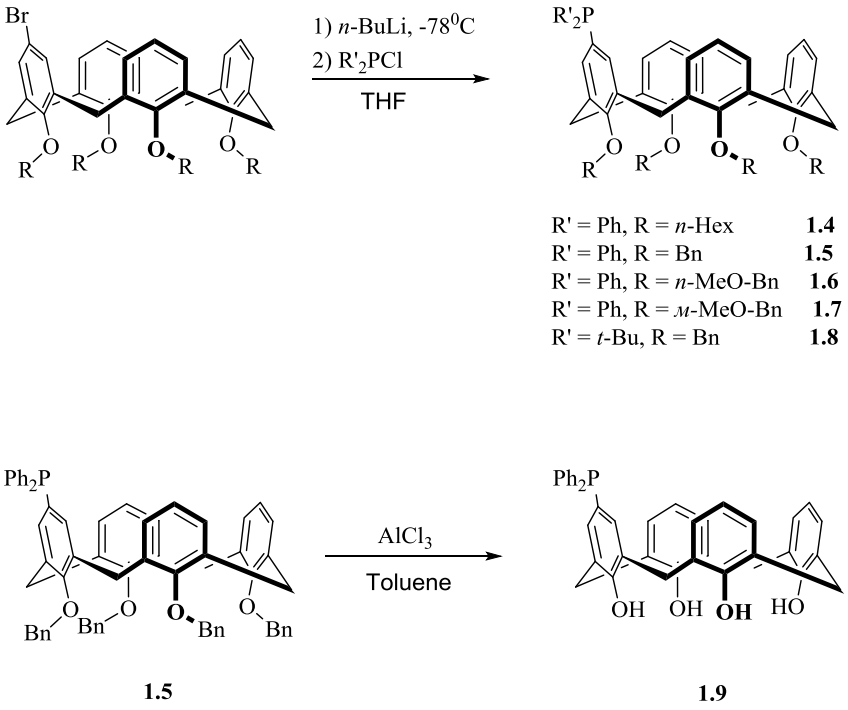


1.1 **1.2** **1.3**

Scheme 1.1. Introduction of P(III)-atoms to the upper crown of calix[4]arene platform.

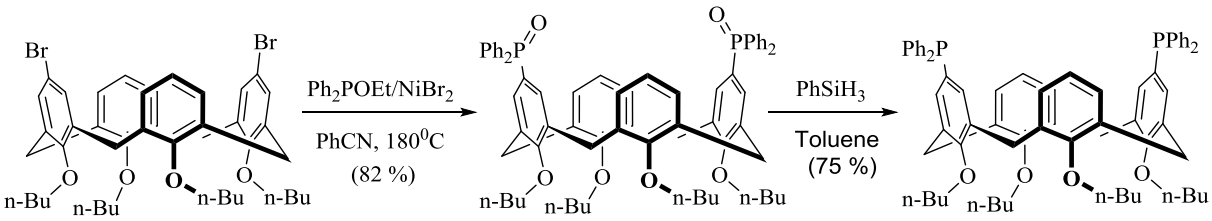
The same compound was obtained also by Kalchenkos et al. using a two-step methodology: first the nickel-catalyzed phosphorylation of **1.1** by Ph_2POiPr yielding phosphine oxide **1.3**, which was then quantitatively reduced to **1.2** with $PhSiH_3$ (Scheme 1.1) [14].

Inspired by Hamada's method, Monnereau et al. prepared the monophosphines **1.4**-**1.8** (Scheme 1.2). The yield of these reactions depended on the substituent (R) attached at the lower rim [15,16]. Reaction of **1.5** with $AlCl_3$ resulted in the formation of **1.9**. ^1H NMR ($CDCl_3$) spectrum of **1.9** is consistent with fast trans annular rotation of the phenoxy groups occurring in solution.



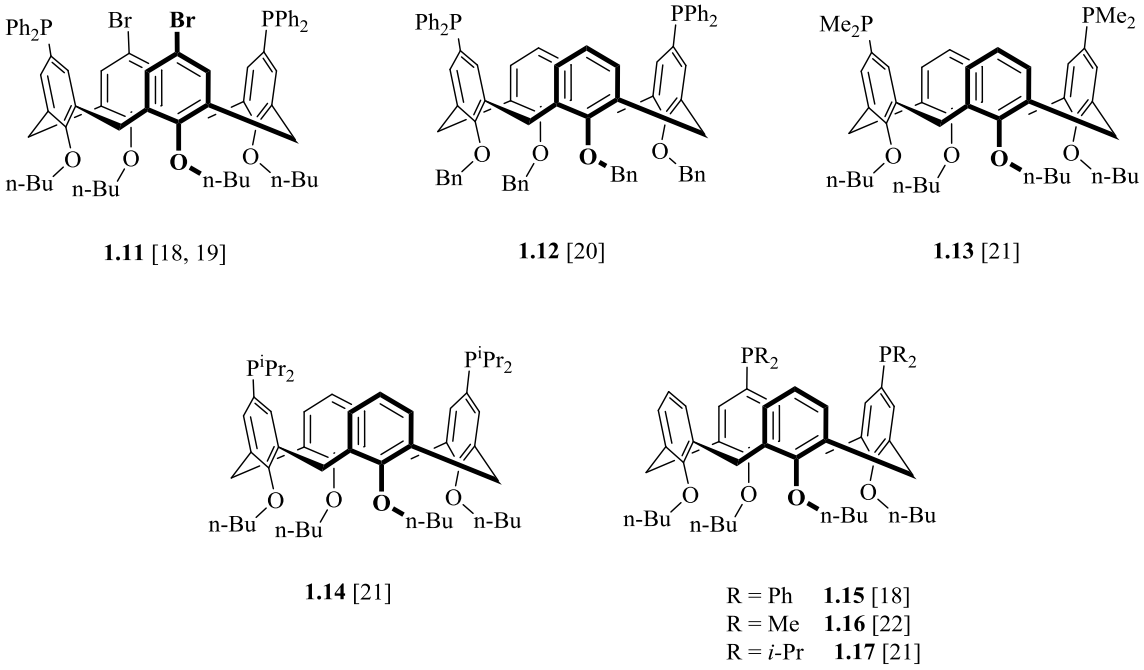
Scheme 1.2. Synthesis of phosphines **1.4**-**1.9** starting from a monobromo calix[4]arene.

It is worth of note that upper-rim diphosphinated versions of the above calixarenes could be prepared either via the modified Arbuzov procedure (**1.10**-**1.17**, Figure. 1.2) (**1.10** Scheme 1.3) [17] or by using Hamada's method [18-21].



1.10

Scheme 1.3. Synthesis of phosphine **1.10** starting from a dibromo calix[4]arene via the modified Arbuzov procedure.



1.11 [18, 19]

1.12 [20]

1.13 [21]

1.14 [21]

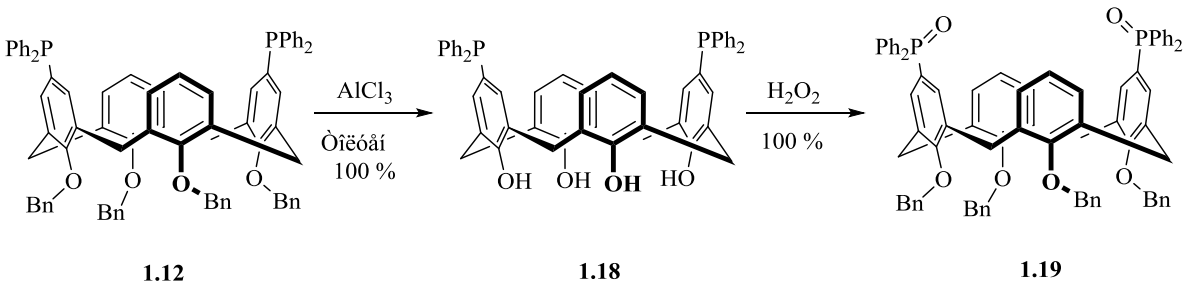
R = Ph **1.15** [18]
R = Me **1.16** [22]
R = *i*-Pr **1.17** [21]

Figure. 1.2. Obtained calix[4]arenyl-diphosphines **1.11-1.17**.

For practical reasons,the air sensitive dialkylphosphines **1.13**, **1.14**, **1.16**, **1.17** were isolated as phosphine oxides. These were then conveniently reduced with $PhSiH_3$ into the corresponding phosphines.

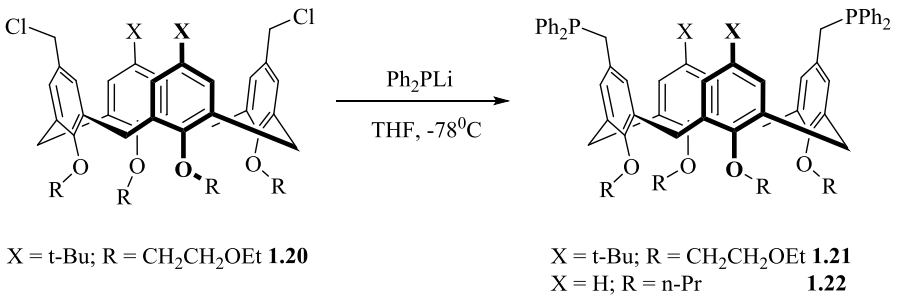
Diphosphine **1.18** was quantitatively obtained by debenzylation of **1.12** with $AlCl_3$ in toluene (Scheme 1.4) [22]. Like monophosphine **1.9**, diphosphine **1.18** exists in solution as several interconverting conformers. An X-ray structure

determination was carried out for the phosphine oxide **1.19** showing a conical structure of the calixarene moiety in the solid state.



Scheme 1.4. Synthesis of diphosphine **1.18**.

Diphosphine **1.21** was synthesised by Matt et al. by reaction of the calix[4]arene **1.20** with two equiv. of *in situ* generated Ph_2PLi (Scheme 1.5) [23]. The same procedure was applied by Kubas et al. for the synthesis of diphosphine **1.22** (Scheme 1.5) [24].



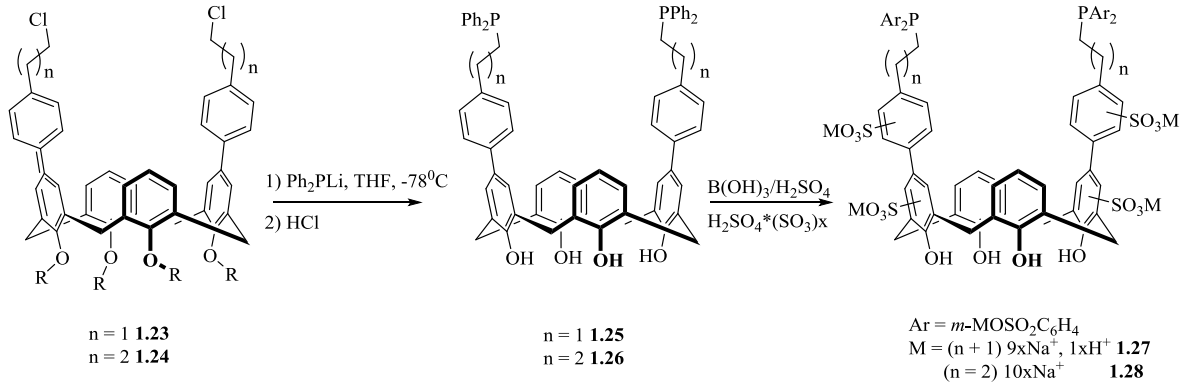
X = t-Bu; R = CH_2CH_2OEt **1.20**

X = t-Bu; R = CH_2CH_2OEt **1.21**
X = H; R = n-Pr **1.22**

Scheme 1.5. Synthesis of diphosphines **1.21** and **1.22**.

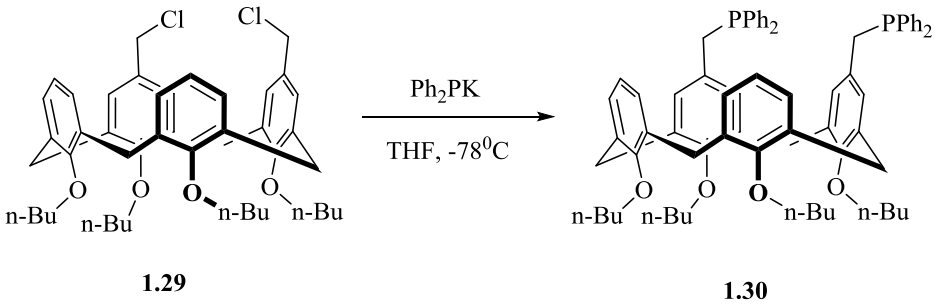
In 2000, Shimizu et al. prepared the water-soluble calix[4]arenyl-phosphines **1.27** and **1.28** in two steps: (a) reaction of Ph_2PLi with halogenides **1.23** and **1.24**, leading to **1.25** and **1.26**; (b) reaction of the resulting phosphines with orthoboric acid in H_2SO_4, and finally with oleum, affording the decasulfonated derivatives **1.27** and **1.28** (Scheme 1.6) [25]. ^{31}P NMR data indicate that during each synthesis several phosphines formed, together with

phosphine oxides. The catalytic applications of these water-soluble ligands were performed in the presence of the corresponding phosphine oxides.



Scheme 1.6. Synthesis of the water-soluble calix[4]arenyl-phosphines **1.27** and **1.28**.

In 2008, Harvey et al. described the synthesis of diphosphine **1.30** prepared by reacting the proximally bis-chloromethylated calix[4]arene with Ph_2PK (Scheme 1.7) [26].

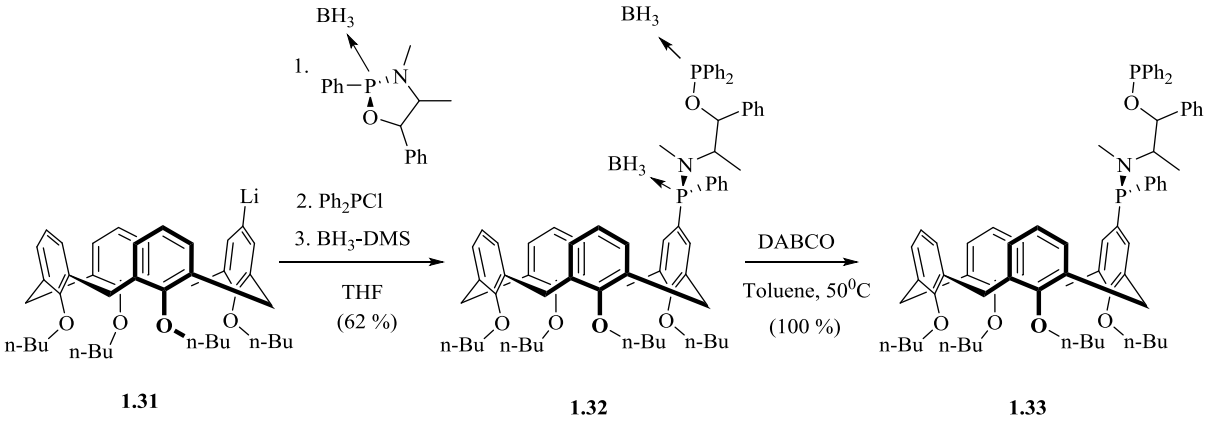


Scheme 1.7. Synthesis of the proximally functionalised calix[4]arene **1.30**.

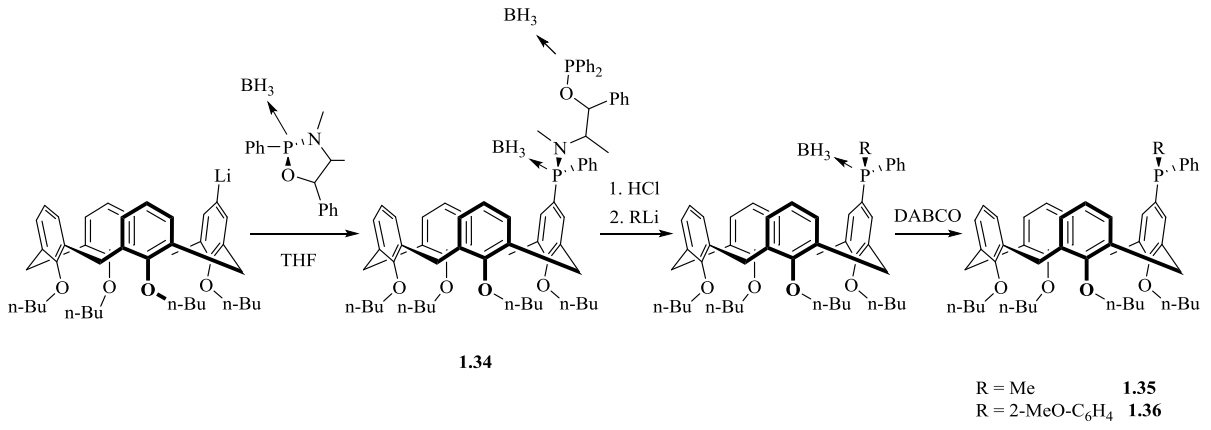
In 2010, Jugé, Harvey et al. achieved the synthesis of the enantiomerically pure aminophosphine-phosphinite **1.33** using Jugé's method. Its synthesis was performed in four steps (Scheme 1.8) [27].

The same autors later applied again Jugé's method in synthesis of monophosphines **1.35** and **1.36** (Scheme 1.9) and diphosphines **1.37**-**1.39**

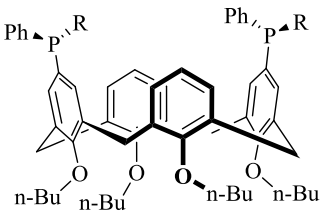
(Figure. 1.3) [28]. P-N bond of intermediate **1.34** broken using HCl, resulting in product – chlorophosphine, which was sub-sequently reacted with the appropriate organolithium reagents.The resulting optically active phosphine-boranes were then treated with DABCO to give the corresponding free phosphine or diphosphine. (Scheme 1.9) [27].



Scheme 1.8. Synthesis of aminophosphine-phosphinite **1.33**.



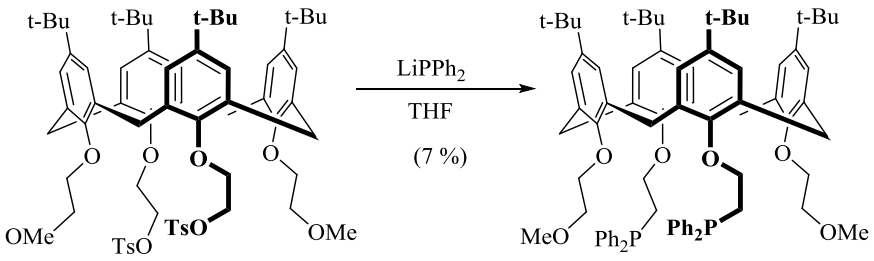
Scheme 1.9. Synthesis of phosphines **1.35** and **1.36**.



R =Me **1.37**
R = 2-MeO-C_2H_4 **1.38**
R = Fc **1.39**

Figure. 1.3. Diphosphines **1.37-1.39**.

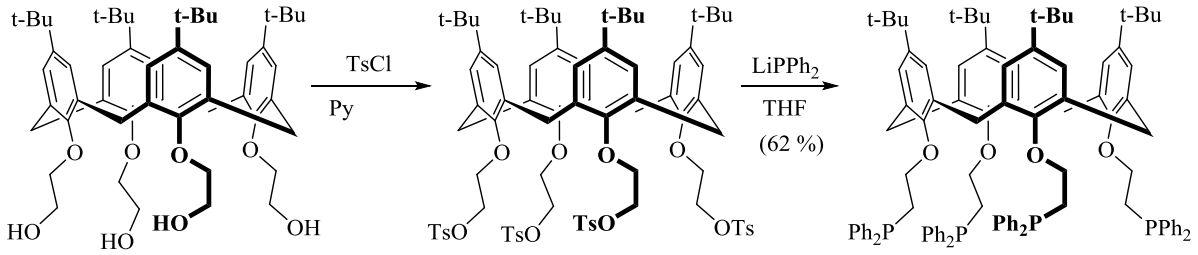
Matt et al. described the synthesis of calix[4]arene **1.41** with two dangling-$CH_2CH_2PPh_2$ moieties attached to distal positions (Scheme 1.10) [29].



1.40 **1.41**

Scheme 1.10. Synthesis of diphosphine **1.41**.

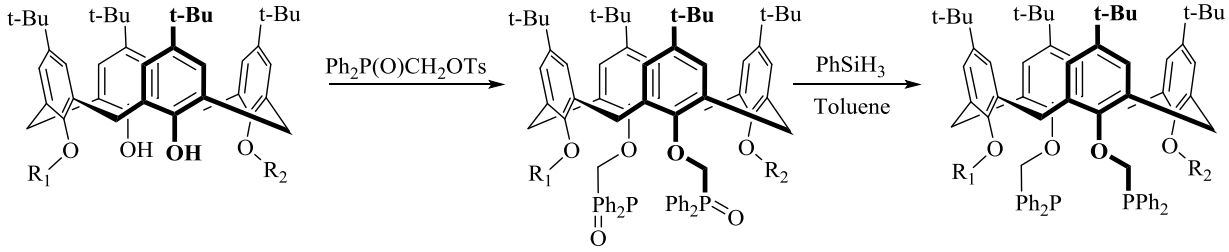
The anchoring of four such groups was achieved by McKervey et al. by reaction of tetratosylate **1.43** (obtained from tetrol **1.42**) with Ph_2PNa [30]. Obtained calix[4]arene (**1.44**), was synthesised again later by Kollár et al. using Ph_2PLi as source of phosphorus (Scheme 1.11) [31].



1.42 **1.43** **1.44**

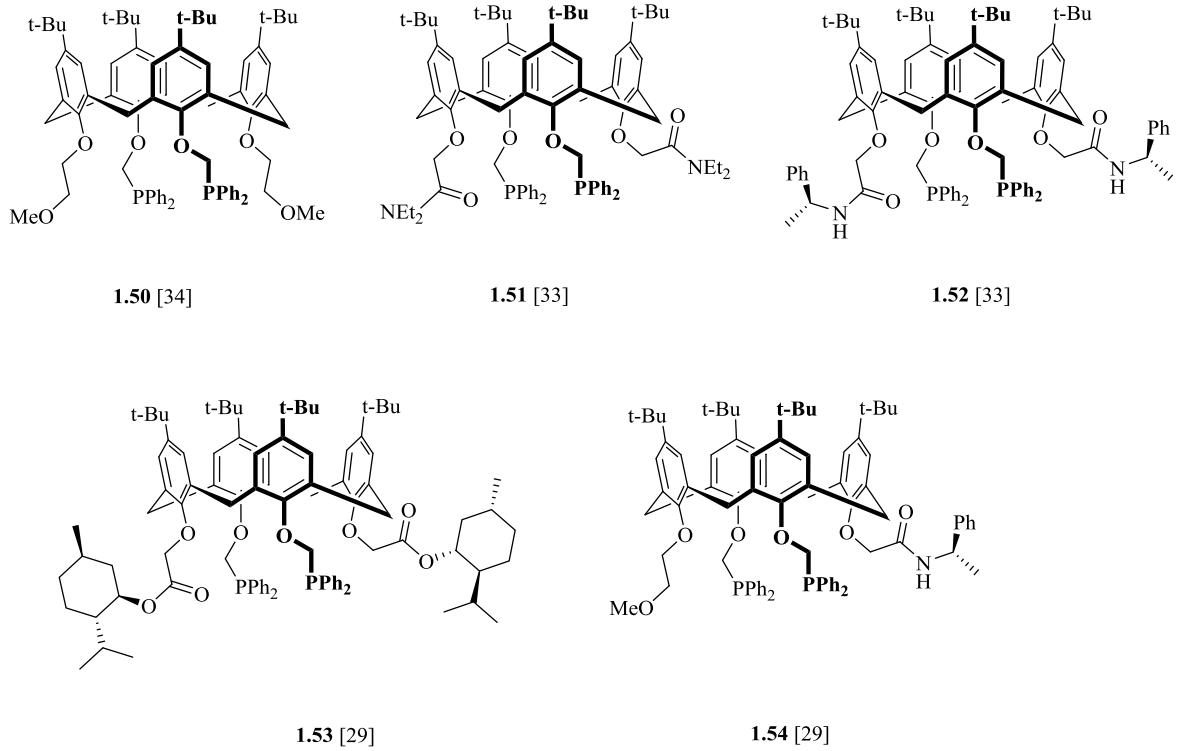
Scheme 1.11. Synthesis of tetraphosphine **1.44**.

A series of calix[4]arenes substituted at the lower rim by two distally positioned CH_2PPh_2 groups [32], were obtained by alkylation of the dihydroxy-dialkylated precursors **1.45-1.49** with $Ph_2P(O)CH_2OTs$ and reduction of the resulting doubly-phosphorylated compounds **1.50-1.54** with $PhSiH_3$ (Scheme 12, Figure. 4) [29,33,34].



1.45 - 1.49 **1.50 - 1.54**

Scheme 1.12. Synthesis of distally substituted diphosphines.

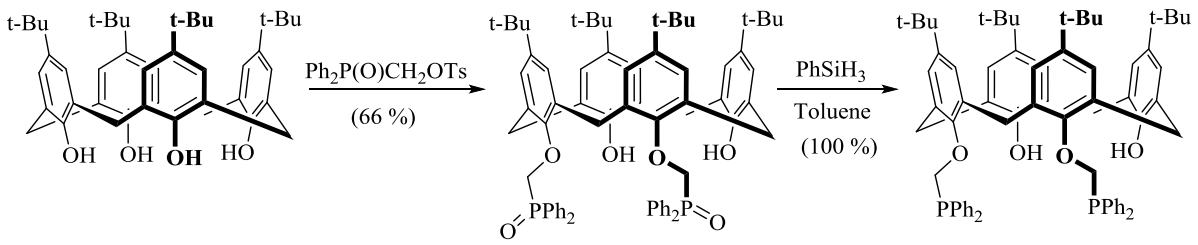


1.50 [34] **1.51** [33] **1.52** [33]

1.53 [29] **1.54** [29]

Figure. 1.4. Diphosphines **1.50**-**1.54**.

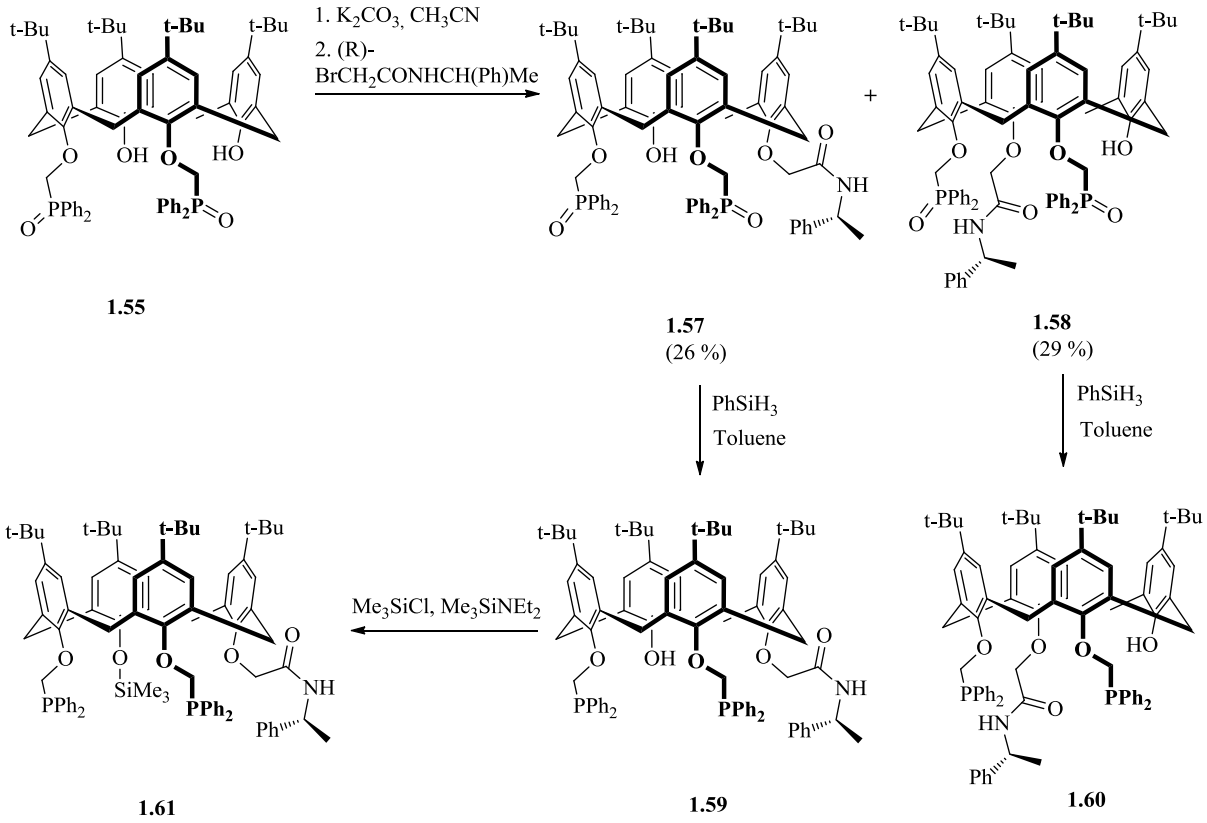
The synthesis of calix[4]arene **1.56**, which contains two -CH_2PPh_2 substituents attached to proximal positions of its backbone, was achieved with the same alkylating reagent than for the preparation of **1.50**-**1.54**, but using NaH as the base [35]. Intermediate **1.55** was obtained with 66% yield [36]. Its reduction with $PhSiH_3$ lead to quantitative formation of **1.56** (Scheme 1.13) [37].



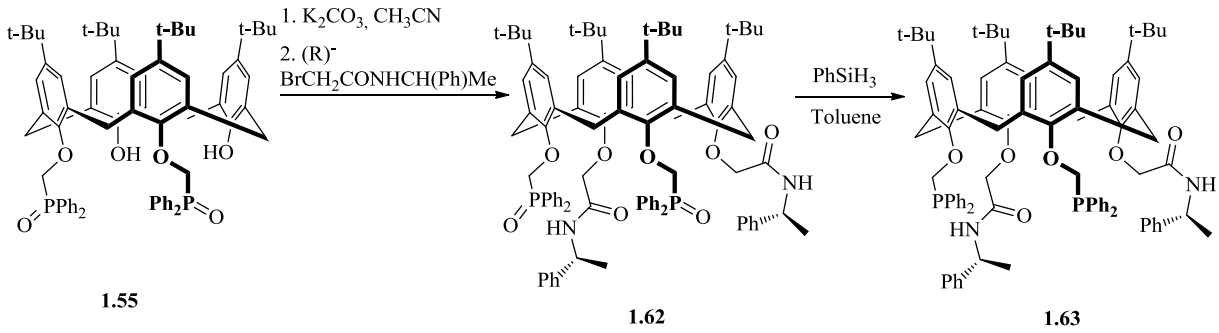
1.55 **1.56**

Scheme 1.13. General synthesis of distal diphosphines.

The dihydroxy-calix[4]arene **1.55** is a useful synthon for the preparation of chiral diphosphines. Treatment of **1.55** with (R)-$BrCH_2C(O)NHCHMePh$ in the presence of 0.5 equiv. of K_2CO_3 yields the two diastereoisomers **1.57** and **1.58**, which were separated by column chromatography (Scheme 1.14). Their reduction with $PhSiH_3$ gave the corresponding optically active diphosphines **1.59** and **1.60**. Alkylation of **1.59** by Me_3SiCl gave selectively the enantiomerically pure diphosphine **1.61** with a cone conformation.



Scheme 1.14. Synthesis of optically pure diphosphines **1.59-1.61**.

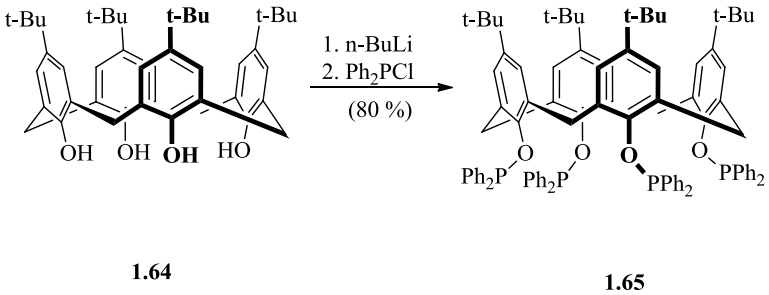


Scheme 1.15. Synthesis of optically pure diphosphine **1.63**.

Repeating the alkylation of **1.55** with two equiv. of (R)-$BrCH_2C(O)NHCHMePh$ lead to formation of **1.62** with high yield. The latter was conveniently converted with $PhSiH_3$, into enantiomerically pure diphosphine **1.63** (Scheme 1.15) [38].

1.1.2. Phosphinites

In 1989, Floriani et al. reported the first P(III)-functionalised calix[4]arenes. Among these is tetraphosphinite **1.65**, which was obtained by deprotonation of **1.64** with a strong base, followed by reaction with Ph_2PCl (Scheme 1.16) [40].

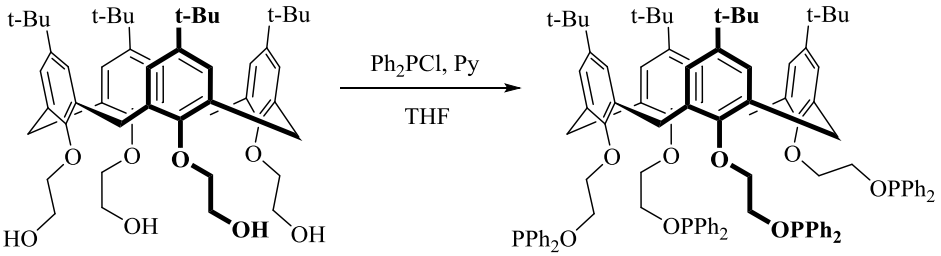


Scheme 1.16. Synthesis of tetraphosphine **1.65**.

This compound was intended to be used as a P_4- platform for forming tetranuclear complexes in which the four metal atoms lie in close proximity and may therefore facilitate synergetic interactions in catalytic reactions. Related

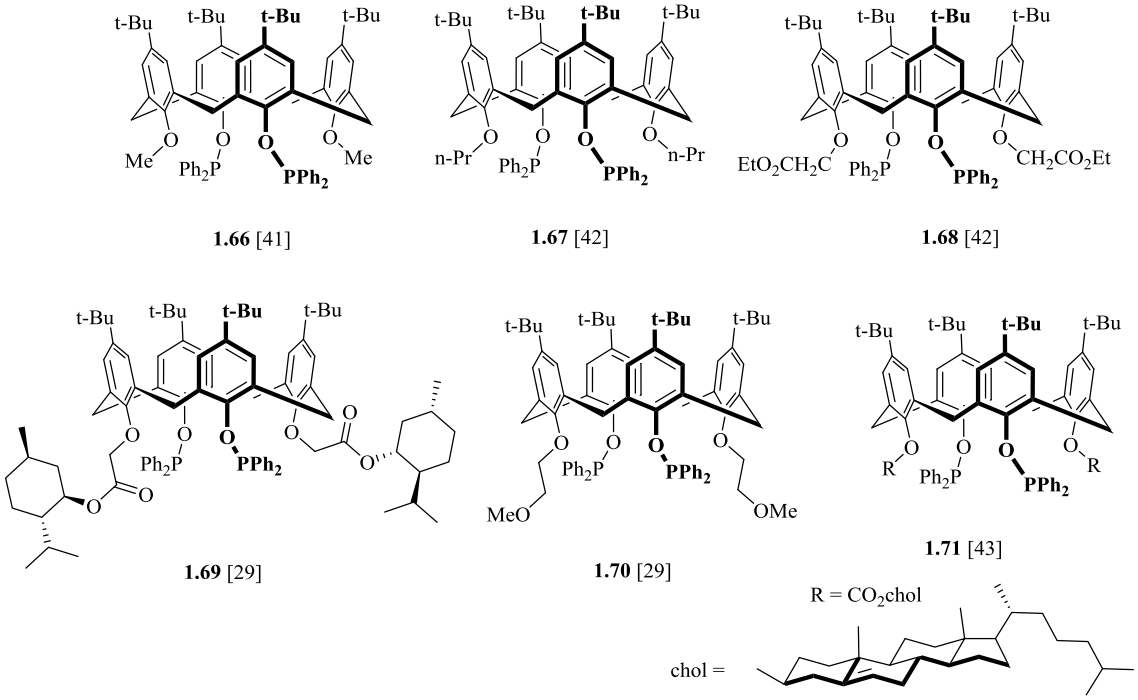
calixarenes bearing only two phosphinito groups, notably **1.66-1.71** (Figure. 1.5), were reported later, independently by Roundhill [41] and Matt [29,42,43].

A calix[4]arene O-substituted by four -$CH_2CH_2OPPh_2$ pending arms **1.72** was obtained by Kollár et al. by reacting tetrol **1.42** with Ph_2PCl in the presence of pyridine (Scheme 1.17) [31].



1.42 **1.72**

Scheme 1.17. Synthesis of tetraphosphinite **1.72**.



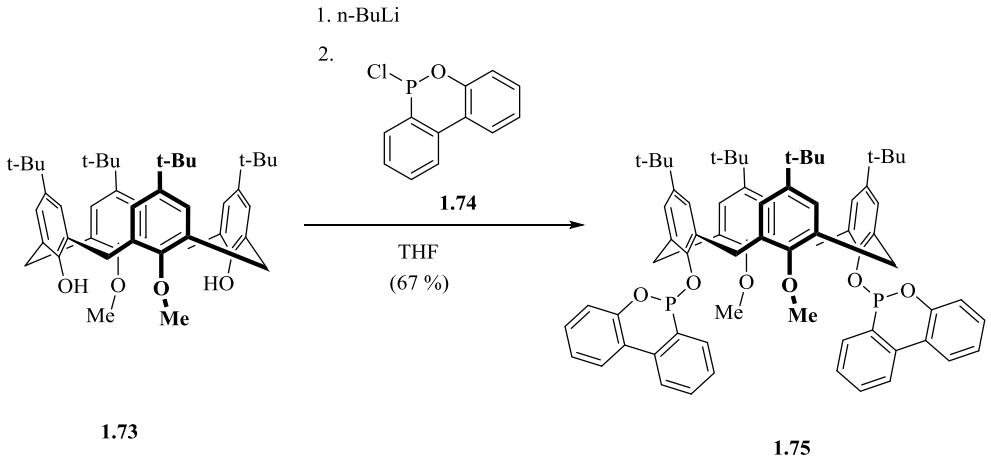
1.66 [41] **1.67** [42] **1.68** [42]

1.69 [29] **1.70** [29] **1.71** [43]

Figure. 1.5. Diphosphinites **1.66-1.71**.

1.1.3. Phosphonites

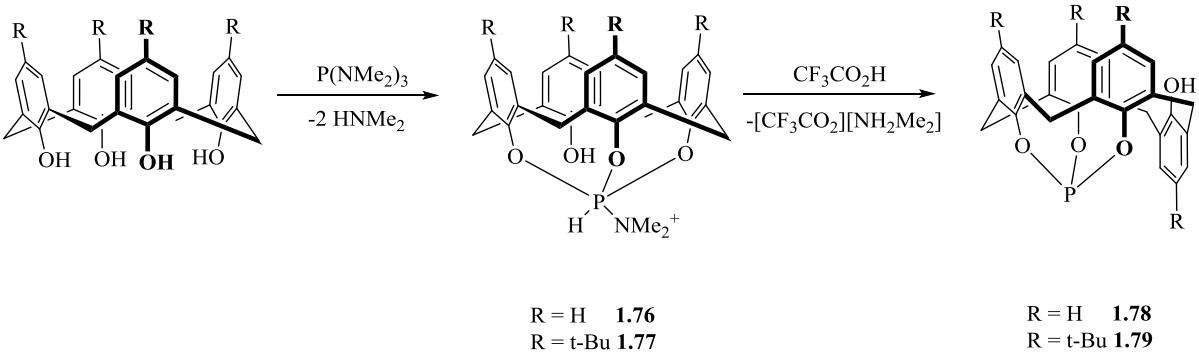
To date, only one phosphonite-calix[4]arene has been used in catalysis, namely **1.75**. Its synthesis involved treatment of dihydroxyl-calix[4]arene **1.73** with n-BuLi and chlorophosphonite **1.74** (Scheme 1.18) [44].



Scheme 1.18. Synthesis of diphosphonite **1.75**.

1.1.4. Phosphites

In 2000, Pringle et al. reported the synthesis of phosphites **1.78** and **1.79** each having their phosphorus atom capping three oxygen atoms of a calix[4]arene skeleton. They were obtained by slow addition of trifluoroacetic acid to a solution of the hexacoordinate phosphorus(V) derivatives **1.76** and **1.77** [45]. Precursors were obtained according to a method previously described by Lattman, by reacting a calix[4]arene with $P(NMe_2)_3$ (Scheme 1.19) [46].



Scheme 1.19. Synthesis of phosphites **1.78** and **1.79**.

Water-soluble phosphite **1.80** (Figure. 1.6), was prepared in the same manner, but starting from p-$(SO_3H)_4$-calix[4]arenes [47].

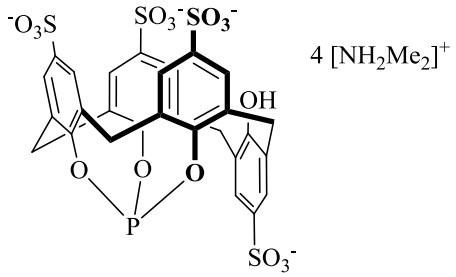
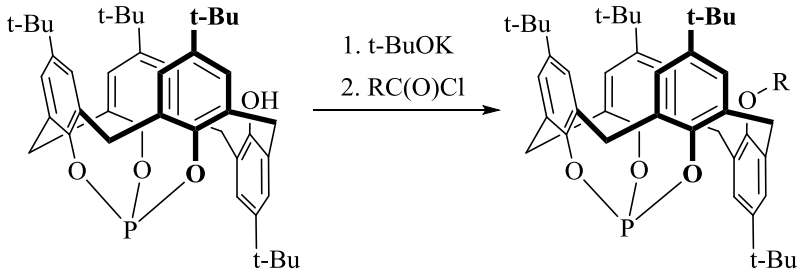


Figure. 1.6. Water-soluble phosphite **1.80**.

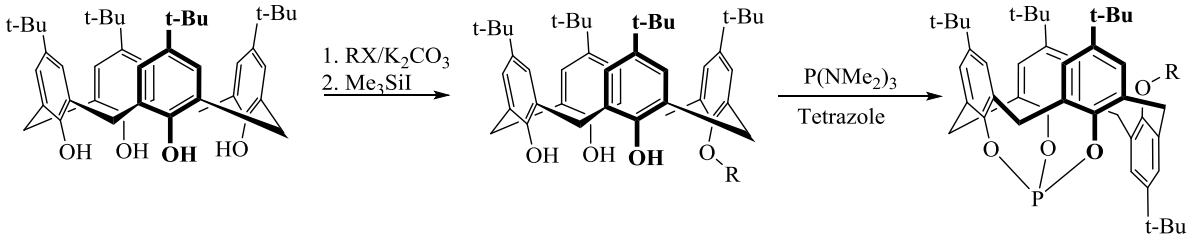
Van Leeuwen et al. obtained calix[4]arene phosphites **1.81** and **1.82** by acylation of **1.79** after treatment with t-BuOK (Scheme 1.20) [48]. All attempt to obtain compounds **1.83-1.86** by the simple alkylation of phosphite **1.79** failed. However, these compounds were synthesized in two steps : (a) monoalkylation of *p-tert*-butyl-calix[4]arene; (b) reaction of the resulting (tris-hydroxy)-(alkyl)-calix[4]arene with $P(NMe_2)_3$ in the presence of tetrazole (Scheme 1.21).



1.79

R = C(O)Me **1.81**
R = C(O)Ph **1.82**

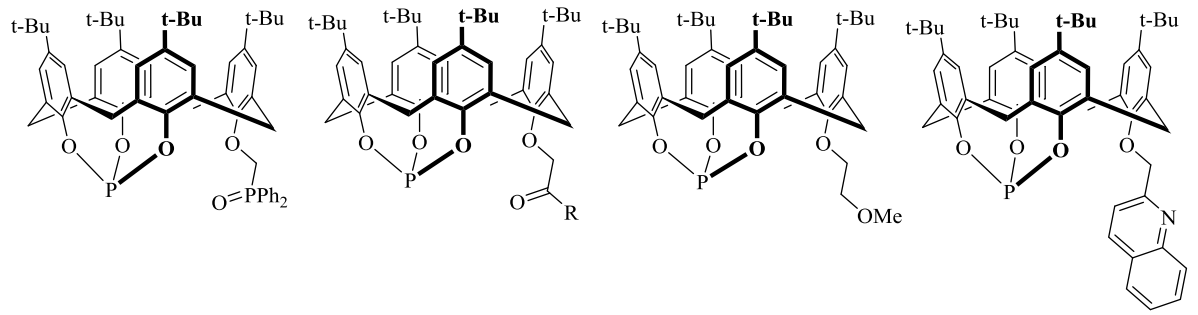
Scheme 1.20. Synthesis of phosphites **1.81** and **1.82**.



R = Me **1.83**
R = CH_2Ph **1.84**
R = CH_2Ph **1.85**
R = i-Pr **1.86**

Scheme 1.21. Synthesis of phosphites **1.83 - 1.86**.

The groups of van Leeuwen and Matt independently developed an alternative synthetic pathway to prepare phosphites with additional coordinating fragment (phosphine oxide, ester, amide, ether, quinoline). Compounds **1.87-1.91** were prepared by reaction of the appropriate mono-O-alkylated precursor with PCl_3/NEt_3 (Figure. 1.7) [29,36,49,50,50,51].



1.87 [51]

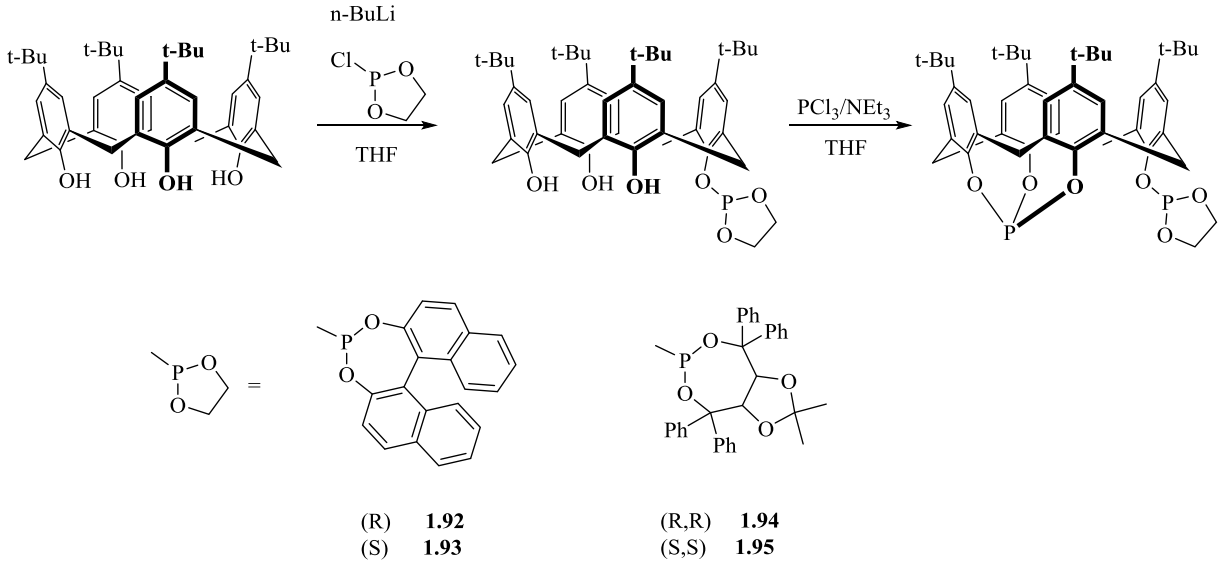
R = OEt **1.88** [51]
R = NEt_2 **1.89** [51]

1.90 [51]

1.91 [50]

Figure. 1.7. Phosphites **1.87 – 1.91**.

van Leeuwen et al. extended this two-step synthetic route to the design of the optically active BINOL-derived phosphites **1.92-1.93** and TADDOL derivatives **1.94-1.95** (Scheme 1.22) [52].



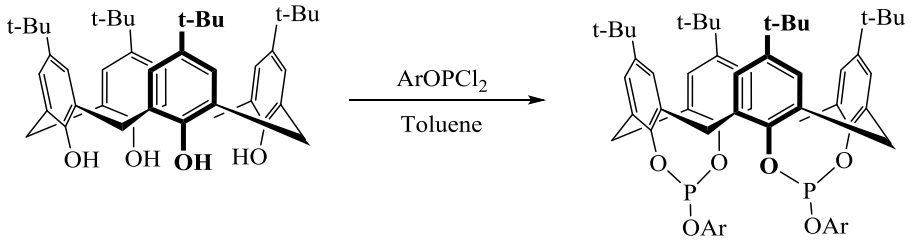
(R) **1.92**
(S) **1.93**

(R,R) **1.94**
(S,S) **1.95**

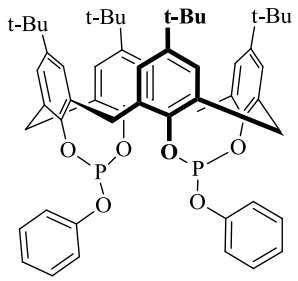
Scheme 1.22. Synthesis of phosphites **1.92 - 1.95**.

In 1999, Paciello and Röper described the synthesis of diphosphites **1.98-1.101**, that have each phosphorus atoms bridging to two neighbor phenolic rings (Figure. 1.8) [53]. Yields of products were 23-65 % after reaction of *p-tert*-butylcalix[4]arene with two equivalents of corresponding aryl-phosphite

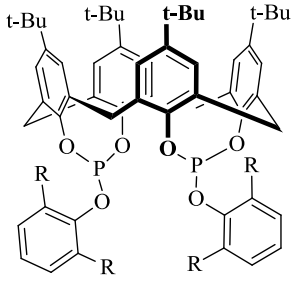
($ArOPCl_2$) in the presence of NEt_3 (Scheme 1.23). Krishnamurty et al. obtained the related diphosphites **1.102-1.104** (Figure. 1.8), using a similar synthetic procedure [54,55].



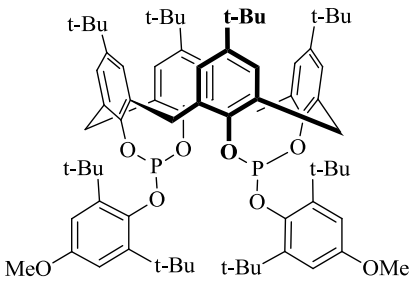
Scheme 1.23. Synthesis of phosphites **1.98 - 1.104**.



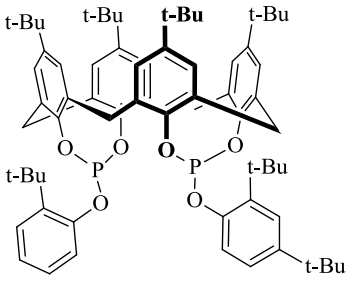
1.98 [53]



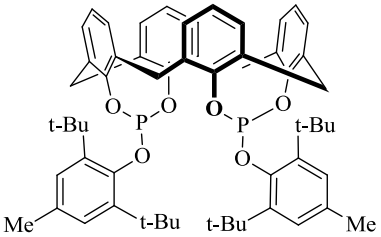
R = Me **1.99** [53]
R = i-Pr **1.100** [53]



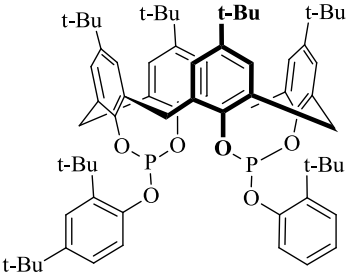
1.101 [53]



1.102 [54]



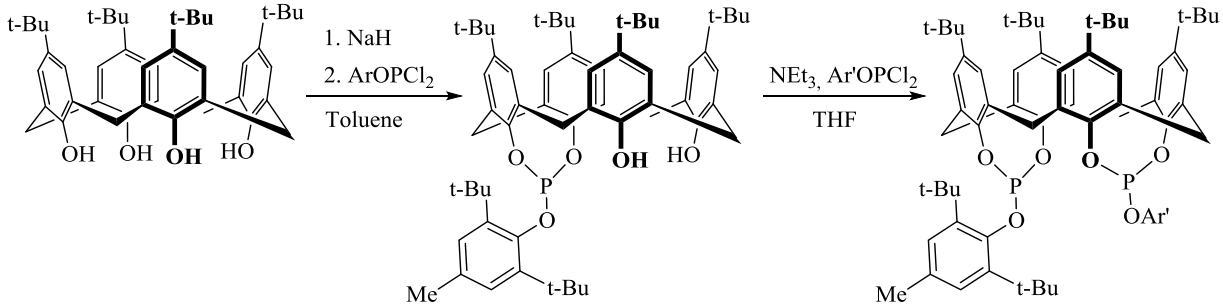
1.103 [55]



1.104 [54]

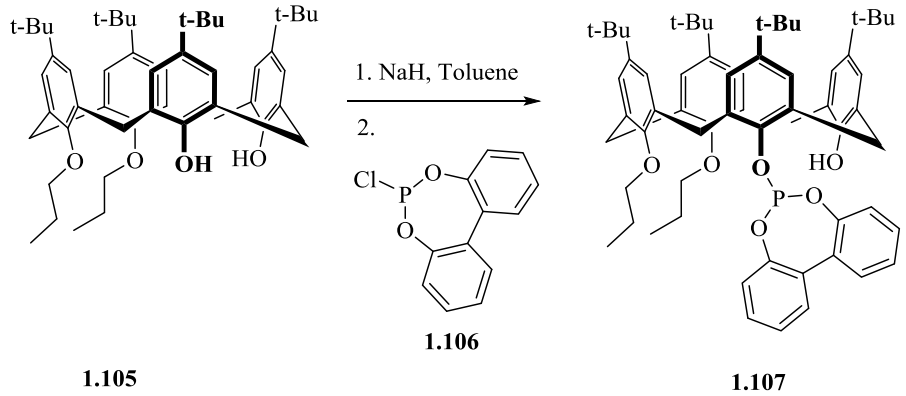
Figure. 1.8. Diphosphites **1.98 – 1.104**.

Krishnamurty also carried out the stepwise construction of related calixarenes having two distinct P(OR) bridging units **1.96** and **1.97** (Scheme 1.24) [56]. Currently, a series of calix[4]arenes phosphites and diphosphites, with phosphorus atom attached to one oxygen atom of the lower rim, was described.



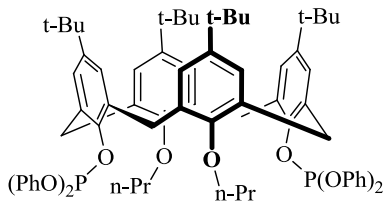
Scheme 1.24. Synthesis of phosphites **1.96** and **1.97**.

A catalytically relevant monophosphite of this family is calix[4]arene **1.105**, which was obtained by mono-deprotonation with NaH of the proximally dipropylated calix[4]arene **1.105**, followed by reaction with one equiv. of [1,1'-biphenyl]-2,2'-phosphorochloridite (**1.106**) (Scheme 1.25) [57].

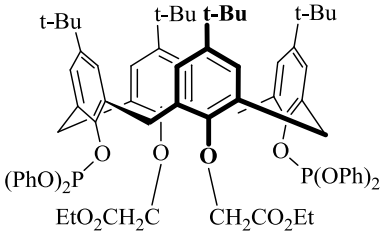


Scheme 1.25. Synthesis of monophosphite **1.107**.

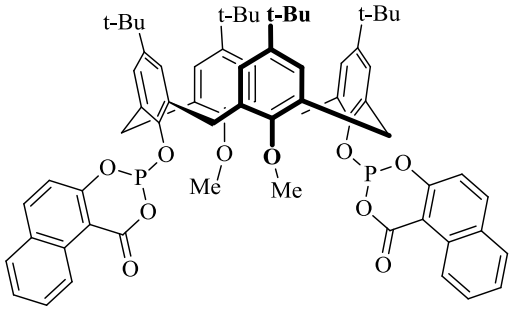
In the calix[4]arene diphosphite series reported to date (**1.108-1.110** [43], **1.111-1.112** [44], **1.113** [58], **1.114** [57], **1.115** [59], **1.116** [60], **1.117-1.118** [61] , **1.119** [60], **1.120-1.124** [62] i **1.125-1.127** [60], Figure. 1.9), all are distally P-substituted. The only reported calix[4]arenes with four $P(OR)_2$ groups binded to their lower rim were described by Schmutzler and Börner in 2001 (**1.146** and **1.147**, Figure. 1.10) [63].



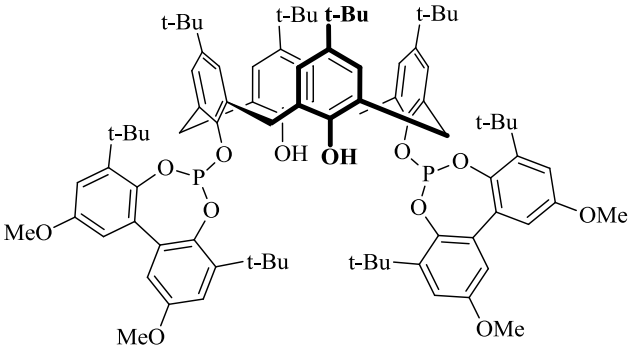
1.108 [43]



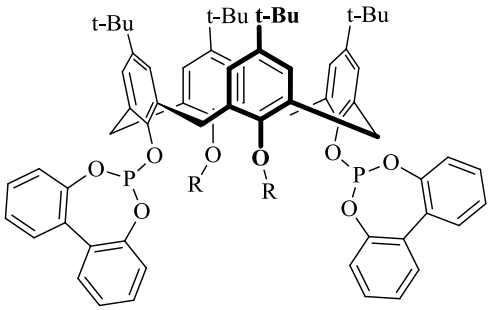
1.109 [43]



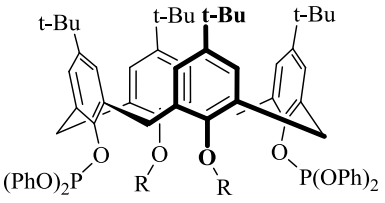
1.111 [44]



1.112 [44]

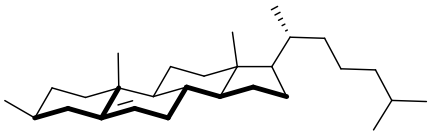


R = CH_3 **113** [58]
R = $CH_2CH_2CH_3$ **114** [57]
R = $CH_2C(O)NEt_2$ **115** [59]

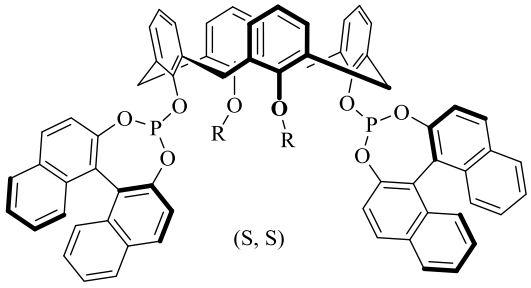


R = CO_2chol

chol =

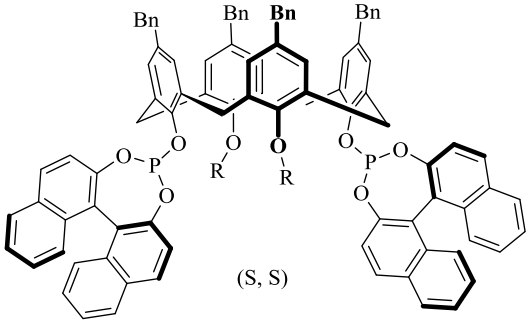


1.110 [43]



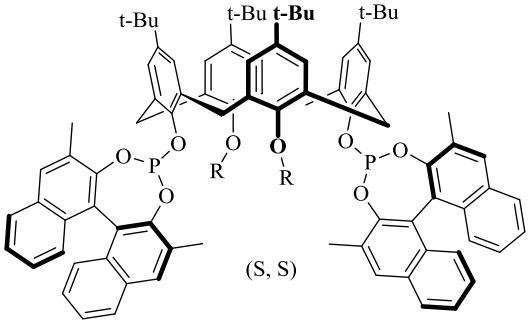
(S, S)

R = $CH_2CH_2CH_3$ **124** [62]
R = CH_3 **125** [60]



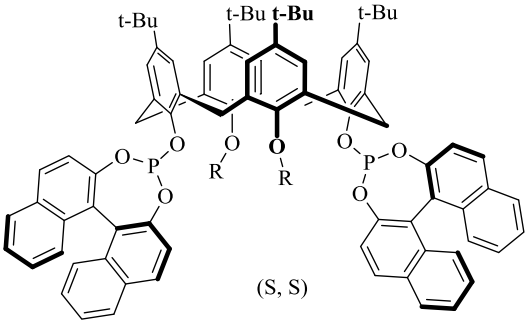
(S, S)

R = CH_2Ph **126** [60]

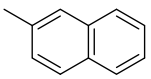
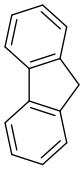


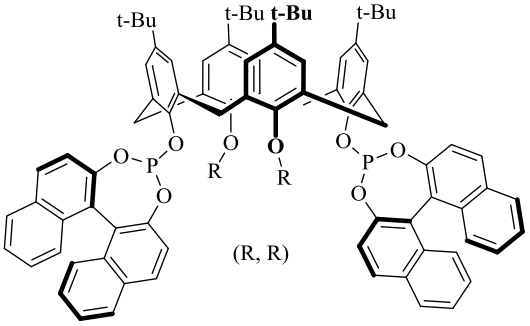
(S, S)

R = CH_2Ph **127** [60]



(S, S)

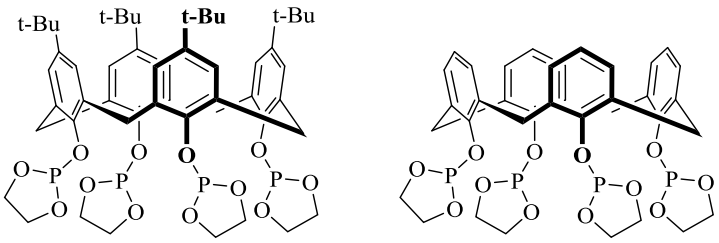
R = CH_3 **116** [60]
R = $CH_2CH_2CH_3$ **117** [61]
R = CH_2Ph **118** [61]
R = $CH_2CH_2CH_2CH_3$ **119** [60]
R =  **120** [62]
R =  **121** [62]



(R, R)

R = $CH_2CH_2CH_3$ **122** [62]
R = CH_2Ph **123** [62]

Figure. 1.9. Diphosphites **1.108 – 1.127**.

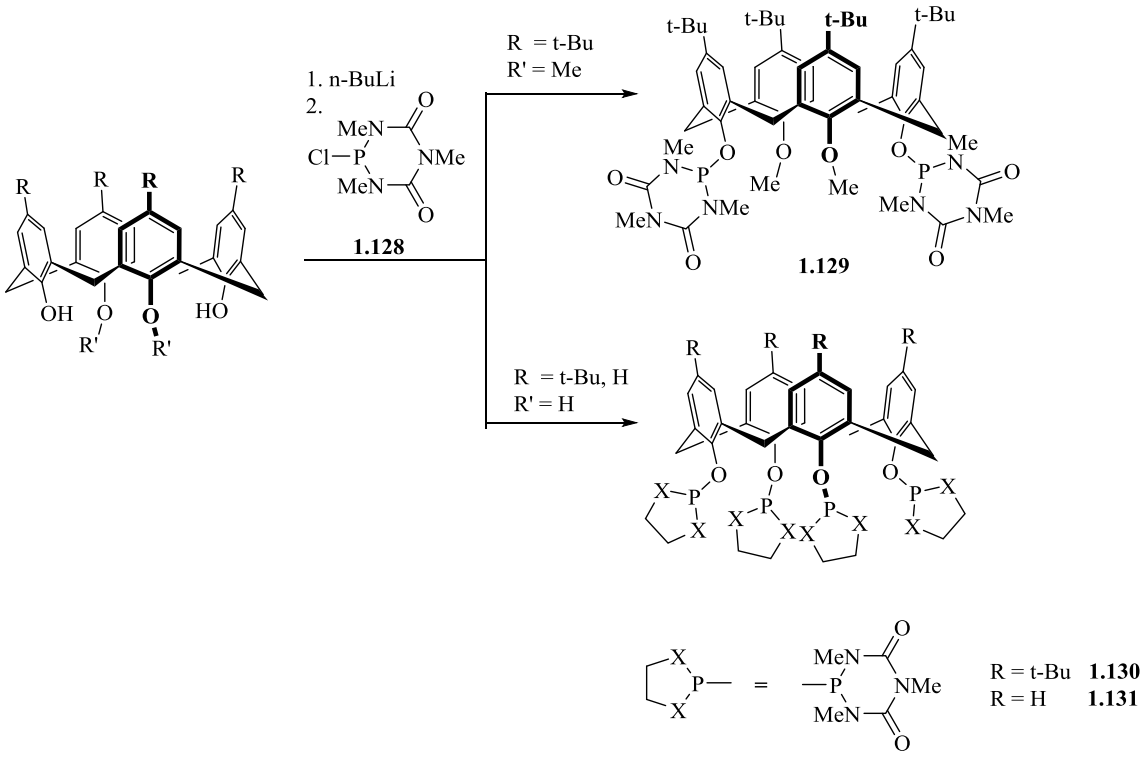


1.146 **1.147**

Figure. 1.10. Diphosphites **1.146** and **1.147**.

1.1.5. Oxy-phosphorus diamides

A series of Biuret-based ligands were reported by Schmutzler and Börner (**1.129** [63], **1.130** [64] and **1.131** [63]), were synthesised by reaction of 2-chloro-1,3,5-trimethyl-1,3,5-triaza-2$\sigma^3\lambda^3$-phosphorin-4,6-dione (**1.128**) with the appropriate, fully deprotonated di- or tetrahydroxy calix[4]arene (Scheme 1.26).

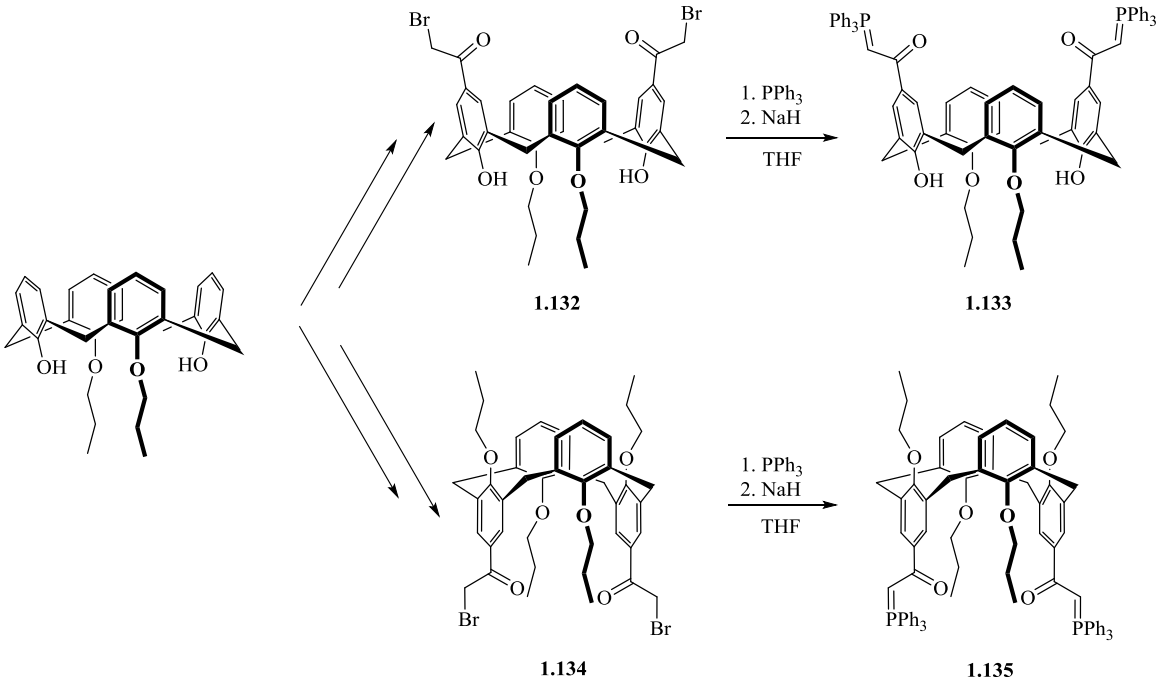


Scheme 1.26. Oxy-phosphorus diamides **1.129-1.131**.

These phosphorus ligands have poor donor properties.

1.1.6. Phosphorus ylides

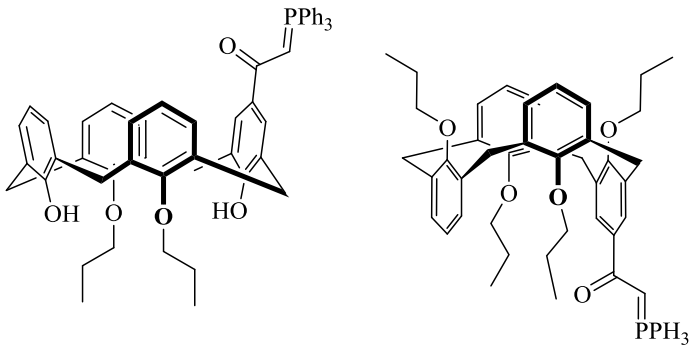
The synthesis of keto-stabilized phosphorus ylides tethered to a calix[4]arene platform was reported by Matt et al. [65]. According to proposed synthetic pathway, reaction of the dibromoacetylated calix[4]arene **1.132** with PPh_3 followed by deprotonation of the resulting phosphonium salt with NaH produced quantitatively the bis-phosphorus ylide **1.133** (Scheme 1.27).



1.132 1.133 1.134 1.135

Scheme 1.27. Phosphorus ylides based on calix[4]arene platform.

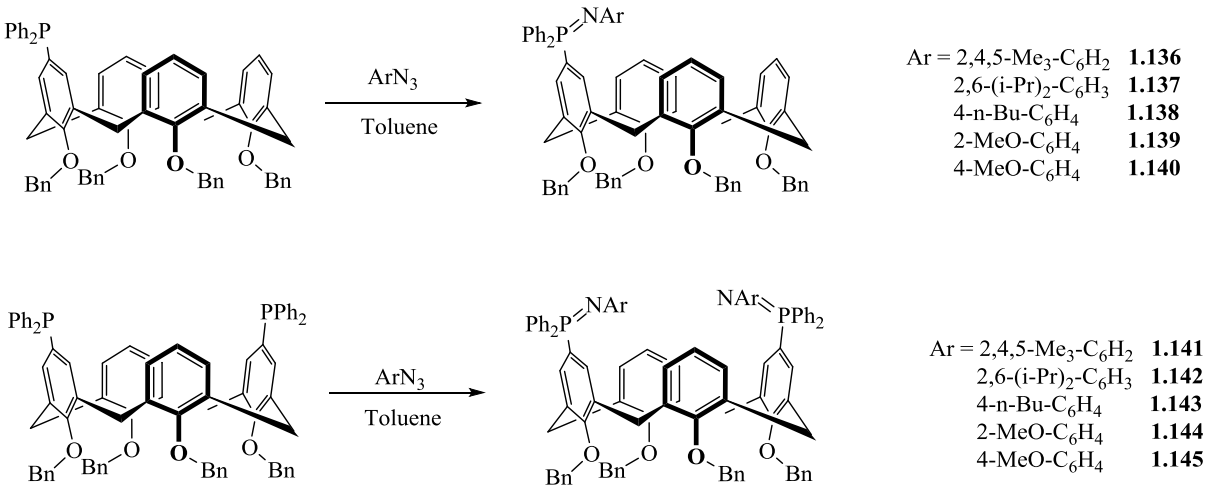
Phosphorus ylide **1.135**, in 1,3 alternate conformation was obtained in the same way, starting from precursor **1.134** (Scheme 1.27). Only known mono phosphorus ylides based on calix[4]arene platform – compounds **1.148** and **1.149** (Figure. 1.11). Their synthesis is similar and starts from corresponding monobromacetylated calix[4]arenes [65]. Such keto-stabilized phosphorus ylides are classical precursors of phosphine-enolate ligands. Nickel complexes with such ligands catalyzes oligomerization/polymerization of ethylene and used in SHOP (Shell higher olefin process) process.



1.148 **1.149**

Figure. 1.11. Mono phosphorus ylides based on calix[4]arene platform **1.148** and **1.149**.

1.1.7. Iminophosphoranes



Scheme 1.28. Iminophosphoranes synthesis.

The synthesis of monoiminophosphorane-calix[4]arenes **1.136-1.140** [66], and diiminophosphorane-calix[4]arenes **1.141-1.145** [67] was done by Sémeril et al. Iminophosphoranes – P(V) derivatives, are quantitatively obtained by using Staudinger condensation of phosphine with azide (Scheme 1.28). They are air-stable, despite sensitivity to moisture; reactions with water lead to decomposition to aniline and phosphine oxide. They are N-donor ligands.

1.1.8. Calix[4]arene phosphoric and phosphonous acids

Subsequent treatment of the corresponding calix[4]arene phosphorus esters with Me_3SiBr and methanolysis of the silyl esters formed lead to phosphoric acids, phosphonous acids, bisphosphonous acids, α-hydroxy and α-amino phosphonous acids (Figure. 1.12) [68,69,70,71,72,73,74,75,76].

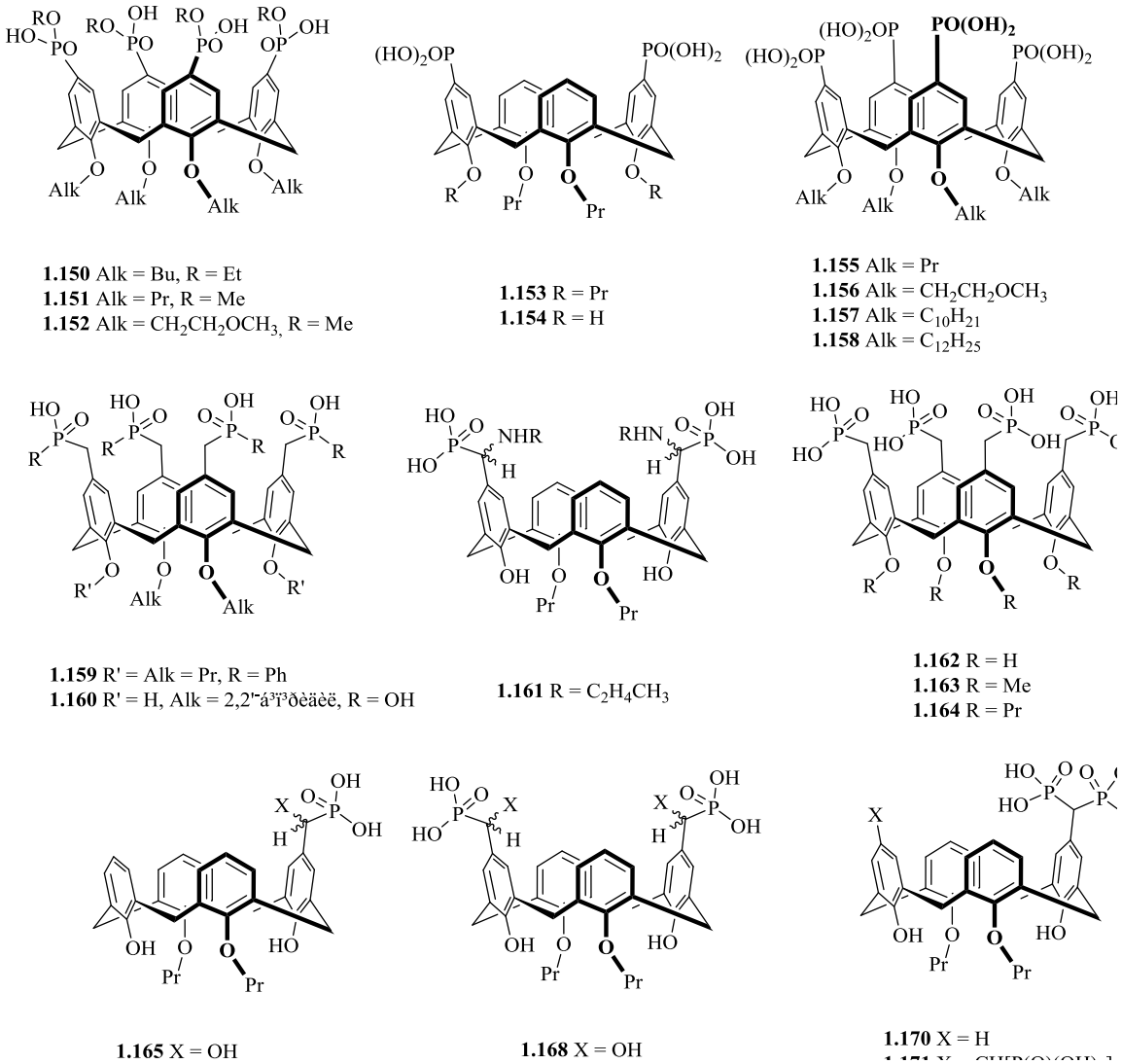
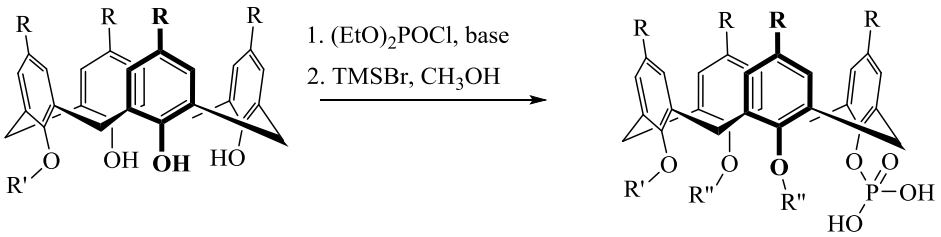


Figure. 1.12. Calix[4]arene phosphoric and phosphonous acids **1.150 - 1.171**.

Calix[4]arenes that have one, two or four dihydroxyphosphoryl groups on the lower rim of the macrocycle were synthesized by reaction with diethylchlorophosphate action in the presence of a base and subsequent reaction with trimethylbromosilane and methanol (Scheme 1.29) [76,77,78].



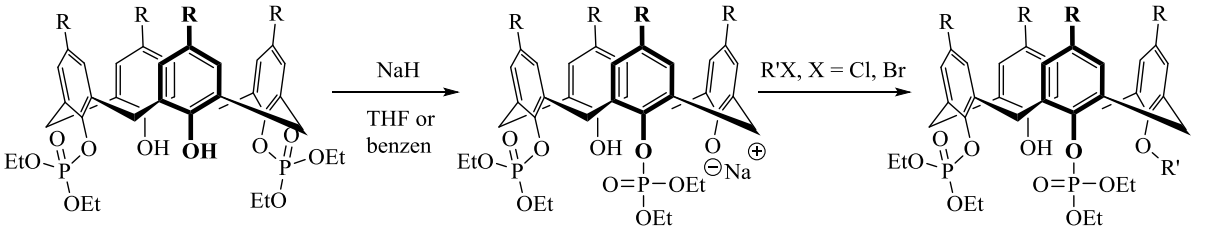
R = H:
1.172 R' = R" = -$PO(OH)_2$
1.173 R' = -$PO(OH)_2$, R" = H
1.174 R' = C_2H_5, R" = H

R = -$C(O)C_{11}H_{23}$
1.175R' = -$PO(OH)_2$, R" = H

R = t-Bu
1.176 R' = R" = -$PO(OH)_2$
1.177 R' = -$PO(OH)_2$, R" = H
1.178 R' = C_2H_5, R" = H

Scheme 1.29. Preparation of calix[4]arene phosphoric acids **1.172 - 1.178**.

Phosphoryl moities in distal position of disubstituted calix[4]arene show some mobility. Phosphotropic isomerization of distally disubstituted calix[4]arene bis-diethylphosphate easily occurs under treatment with 1 mole of strong base – NaH or n-BuLi in THF or benzene and lead to proximally disubstituted calix[4]arene bis-diethylphosphate (Scheme 1.30) [79,80].



1.179 R = H
1.180 R = t-Bu

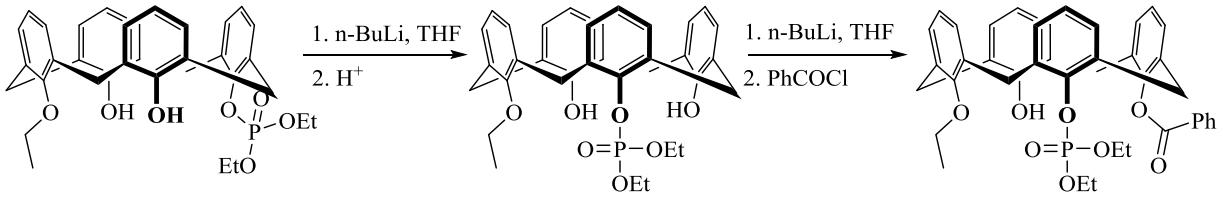
1.181 R = H R' = $CH_2C(O)OMe$
1.182 R = H R' = PhCO
1.183 R = t-Bu R' = $CH_2C(O)OMe$
1.184 R = t-Bu R' = PhCO

Scheme 1.30. Phosphotropis isomerization of distally disubstituted calix[4]arene bis-diethylphosphate.

Inherently chiral calix[4]arenes **1.181-1.184** could be obtained by simple alkylation or acylation of formed mono-sodium salt. They have no plane of

symmetry due to asymetric arrangement of achiral substituent on the lower rim. This substitution type is called AABH.

Reaction of 25-ethyl-27-diethoxyphosphoryl-calix[4]arene **1.174** with 1 mole of n-BuLi also results in phosphotropic isomerization (Scheme 1.31) [80,81]. Hydrolysis of obtained lithium salt with acid lead to the formation of chiral calix[4]arene with ABHH substitution type.

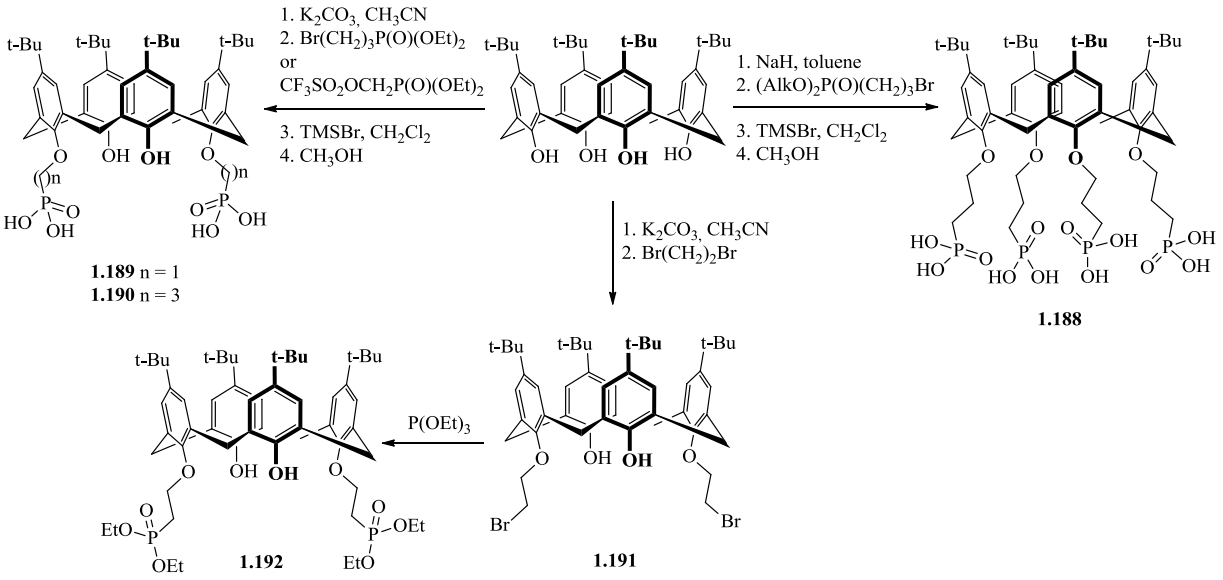


1.185 **1.186** **1.187**

Scheme 1.31. Synthesis of inherently chiral calix[4]arene phosphonate **1.187**.

Calix[4]arenes, in which the phosphonic acid groups are connected to the calixarene platform by a methylene, ethylene or propylene bridges, were synthesized by subsequent treatment of the corresponding calix[4]arene phosphonates (Scheme 1.32) with Me_3SiBr and methanolysis of the silyl esters formed [82,83,84,85].

Calix[4]arene bisphosphonate **1.192** was prepared by the Arbuzov reaction of bis-bromoethylcalix[4]arene **1.191** with triethylphosphite (Scheme 1.32). Attempts to alkylate p-tert-butylcalix[4]arene with diethyl 2-bromoethylphosphonate in acetonitrile–K_2CO_3 failed and resulted in complete decomposition of the reagent and formation of diethylvinylphosphonate.



Scheme 1.32. Synthesis of calix[4]arene phosphoric acids by Williamson alkylation (**1.188** – **1.190**) and Arbuzov reaction (**1.192**).

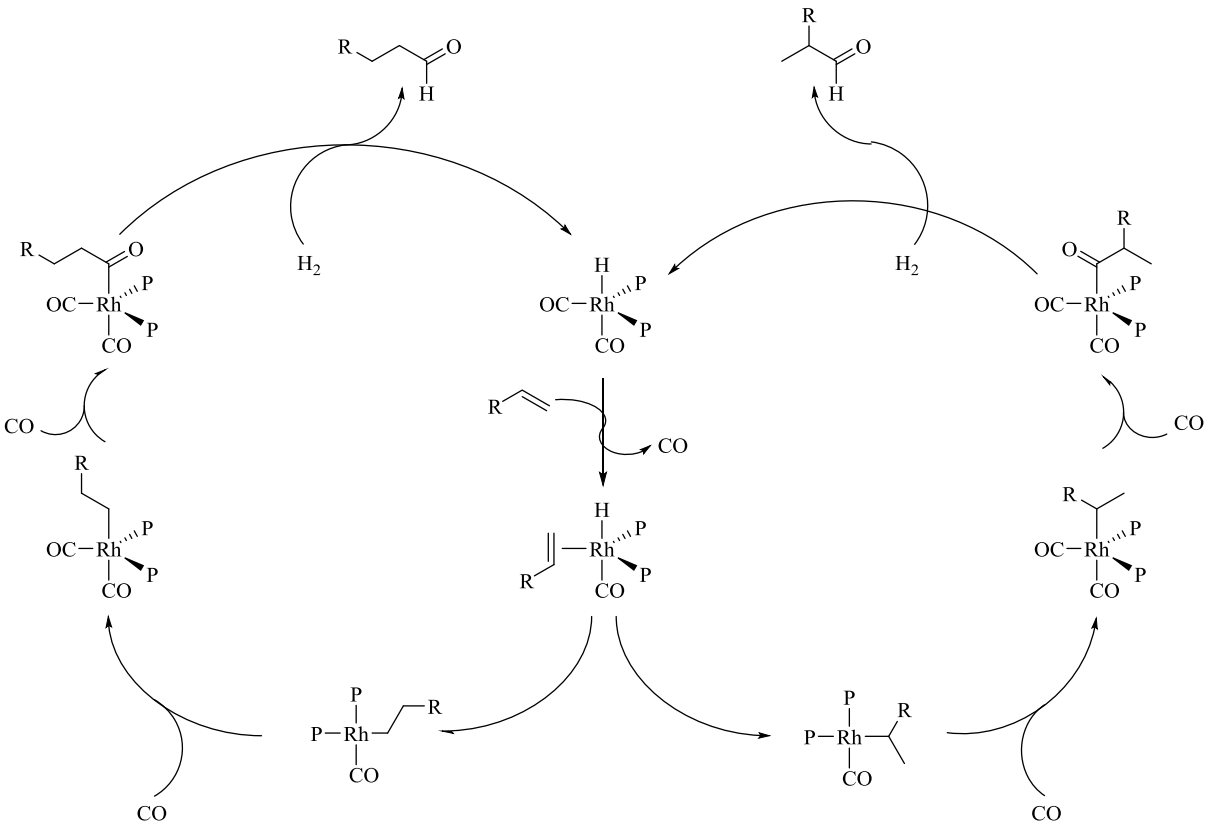
Calix[4]arene phosphoric acids has found their application in complexation with cations (organic and inorganic) and have some biological activity. Their possible application in asymmetric catalysis was not yet reported.

1.2. Use of P (III) and P (V)-containing calix[4]arenes in catalysis

1.2.1. Olefin hydroformylation

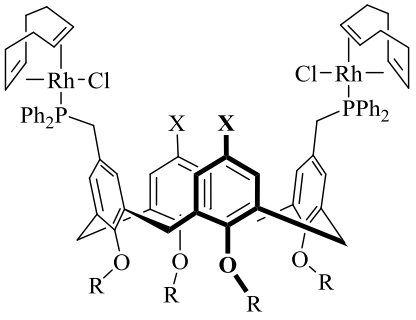
The hydroformylation, also known as oxo-synthesis, is an important widely used process to prepare aldehydes from alkenes [86]. This chemical reaction is formally adding aformyl group (CHO) and an hydrogen atom to a C-C double bond. This process has been subjected to continuous development since its discovery in 1938, in particular using rhodium catalysts.

For the rhodium-catalyzed hydroformylation reaction, the formation of the two regioisomers in different proportions (linear and branched aldehydes) can be explained by the presence in the catalytic cycle (Scheme 1.33) of two types of rhodium-alkyl intermediate, *[LRh-CH_2CH_2R]* (linear isomer) *and [LRh-CH(Me)R]* (branched isomer).

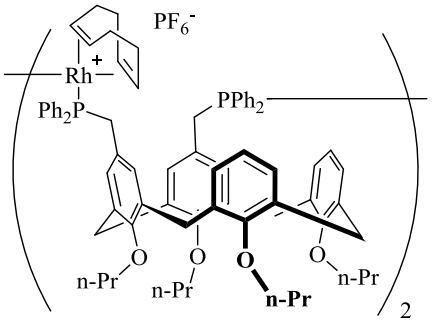


Scheme 1.33. Catalytic cycle of rhodium-catalyzed olefin hydroformylation.

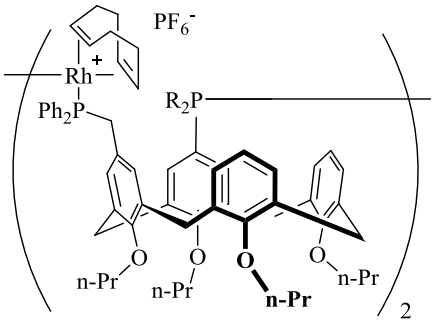
One efficient way to drive the hydroformylation reaction towards the formation of linear aldehydes consists in using chelating diphosphines that display a large natural bite angle [10]. The large PRhP angle of the intermediate forces the phosphorus substituents to be bent towards the metal centre, hence forming a tight molecular pocket. The resulting steric pressure exerted on the metal ion by the substituents then favours the transfer of the hydrido atom on the C2 carbon atom of the coordinated olefin, rather than to the terminal atom. The linear alkyl intermediate is the one that eventually leads to the linear aldehyde.



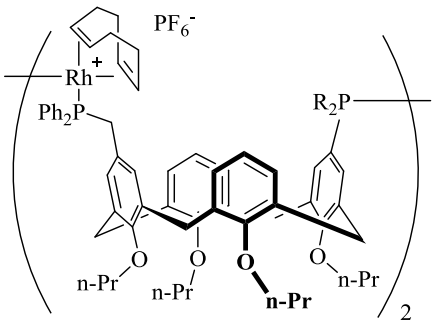
1.192 X = t-Bu, R = CH_2CH_2OEt
1.193 X = H, R = n-Pr



1.194



1.195 R = Ph
1.196 R = Me
1.197 R = i-Pr



1.198 R = Ph
1.199 R = Me
1.200 R = i-Pr

Figure. 1.13. Bis-rhodium complexes **1.192 - 1.200** applied in olefin hydroformylation.

Bis-rhodium complexes **1.192 - 1.200** were used in olefin hydroformylation – 1-hexene and styrene. They has shown high selectivity – linear aldehyde forms in large excess, but, with low catalytic activity (TOF of 11-250) (Table 1.1).

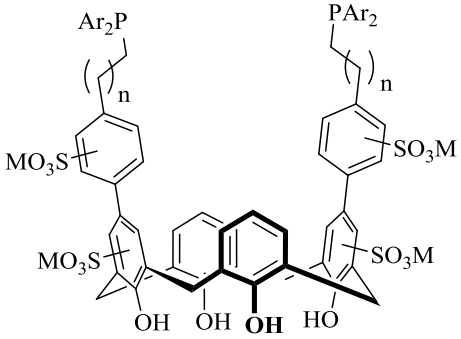
Table 1.1

*Rhodium-catalysed hydroformylation using complexes **1.192 – 1.200**.*

№	*Rh complex*	*1-Hexene*		*Styrene*	
		TOF	*l/b*	*TOF*	*l/b*
1.	**1.193** [24]**	-	-	58	14:86

2.	**1.194** [26]*	250	2.5	-	-
3.	**1.195** [21]*	250	1.7	11	6:94
4.	**1.196** [21]*	106	1.7	11	5:95
5.	**1.197** [21]*	211	1.8	65	11:89
6.	**1.198** [21]*	141	1.7	80	8:92
7.	**1.199** [21]*	51	1.8	35	6:94
8.	**1.200** [21]*	97	1.9	82	10:90

Conditions: *THF, 71 bar CO/H_2 (1: 1), 50 ˚C. **Toluene/CH_2Cl_2 = 1/4, 55 bar CO/H_2 (1: 1), 70 ˚C. TOF in mol(olefin) mol(Rh)$^{-1}$ h^{-1}.



Ar = *m*-$MOSO_2C_6H_4$
M = (n + 1) 9xNa^+, 1xH^+ **1.27**
(n = 2) 10xNa^+ **1.28**

Figure. 1.14. Water-soluble phosphites **1.27** - **1.28** used in olefin hydroformylation.

Water-soluble phosphites **1.27** and **1.28** (Figure. 1.14), were both used in hydroformylation of 1-octene. Catalytic systems were prepared by mixing ligand and $[Rh(acac)(CO)_2]$ in water [25]. In these biphasic aqueous sytems, catalyst are believed to behave as an inverse phase-transfer agent. After 12 h, 1-octene

was converted into aldehydes with 40 % (**1.27**) and 73 % (**1.28**) yield (Table 1.2).

Table 1.2

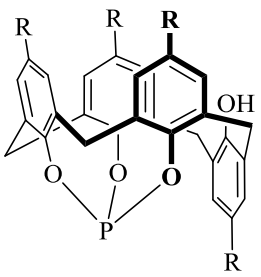
*Rhodium-catalysed hydroformylation using phosphites **1.27** – **1.28**.*

№	*Catalytic system*	*Conversion, %*	*Aldehyde yield, %*	*l/b*
1. [25]	**1.27**/[Rh(acac)$(CO)_2$]	55	40	3.0
2. [25]	**1.28**/[Rh(acac)$(CO)_2$] (first use)	95	73	1.7
3. [25]	**1.28**/[Rh(acac)$(CO)_2$] (second use)	97	84	1.7
4. [25]	**1.28**/[Rh(acac)$(CO)_2$] (third use)	98	86	1.9
5. [87]	**TPPTS**/[Rh(acac)$(CO)_2$]/ DMCD	26	21	2.4

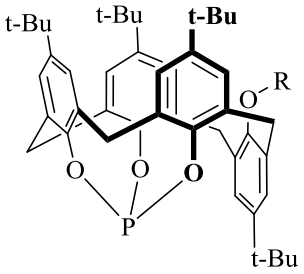
Conditions: 1-octene: P: Rh = 250: 4: 1, water, 40 bar CO/H_2 (1: 1), 100 ˚C, 12 h.

In these experiments, the observed l/b ratios were close to 0.3. The above water-soluble catalysts were more efficient than Monflier's system based on tris-(3-sulfophenyl)phosphine trisodium salt (TPPTS) and (2,6-di-O-methyl)--cyclodextrin (DMCD) (Table 2) [87].

Van Leeuwen et al. studied the conformational influence of the calixarene moiety of phosphites **1.81** – **1.86** (Figure. 1.15) in hydroformylation of 1-octene [48]. All these ligands led to active catalytic systems, with the l/b ratios ranging from 1.3 to 2.0.The authors observed that the activities were strongly dependant on the calix[4]arene conformation.



R = H **1.78**
R = t-Bu **1.79**



R = C(O)Me (up–up-out–down) **1.81**
R = C(O)Ph (up–up-out–down) **1.82**
R = Me (up–out–up-up) **1.83**
R = CH_2Ph (up–up-out–up) **1.84**
R = CH_2Ph (up–out–up-up) **1.85**
R = i-Pr (up–up-out–up) **1.86**

Figure. 1.15. Phosphites **1.78 - 1.86** (the 'up-down' notation is used, taking the arene ring that is not connected to the phosphorus atom as a reference. "Up" – phenyl rings are pointing towards the same side of the molecule, "down" – phenyl rings are pointing towards the opposite side of the molecule, and an "out" – rings are pointing away from calix[4]arene) [48].

In calix[4]arenes **1.83** and **1.85** (Figure. 1.15), the phosphorus lone pairs are embedded in the calix[4]arene cavity, thus hampering metal binding and impeding olefin coordination. As expected, these effects slowed down the reaction rate with respect to less crowded ligands. Thus for example, phosphites **1.84** and **1.86**, which possess a much more accessible phosphorus lone pair, and in which the R group grafted at the fourth oxygen atom can easily move away from the P atom (TOF = 1900, 1800, 7200 and 7300 mol (olefin) mol (Rh) $^{-1}$ h $^{-1}$, for corresponding **1.83**, **1.85**, **1.84** i **1.86**, Table 1.3).

Ligands **1.81** and **1.82**, thanks to the auxiliary ester functional groups that are capable of binding metal cation and therefore to slow a little bit the rate of the reaction, did not show high selectivity in the formation of linear products (Table 1.3).

Table 1.3

*Rhodium-catalysed hydroformylation using phosphites **1.91** – **1.96**.*

№	*Phosphite*	*Conversion, %*	*Aldehyde yield, %*	*TOF*	*l/b*
1.	**1.81**	97	79	4700	1.6
2.	**1.82**	97	84	5000	1.2
3.	**1.83**	78	53	1900	2.0
4.	**1.84**	92	84	7200	1.3
5.	**1.85**	77	60	1800	1.4
6.	**1.86**	96	90	7300	1.4

Conditions: 1-octene: P: Rh = 6370: 20: 1, toluene, 20 bar CO/H_2 (1: 1), 100 ˚C, 12 h.

Concomitantly, the group of Pringle studied the hydroformylation of 1-hexene with [RhL(CO)(acac*)] complexes (acac * = tBuCOCHCOtBu; L = Phosphite **1.78** or **1.79**;. Figure. 1.15). Two calix[4]arenes used in this study are in conformation up-up-down-out [88]. Hydroformylation at 160 ˚C in toluene at 61 bar CO/H_2 (1: 1) leads to complete conversion after 3 h. The observed ratio l/b is 1.2. Both phosphites, probably because of their bulkiness, yield very unstable rhodium complexes, with good catalytic activity but with low selectivity towards the formation of linear aldehyde. Addition of a large excess of ligand has little effect on the catalytic activity, supporting the idea that the active catalysts are rhodium-monophosphites complexes.

The influence of an oxygen-containing side group in phosphite analogues **1.87 – 1.91** (Figure. 1.7) was investigated in the hydroformylation of 1-octene [51]. Phosphites **1.87 – 1.91** (Figure. 1.7) are in conformation up-up-up-out, in other words, phosphorus atom is in a relatively open environment and thus suitable for the coordination to the metal. The presence of substituents having

phosphoryl, amide or ester groups, which have donor properties, has a positive effect on the reaction regioselectivity. For example, the l/b ratio was 3.6 with ester **1.88** (Table 1.4), while the ratio with phosphite **1.90** l/b was only 1.4. Interestingly, the activity decreases with the increase of the donor properties of the auxiliary oxo group: **1.90** (R = $CH_2CH_2OCH_3$) > **1.87** (R = $CH_2P(O)Ph_2$) > **1.88** (R = CH_2CO_2Et) > **1.89** (R = CH_2CONEt_2) (Table 1.4). This fact suggests that in the process of catalysis, occurs formation of P, O-chelates, which prevent olefin binding.

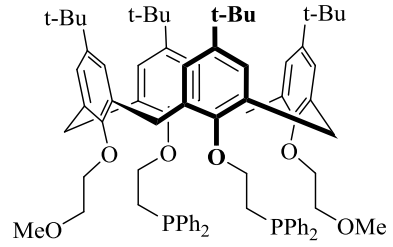
Table 1.4

*Rhodium-catalysed hydroformylation using phosphites **1.87** – **1.91**.*

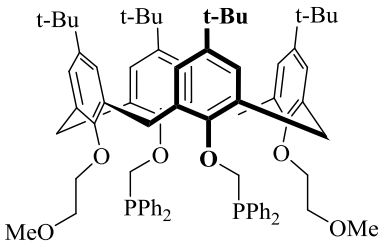
№	*Phosphite*	*Conversion, %*	*Aldehyde yield, %*	*TOF*	*l/b*
1.	**1.87**	100	89	2450	2.4
2.	**1.88**	100	90	1300	3.6
3.	**1.89**	100	86	950	2.7
4.	**1.90**	100	96	4400	1.4

Conditions: 1-octene: P: Rh = 5000:10:1, toluene, 22 bar CO/H_2 (1: 1), 80 ˚C.

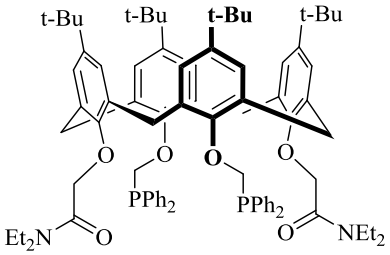
Functionalized diphosphines **1.41** and **1.50** – **1.52** (Figure. 1.16) were tested in hydroformylation of styrene. Experiments were carried out at 40 ˚C under 40 bar of CO/H_2 with synthesized complexes [Rh(**1.51**)(CO)]BF_4 (**1.201**) (Figure. 1.17) and [Rh(L)(nbd)]BF_4 (L = **1.41**, **1.50** and **1.52**) [29,33,34].



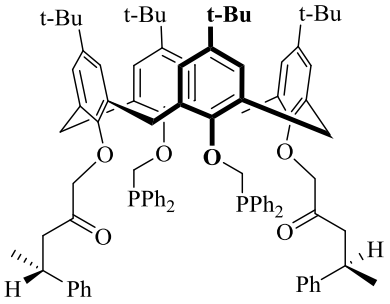
1.41



1.50



1.51



1.52

Figure. 1.16. Phosphines **1.41**, **1.50 - 1.52**.

These complexes showed low activity but high selectivity for the formation of branched aldehydes (95%) (Table 1.5).

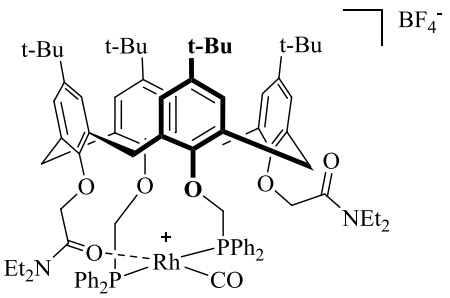
Table 1.5

*Rhodium-catalysed hydroformylation using phosphines **1.41**, **1.50 – 1.52**.*

№	*Phosphine*	*Styrene/Rh*	*Conversion, %*	*Aldehyde yield, %*	*TOF*	*l/b*
1.	**1.41**	870/1	100	89	7	5:95
2.	**1.50**	600/1	100	90	7	5:95
3.	**1.51**	500/1	100	86	1	5:95
4.	**1.52**	300/1	100	96	7	5:95

Conditions: toluene, 40 bar CO/H_2 (1: 1), 40 ˚C.

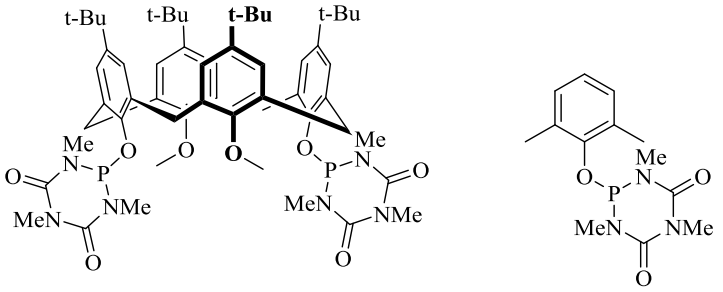
The reason for low rates may be the partial encapsulation of catalytic center or competitive binding on catalytic center by the functional side groups, both phenomena making difficult for the olefin to coordinate.



1.201

Figure. 1.17. Complex **1.201**.

Bis-phosphorus ligand **1.129** (Figure. 1.18), was tested in the reaction of hydroformylation of 1-octene [63]. Catalytic systems were generated by the reaction of the ligand **1.129** with [Rh(acac)(cod)].



1.129 **1.202**

Figure. 1.18. Oxyphosphoramides **1.129** and **1.202**.

This system gave high activity but low selectivity towards the linear aldehyde even in the presence of a large excess of ligand (ratio l/b in the range of 1.0 to 1.4) (Table 1.6). A possible explanation for these results could be that

the ligand is so wealy bound to the metal that unsaturated rhodium intermediates could be easily generated.

The effect of the presence of calix[4]arene backbone could not be confirmed by the results obtained with ligand **1.202** (Figure. 1.18), which also shows a low selectivity l/b = 0.8!

Table 1.6

*Rhodium-catalysed hydroformylation using **1.129** i **1.202**.*

№	*Ligand*	*L/Rh*	*p(CO/H₂), bar*	*Aldehyde yield, %*	*l/b*
1.	**1.129**	2:1	50	88.4	1.0
2.	**1.129**	10:1	50	86.6	1.4
3.	**1.202**	4:1	40	95.9	0.8

Conditions: THF, 1-octene:[Rh(acac)(cod)] = 15.700:1, CO/H_2 (1: 1), 100 ˚C, 3 h.

Diphosphinites **1.67**, **1.68** and **1.71** (Figure. 1.19) with $[Rh(acac)(CO)_2]$ were effective for hydroformylation of 1-octene [43]. Propyl substituent replacement on $CH_2C(O)OEt$-group (ie the use of a ligand **1.68**) led to a decrease in activity, but an increase in regioselectivity (l/b = 2.5) (Table 1.7). In addition, the l/b ratio increased to 3.1 using 2 equivalents of ligand instead of one. In the hydroformylation of styrene diester, **1.68** showed good activity and selectivity of the formation of branched aldehydes. Replacement of auxiliary CO_2Et functions with bulky ester cholesterol-containing groups (ligand **1.71**) increased the proportion of the linear aldehyde (l/b = 41:59) (Table 1.7).

Table 1.7

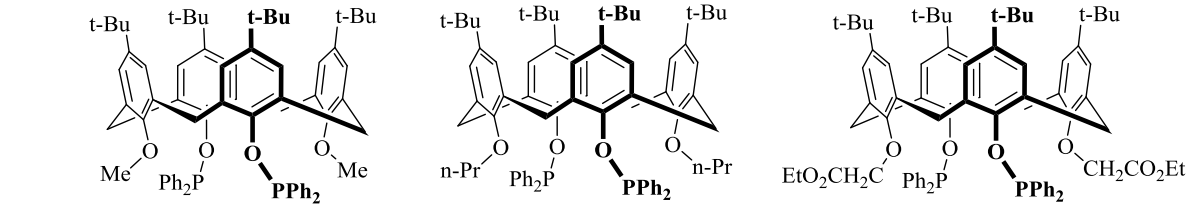
*Rhodium-catalysed hydroformylation using **1.67**, **1.68** i **1.71** [43] and **1.111** – **1.115** [44].*

№	Ligand	*1-Octene*		*Styrene*	
		TOF	*l/b*	*TOF*	*l/b*
1.	**1.67**	2625	1.6	854	34 : 66
2.	**1.68**	1032	2.5	891	36 : 64
3.	**1.71**	1219	2.2	210	41 : 59
4.	**1.111** (L/Rh=1:1)	1204	2.3	2033	33 : 67
5.	**1.111** (L/Rh=2:1)	156	5.0	1975	37 : 63
6.	**1.112** (L/Rh=1:1)	629	3.2	140	34 : 66
7.	**1.112** (L/Rh=2:1)	247	9.6	28	12 : 88
8.	**1.115** (L/Rh=1:1)	1045	2.7	789	27 : 73
9.	**1.115** (L/Rh=2:1)	65	10.6	587	25 : 75

Conditions: olefin:P:[Rh(acac)$(CO)_2$] = 2500:1:1, toluene, 20 bar CO/H_2 (1:1), 80 ˚C. TOF in mol(olefin) mol(Rh)$^{-1}$ h^{-1}.

Catalytic system, obtained by combining diphosphite **1.111** (Figure. 1.19) with one equivalent of [Rh(acac)(cod)] produces an active catalyst for the transformation of 1-octene to aldehydes, but the selectivity for linear aldehydes was disappointing here again (*l/b* = 1.1) (Table 1.7) [44]. As expected, the increase in the rhodium/ligand ratio led to a reduced reaction rate and a slight increase of the selectivity towards the linear product (*l/b* = 1.4) (Table 1.7). A mixture of N,N-dietylacetamid-diphosphite **1.115** (Figure. 1.19) and [Rh(acac)$(CO)_2$] in a 3:1 ratio was tested in the reaction of hydroformylation of propylene. The experiments were carried out at a 4 bar pressure and with CO/H_2/propylene = 1:1:1 ratios in the presence of a large amount of tryphenylphosphine (PPh_3 : **1.115** : Rh = 300 : 3: 1). The reaction yields *n*-butanal with high selectivity (l/b = 18.5). The initial reaction rate increases 17 times when the number of PPh_3 was reduced to 150 equivalents relative to

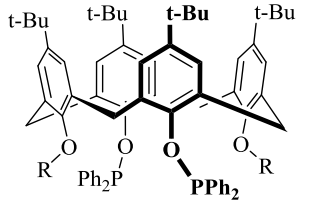
rhodium; however, the ratio l/b decreases to 13.3. Even higher regioselectivity was observed in the case of 1-butene (*l/b* = 24.5; conditions: PPh_3 : **1.115** : Rh = 150: 3 : 1, 2.7 bar CO/H_2 at 100˚C in toluene).



1.66

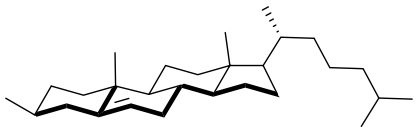
1.67

1.68

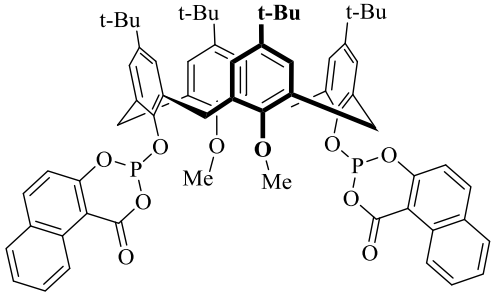


R = CO_2chol

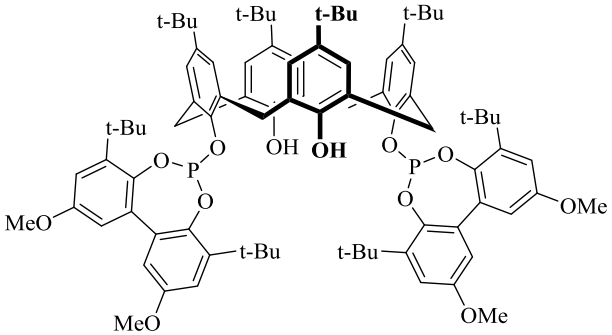
chol =



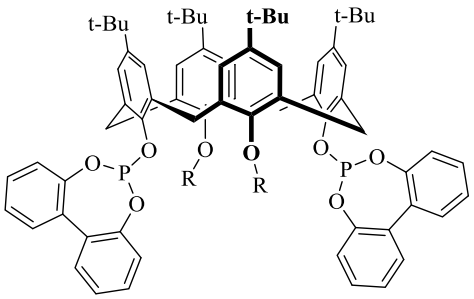
1.71



1.111 [44]



1.112 [44]



R = $CH_2C(O)NEt_2$ **115** [59]

Figure. 1.19. Diphosphinites **1.66 - 1.71** and diphosphites **1.111 – 1.115**.

Carrying hydroformylation of butene-1 in the absence of triphenylphosphine led, after optimizing conditions to a l/b ratio of 51 (**1.115**:Rh

= 2:1, 1.6 bar CO/H_2, 70˚C in tetraglyme). In the case of 1-octene, selective formation of linear aldehyde was also observed (l/b = 31). The same catalytic system was also tested at 75˚C in tetraglyme and under a pressure of 6,5 bar CO/H_2/butene: n-valeric aldehyde was obtained as a main aldehyde (l/b = 6.3) [63].

The relatively high selectivies for the formation of linear aldehydes observed with octene and styrene are likely to result from steric effects caused by the formation of intermediates where R-substituents are bent to the coordinating metal to form a tight pocket around him. As a result of this, the hydride migration, which yields linear intermediate "Rh-n-alkyl" instead of "Rh-i-alkyl", is favored.

Inspired by these observations, Sémeril et al. decided to increase the ligand bulk of such diphosphites by replacing the two Oph substituents of each phosphorus atom with the binol derived (R or S)- (1,1'-binaphthalene-2,2'-diyl) group [61,62].

The diphosphites **1.117** - **1.118**, **1.120** - **1.123** (Figure. 1.20), obtained this way, were then tested in the hydroformylation of 1-octene and their catalytic performances compared with the ones of **1.108** (Figure. 1.9).

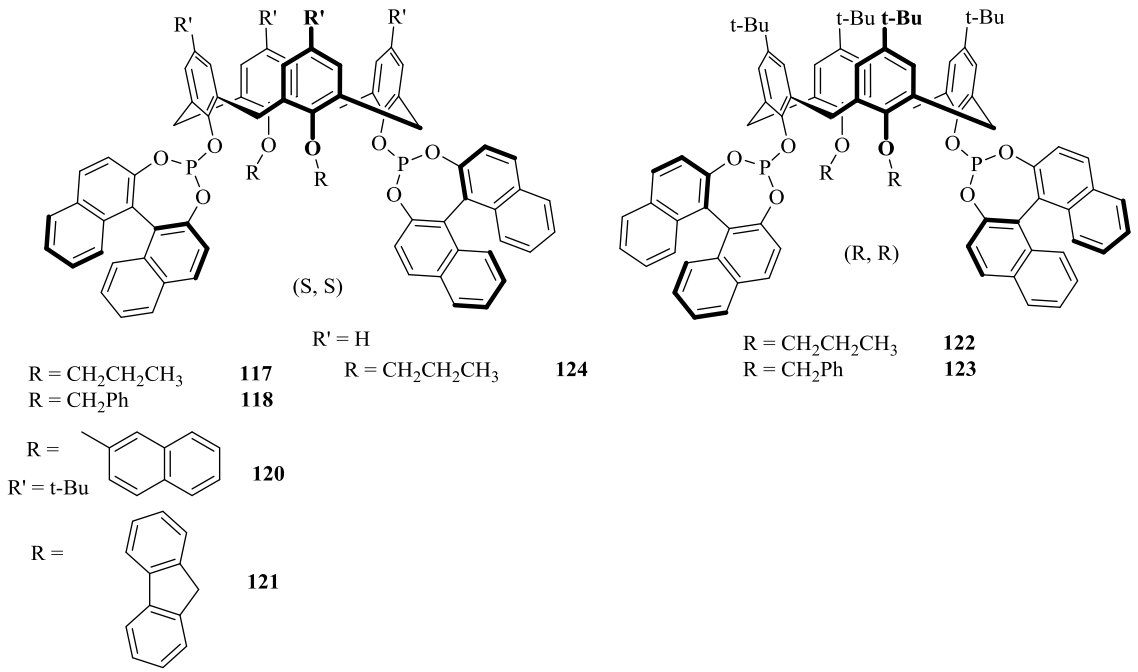
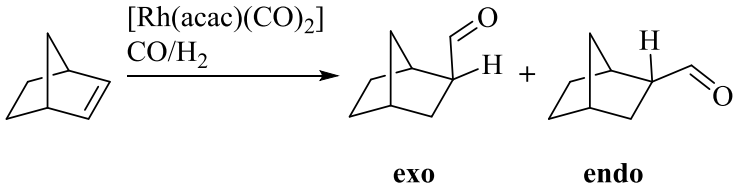


Figure. 1.20. Diphosphites **1.117 - 1.118**, **1.120 - 1.123**.

Going from **1.108** to **1.120** – **1.123**, the l/b ratio increased from 5.0 to 58.0. In addition, modifying ligand with sterically hindered two auxiliary groups can vary considerably both reactivity and regioselectivity. Efficiency of the catalytic system at first is increases till reach some preferable bulkines of ligand and is reduced by the further growth of two auxiliary substituents.

Optically pure diphosphites **1.117** – **1.118**, **1.120** – **1.123** were additionally used in asymmetric hydroformylation of norbornene (Scheme 1.34) [62]. All ligands showed very high selectivity towards exogenous aldehyde (exo/endo from 82.7/17.3 up to 100/traces), but ee observed were low. Best ee was obtained with **1.121** fluorenyl ligand (ee = 52%).

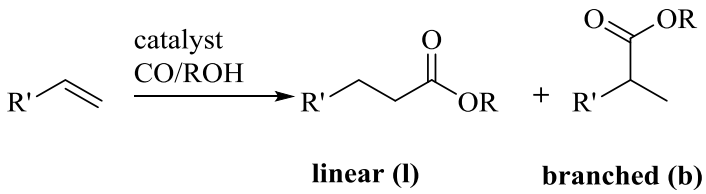


Scheme 1.34. Hydroformylation of norbornene.

Use of tetraphosphine **1.44** and tetraphosphinite **1.72** in styrene hydroformylation with platinum and rhodium [31] showed that for both metals and for both ligands, an increase in reactivity and for the l/b ratio were observed with increasing temperature.

1.2.2. Olefin hydroalkoxycarbonylation

Alkoxycarbonylation is a simple way to get esters from olefins, carbon monoxide and alcohols (Scheme 1.35). This reaction is interesting from a scientific and commercial point of view.



Scheme 1.35. Olefin hydroalkoxycarbonylation.

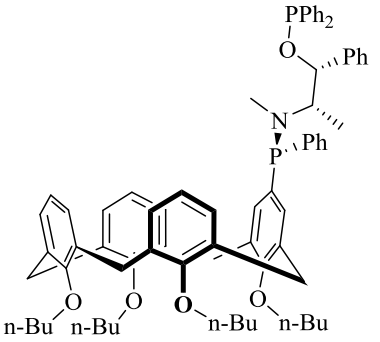
Tetraphosphine **1.44** and tetraphosphinite **1.72** were used in the hydroalkoxycarbonylation of styrene in the presence of a palladium precursor using methanol or tert-butanol. In harsh reaction conditions (140 bar CO, 48 h, 130 °C) **1.72** was inactive but **1.44** showed significant catalytic activity (conversion up to 42%) but low selectivity - l/b ratio = 37.7: 62.3. These results were rationalized by the authors from the possibility of formation of various catalytically active complexes which reduces the selectivity of the reaction.

1.2.3. Olefin hydrogenation

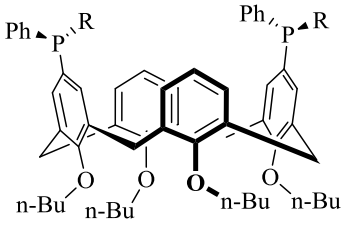
Olefin hydrogenation is the addition of dihydrogen to an olefinic carbon–carbon double bond to generate a saturated compound. It is a very common

reaction in organic synthesis, and is especially valuable in its asymmetric version for the production of fine chemicals [89,90].

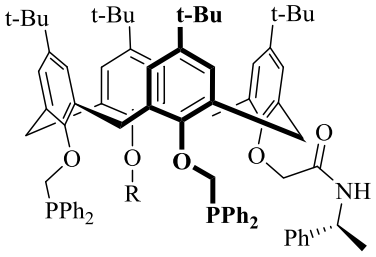
Jugé and Harvey reported the use of the P-chirogenic aminophosphine-phosphinite **1.33** (Figure. 1.21) in the hydrogenation of methyl-2-acetamidocinnamate in benzene [28], with *ee* up to 95 %.



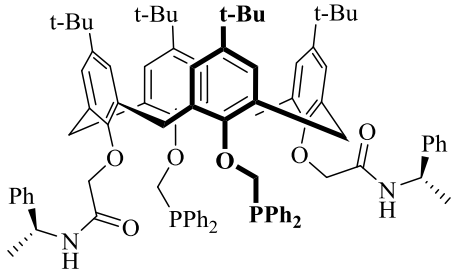
1.33



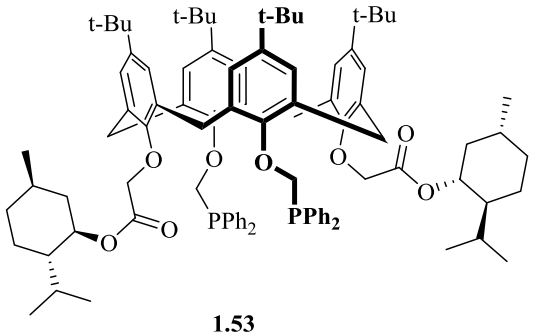
R =Me	**1.37**
R = 2-MeO-C_2H_4	**1.38**
R = Fc	**1.39**



R = H	**1.59**
R = $SiMe_3$	**1.61**
R = (R)-$CH_2C(O)NHCHMePh$	**1.63**



1.54



1.53

Figure. 1.21. Chiral phosphines **1.33 – 1.63**.

Table 1.8

Rhodium-catalysed hydrogenation of dimethyl itaconate using diphosphines ***1.52***, ***1.59***, ***1.61***, ***1.63***,.

№	*Complex*	*Time, h.*	*ee, %*	*TOF, mol(olefin) mol(Rh)-1 h-1*
1.	[Rh(cod)(**1.59**)]BF_4	0.10	48	2000
2.	[Rh(cod)(**1.61**)]BF_4	0.17	25	1176
3.	[Rh(cod)(**1.63**)]BF_4	0.75	0	267
4.	[Rh(cod)(**1.52**)]BF_4	20	0	10

Conditions: olefin:[Rh(acac)(cod)] = 200:1, H_2 20 bar, methanol.

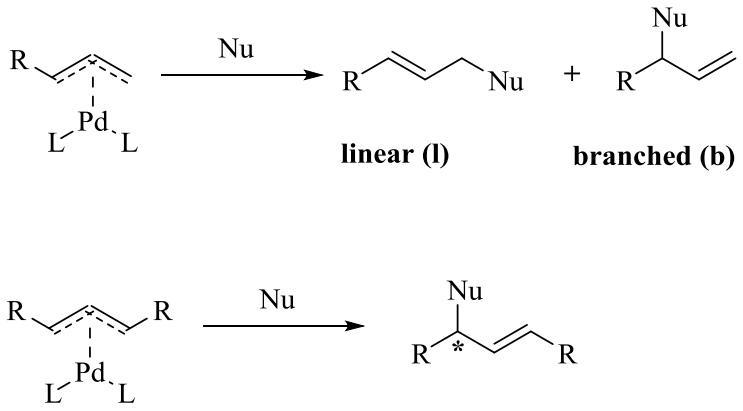
In addition, the inherently chiral calix[4]arenes **1.59** and **1.61** has shown good results (Table 1.8). These results demonstrates that an inherently chiral calix[4]arene skeleton is able to transfer chiral information to the catalytic centre.

In the asymmetric hydrogenation of dimethyl itaconate and α-(acylamino)acrylate performed with the *in situ* generated catalytic systems from [Rh(nbd)$_2$]BF_4 and ligands **1.92-1.95** (Scheme 1.22), was obtained *ee* up to 94% [52]. Even higher enantioselectivities could be obtained with the binol-derived **1.116-1.127** (Figure. 1.9) [60]. For example, using diphosphite **1.117** in the hydrogenation of methyl-(Z)-2-(acetamido)acrylate and methyl-(Z)-2-(acetamido)cinnamate led to ee's of 98 and 96%, respectively.

1.2.4. Tsuji–Trost reaction

The Tsuji–Trost reaction is the metal-catalyzed nucleophilic substitution of allylic substrates. Products from asymmetric substrates are linear (l) and branched (b) isomers with ratio depending on the catalytic system (Scheme 1.36). If the catalyst is optically active, the reaction may have chiral induction,

leading to the formation of branched product with some selectivity in favor of one enantiomer [91].



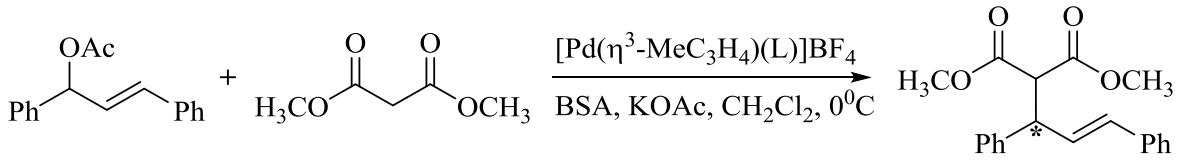
Scheme 1.36. The palladium-catalyzed Tsuji–Trost reaction.

Table 1.9

*Palladium-catalysed allylic alkylation of 1,3-diphenylprop-2-enyl acetate using diphosphines **1.41-1.77**.*

№	*Complex*	*Time, h.*	*ee, %*	*TOF, mol(olefin) mol(Rh)-1 h-1*
1.	[Pd(η^3-MeC_3H_4)(**1.41**)]BF_4	5	-	20
2.	[Pd(η^3-MeC_3H_4)(**1.50**)]BF_4	4	-	25
3.	[Pd(η^3-MeC_3H_4)(**1.77**)]BF_4	4	8	25
4.	[Pd(η^3-MeC_3H_4)(**1.52**)]BF_4	3	16	33
5.	[Pd(η^3-MeC_3H_4)(**1.54**)]BF_4	5	6	20
6.	[Pd(η^3-MeC_3H_4)(**1.59**)]BF_4	3.3	67	30
7.	[Pd(η^3-MeC_3H_4)(**1.61**)]BF_4	3.3	45	30
8.	[Pd(η^3-MeC_3H_4)(**1.63**)]BF_4	3.8	0	26

Matt and coworkers studied the allylic alkylation of 1,3-diphenylprop-2-enyl acetate with dimethyl malonate catalysed by $[Pd(\eta^3\text{-}MeC_3H_4)(\mathbf{L})]BF_4$ complexes (as a ligand – chiral phosphine from Figure. 1.21) (Scheme 1.36) [29,38]. For all the catalysts tested, full conversion was observed along with low selectivity (*ee* = 0-16 %; Table 1.9), probably because in the corresponding active species the chiral centres are remote from the π-allyl moieties. Significantly higher inductions were obtained with the inherently chiral calix[4]arenes **1.61** (*ee* = 45 %) and **1.59** (*ee* = 67 %) (Table 1.9).



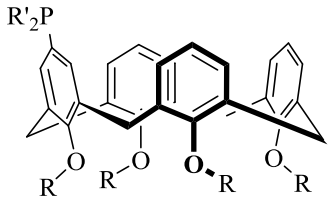
Scheme 1.37. Allylic alkylation of 1,3-diphenylprop-2-enyl acetate.

Jugé et al. tested the P-chirogenic calixarenyl phosphines **1.35-1.39** (Figure. 1.21) in the palladium catalysed allylic substitution of (E)-1,3-diphenylprop-2-en-1-yl acetate by dimethyl malonate andbenzylamine [28]. In all cases, high yields were observed, but with low ee values.

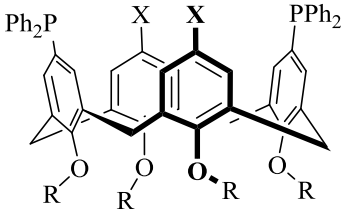
1.2.5. Cross-coupling reactions

Cross-coupling is a general term for organic reactions in which two different organic fragments are coupled together by means of a transition metal catalyst [92]. Only three types of cross-coupling reactions were studied with catalysts containing a phosphinated calix[4]arene : Suzuki–Miyaura (boronic acid/ArX) [93], Kumada–Tamao–Corriu (Grignard/ArX) [94] and Mizoroki–Heck (carbon–carbon double bond/ArX) [95]. Phosphines **1.4-1.7** and **1.9** (Figure. 1.22) were studied in palladium-catalyzed Suzuki-Miyaura reaction, with phenylboronic acid and aryl halides [15]. Those phosphines were further tested in a nickel-catalysed Kumada–Tamao–Corriu [16]. Complex

[NiCp(**1.12**)]BF_4 tested in Kumada–Tamao–Corriu [97]. All ligands showed good results - conversion in the 40-80% range.



R' = Ph, R = *n*-Hex **1.4**
R' = Ph, R = Bn **1.5**
R' = Ph, R = *n*-MeO-Bn **1.6**
R' = Ph, R = *м*-MeO-Bn **1.7**
R' = *t*-Bu, R = Bn **1.8**
R' = Ph, R = H **1.9**



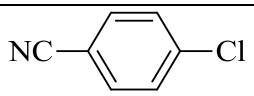
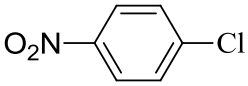
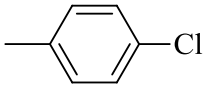
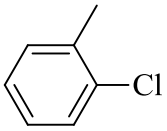
X = H, R = n-Bu **1.10**
X = Br, R = n-Bu **1.11**
X = H, R = Bn **1.12**

Figure. 1.22.

In contrast to these results, diphosphines **1.10** and **1.11** (Figure. 1.22) in the palladium catalysed cross-coupling has showed activity that only slightly exceeds the activity of PPh_3 [98].

Table 1.10

*Nickel-catalysed Kumada–Tamao–Corriu of aryl chlorides at room temperature using phosphine **1.5** and **1.8**.*

№	*Substrate*	*Time, h.*	*Conversion (%)*	
			1.5	***1.8***
1.		6	72.2	88.2
2.		6	66.7	92.3
3.		24	62.5	80.9
4.		24	45.2	64.4

Conditions: ArCl:PhMgBr:P:Pd = 100:200:6:3, dioxane, 25 ˚C.

1.3. Conclusion

Based on the review of the literature one could pointed that at present time a large number of phosphorus-containing calix[4]arenes are widely used in a broad range of metal-complex catalized reactions. However, catalyzed asymmetric reactions are still rare. The use of calix[4]arenes phosphoric acids in catalysis has not been described in the literature.

CHAPTER 2

CALIX[4]ARENES FUNCTIONALIZED WITH P(III)-GROUPS, SYNTHESIS AND CATALYTIC PROPERTIES

Catalysis is now a major tool to carry out organic transformations. Catalysis is commonly divided in homogeneous catalysis, where catalysts and reagents are in the same phase and heterogeneous catalysis where the catalytic reaction is carried out in multiphasic conditions. Even if homogeneous catalysts are often better defined and more selective, heterogeneous catalysts are much employed in industry because of the easier separation between catalysts and products at the end of the reaction, since the cost of the separation steps from the reaction mixture is estimated to be around 80% of the total cost for most chemical processes [99]. To try to benefit from the advantages of both homogeneous and heterogeneous catalysis [99], a lot of efforts have been devoted in the last decades to develop supported homogeneous catalysis by grafting homogenous catalysts on various supports like inorganic supports [100] polymers [101] dendrimers [102].

Additional interactions in the substrate-ligand complex due to the complexity of the structure of ligand groups capable of further interactions - hydrogen, π-stacking, etc. Have been proved to play a very important role in catalysis[103,104]. For this reason, I was aked to develop new chiral ferrocene phosphine ligand on a tetrahydroxy-tetra-para-*tert*-butylcalix[4]arene platform (see figure 2.1).

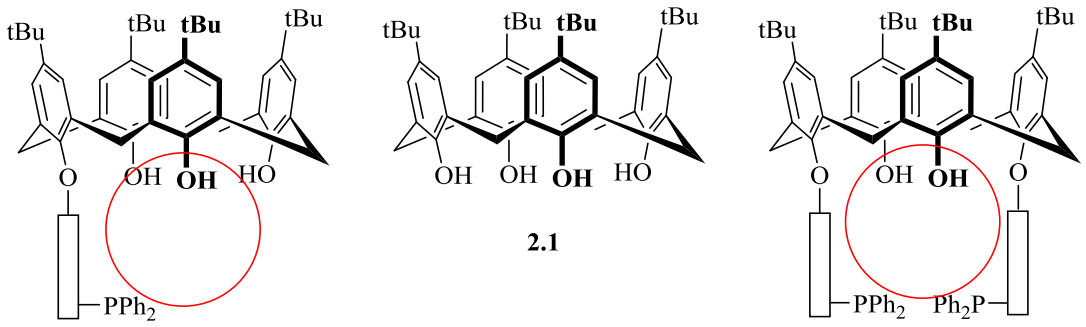
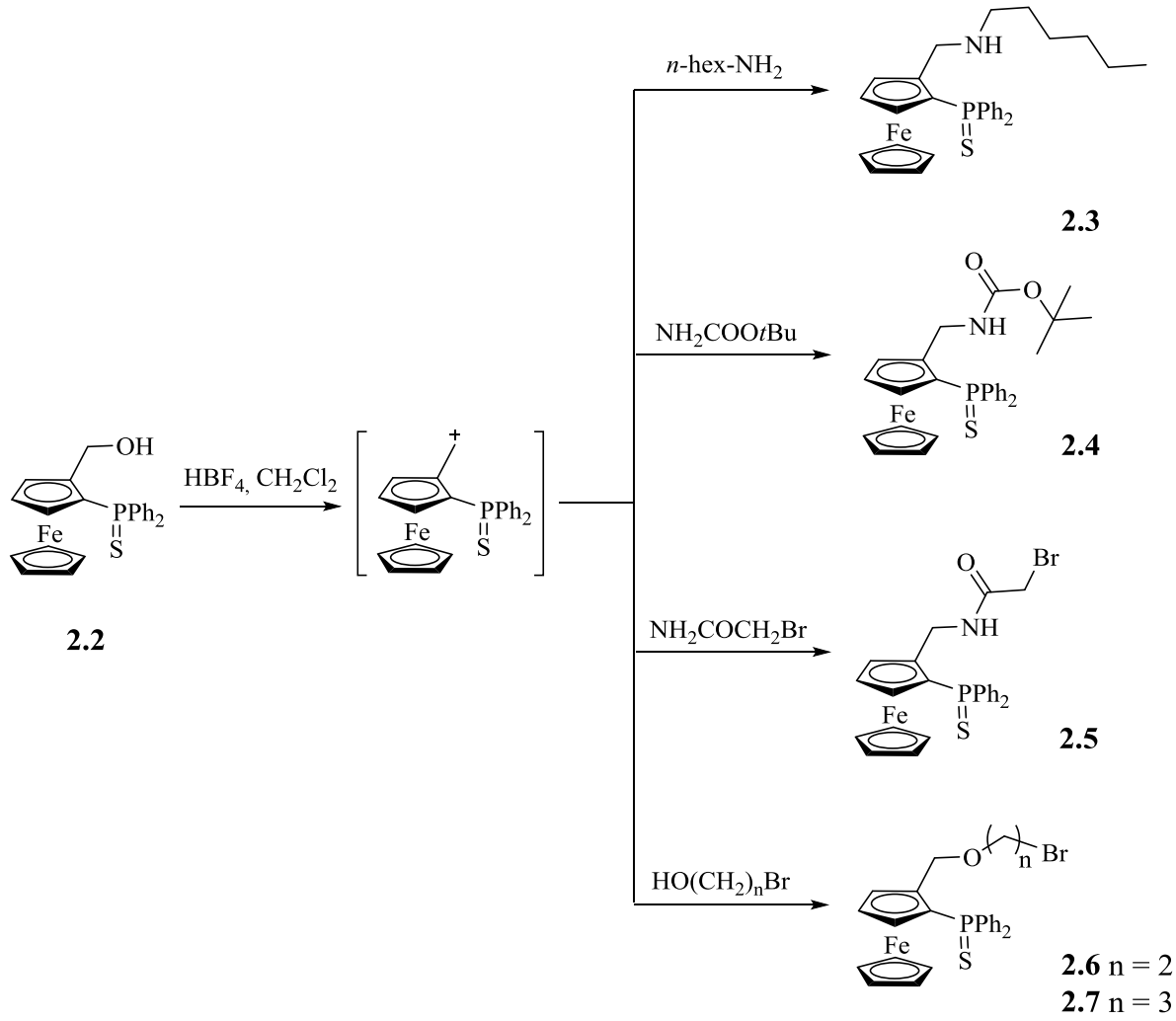


Figure. 2.1.

2.1. Synthesis of new ferrocene derivatives for ligand grafting

The synthesis of the different ferrocene ligands ready for grafting is presented in Scheme 2.1. All syntheses are based on the specific reactivity of the alcohol **2.2**, which can be very efficiently activated by a strong acid like tetrafluoroboric acid, the carbocation-type intermediate being efficiently quenched by various nucleophiles [105]. These one-pot syntheses are realized within 5 minutes, including a chromatographic separation on silicagel. The reactions described in this article have been carried out with racemic **2.2**, but both pure enantiomers are easily available [106], and then compounds **2.3** – **2.7** in enantiomerically pure form should be easily available as well. The isolated yields in the desired products were good to excellent (from 61 to 95%). Compound **2.4** is a BOC-protected form of 2-thiodiphenylphosphino (aminomethyl) ferrocene which could be like compound **2.3**, tether to various supports by reaction with an electrophilic reagents when compounds **2.5** – **2.7** need nucleophilic reagents to be grafted.



Scheme 2.1. Synthesis of new ferrocene derivatives for ligand grafting **2.3** – **2.7.**

Monocrystals suitable for X-ray diffraction analysis of compounds **2.5** – **2.7** could be obtained by slow diffusion of hexane into dichloromethane solution. Molecular view of the 3 structures are represented in Figures 2.2, 2.3 and 2.4. Compounds **2.6** and **2.7** differ only by the length of the O-$(CH_2)_n$-Br chain, 2 CH_2 for **2.6** and 3 CH_2 for **2.7**. The bond lengths and angle within the $Fc(PS(C_6H_5)_2)CH_2X$ (X=N, O) framework are similar within experimental errors. In compounds **2.6** and **2.7**, the Cp rings are roughly eclipsed with twist angle of 2.8(6)° and 2.5(5) respectively, whereas in **2.5**, the Cp rings are rather eclipsed with a twist angle of 18.3(8)°. In the 3 compounds, as usual for such substituted ferrocene, the S atom is endo with respect to the Cp ring to which it

is attached with distances from the Cp of 1.23(2), 1.34(1) and 1.256(7) Å respectively for **2.5**, **2.6** and **2.7**. In compound **2.6** and **2.7**, the O1 is exo with respect to the Cp ring and the C2-C21-O1 plane is roughly perpendicular to the Cp with a dihedral angle of 88.3(4)° and 79.3(2)° respectively, whereas in compound **2.5** the N1 atom is endo with respect to the Cp ring and the dihedral angle between the Cp and the C2-C21-N1 plane is -32.9(9)°. In compound **2.5**, the N1-C22 distance, 1.304(11) Å is shorter than the N1-C21 of 1.444(11) Å indicating a partial double bond character as also underlined by the nearly planar arrangement of the four C21-N1-C22-O1 atoms: the largest deviation from the mean plane being 0.012(7) at C(22).

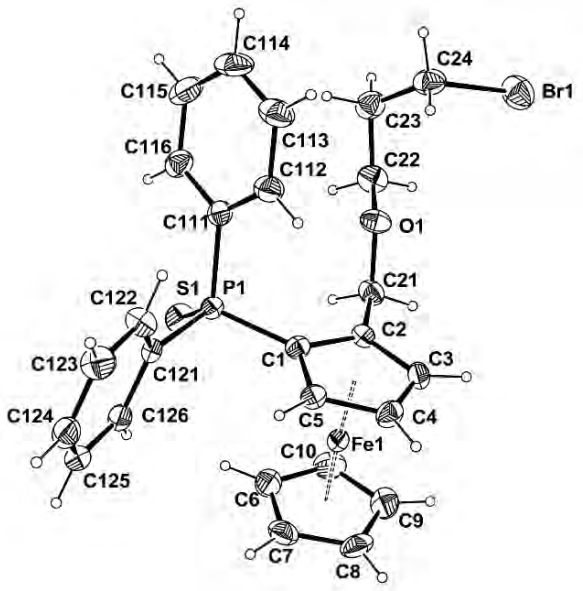


Figure. 2.2. Molecular view of compound **2.5** with the atom labeling scheme. Ellipsoids are drawn at the 50% probability level. H aroms are represented as small circle of arbitrary radii.

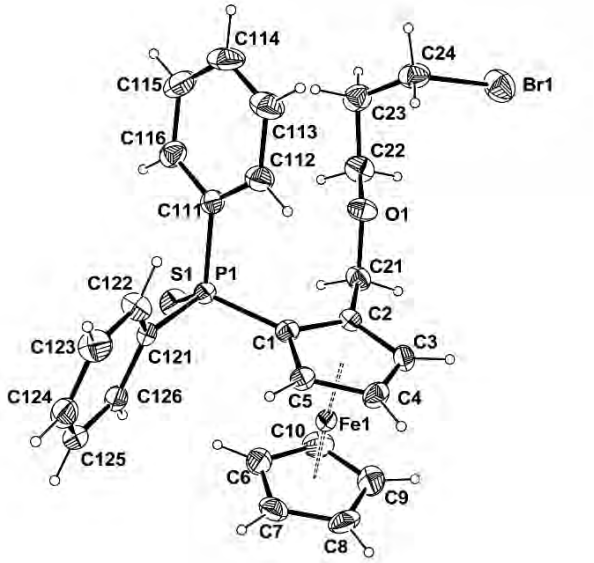


Figure. 2.3. Molecular view of compound **2.6** with the atom labeling scheme. Ellipsoids are drawn at the 50% probability level. H aroms are represented as small circle of arbitrary radii.

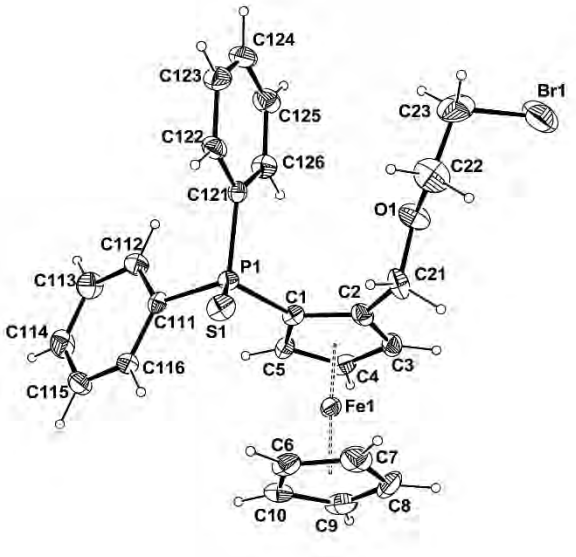
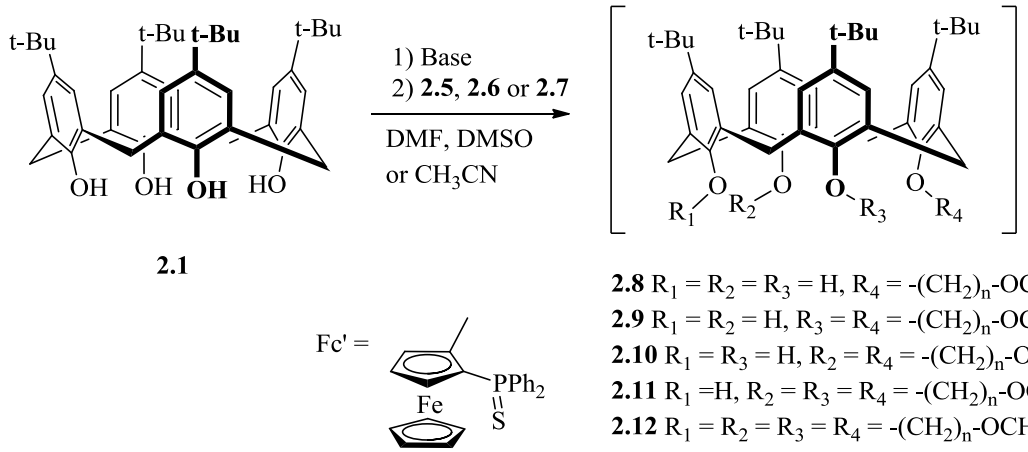


Figure. 2.4. Molecular view of compound **2.7** with the atom labeling scheme. Ellipsoids are drawn at the 50% probability level. H aroms are represented as small circle of arbitrary radii.

Thus, ferrocenyl phosphines **2.5** - **2.7** was planned to be grafted to the lower rim of calix[4]arene macrocyclic skeleton using known methods for alkylation of phenolic hydroxyles: NaOH in DMSO-water, CH_3ONa in absolute DMF, NaH in absolute DMF, $Ba(OH)_2$ in absolute DMF and K_2CO_3 in acetonitrile (Scheme 2.2).



2.1

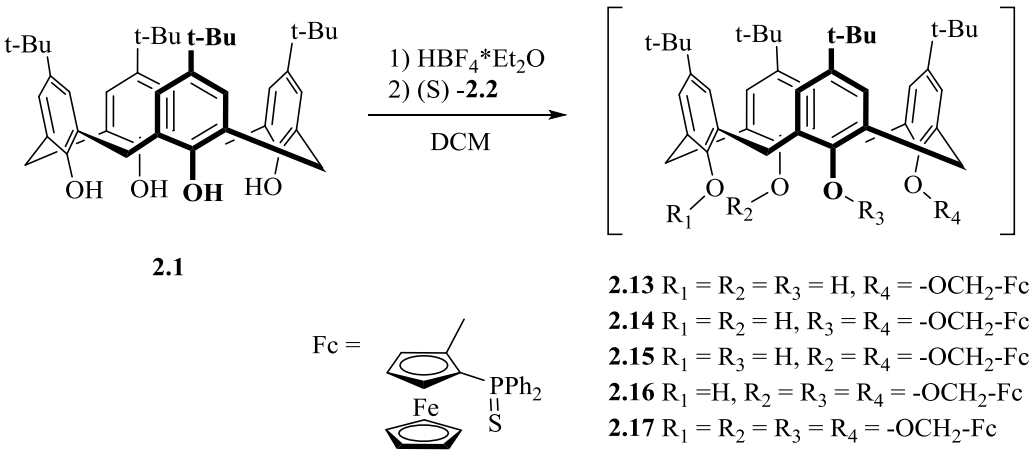
2.8 $R_1 = R_2 = R_3 = H$, $R_4 = -(CH_2)_n-OCH_2-Fc'$
2.9 $R_1 = R_2 = H$, $R_3 = R_4 = -(CH_2)_n-OCH_2-Fc'$
2.10 $R_1 = R_3 = H$, $R_2 = R_4 = -(CH_2)_n-OCH_2-Fc'$
2.11 $R_1 = H$, $R_2 = R_3 = R_4 = -(CH_2)_n-OCH_2-Fc'$
2.12 $R_1 = R_2 = R_3 = R_4 = -(CH_2)_n-OCH_2-Fc'$

Scheme 2.2.

However, in all conditions used, the reaction did not occur. A possible reason is the low electrophilic properties of reagents along with strong steric hindrance on calixarene **2.1**. Degradation of ferrocenyl compounds **2.6** or **2.7** was usually observed.

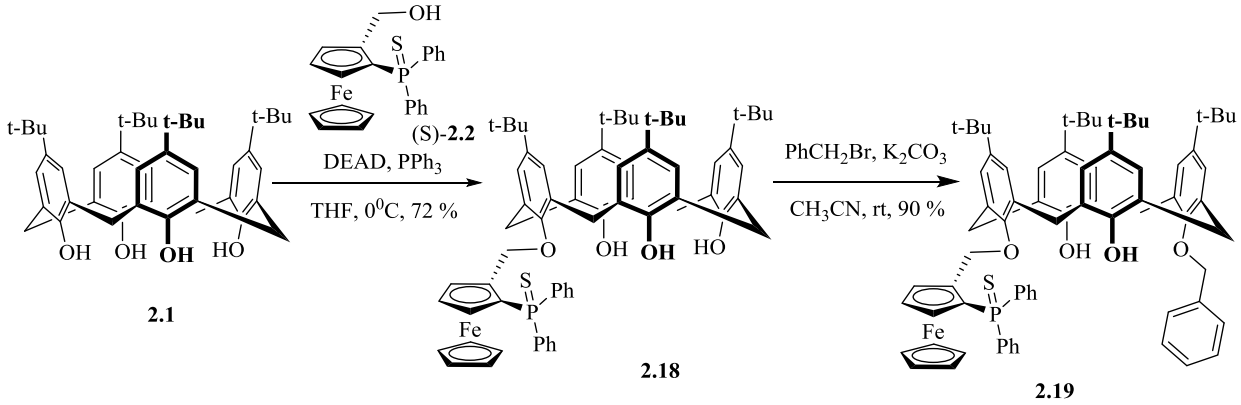
2.2. Synthesis of new chiral ferrocene phosphino calix[4]arenes in enantiomerically pure form

We next tried to carry out the reaction of alcohol **(S)-2.2** with calix[4]arene **2.1** after activation by tetrafluoroboric acid. However, this method failed: **(S)-2.2** was fully decomposed under these conditions without the formation of any of desired product (Scheme 2.3).



Scheme 2.3.

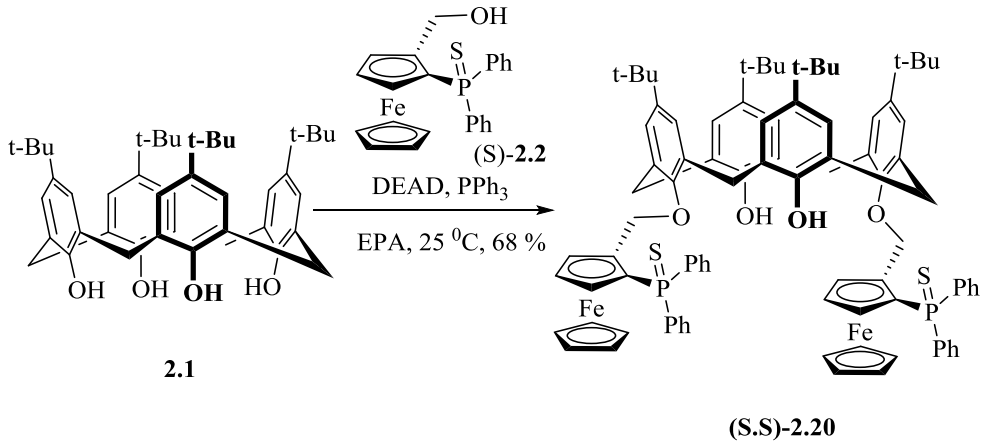
We then decided to use milder conditions to activate phenol **2.1**. Using classical Mitsunobu reaction conditions (PPh_3, diethyl azodicarboxylate (DEAD)), which have been successfully applied to the selective O-alkylation of calix[4]arenes [107,108,109,110]. We were able to synthesize selectively the monosubstituted compound **(S)-2.18** from 4-tert-butylcalix[4]arene **2.1** in THF at 0°C with 72% yield (Scheme 2.4). Subsequent alkylation of calixarene **(S)-2.18** using benzyl bromide under basic conditions in acetonitrile at room temperature was totally selective yielding exclusively the distally disubstituted compound **(S)-2.19** (see Scheme 2.4).



Scheme 2.4.

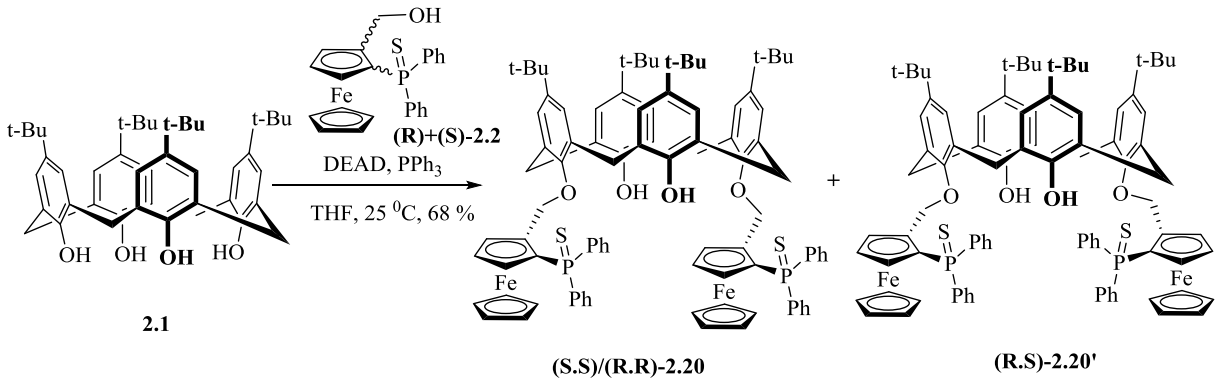
This kind of regioselectivity is usual in monosubstituted calixarenes and is usually explained by interplaying of the intramolecular hydrogen bonds between the OH groups at the lower rim of the macrocycle.

When the Mitsunobu condensation of calixarene **2.1** with ferrocenylmethanol **(S)-2.2** was carried out at RT instead of 0 °C, the distal bi-thiophosphinoferrocenyl calixarene **(S,S)-2.20** (see Scheme 2.5) was formed in good yields after 35 h. Similar distal substitution has been observed for alkylation of hydroxycalixarenes in Mitsunobu conditions [110].



Scheme 2.5.

To probe that no erosion of enantiomeric purity of the ferrocene parts occurs during the synthesis of **(S,S)-2.20**, we carried out in the same conditions the reaction between **2.1** and racemic **2.2** instead of enantiomerically pure **(S)-2.2**. Two diasteroisomers were then found in the reaction mixture in a 1/1 ratio, which could not be separated. Some ^{31}P or ^{1}H NMR signals of the meso diastereoisomer **(R,S)-2.20'** could be identified. These signals are absent from the spectrums of **(S,S)-2.20** showing that **(S,S)-2.20** is diastereoisomerically pure and therefore enantiomerically pure. We can also imagine that no erosion of of enantiomeric purity of the ferrocene part occurs during the synthesis of **(S,S)-2.18**, in milder conditions (0°C instead of RT). (Scheme 2.6).



Scheme 2.6.

Single crystals suitable for X-ray diffraction analysis were obtained by slow evaporation of acetonitrile solutions of compounds **(S)-2.18** and **(S,S)-2.20**. A molecular view of compound **(S)-2.18** is represented in Figure 2.5. As observed in related calixarenes substituted with ferrocenyl moieties, the calixarene in **(S)-2.18** has an irregular cone conformation with a dihedral angle between the two distal phenyl rings bearing a hydroxyl group of 77.5(5)° whereas the dihedral angle between the other two distal phenyl rings, bearing respectively a hydroxyl and the ferrocenyl group, is 55.0(2)°. Within the ferrocenyl moiety, the two Cp rings are nearly parallel with a dihedral angle of 3.2(3)° and the substituted Cp ring is nearly coplanar with the bisecting plane of the calixarene ring (defined by the O1, C111, C311 and O3 atoms) with a dihedral angle of 11.61(4)°. As expected, intramolecular O-H···O hydrogen bonding between the hydroxyl groups are present in the crystals of of compound **(S)-2.18** (see Table 2.1).

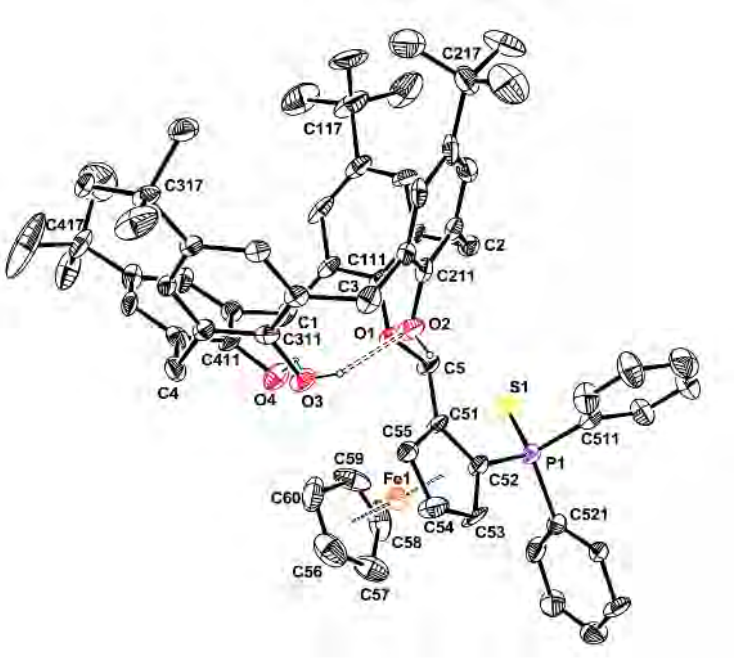


Figure. 2.5. Ortep view of compound **(S)-2.18** with the atom labeling scheme. Ellipsoids are drawn at the 30% probability level. The H atoms attached to carbon atoms have been omitted for the sake of clarity. Hydrogen bonds between the hydroxyl groups are represented as dashed line.

Table 2.1

Intramolecular O-H···O hydrogen bonding between the hydroxyl groups in the crystal of **(S)-2.18**.

D—H···A	*D—H*	*H···A*	*D···A*	*D—H···A*
O3—H3···O2	0.82	1.99	2.672 (11)	139.8
O4—H4···O3	0.82	2.04	2.654 (11)	131.7

In the crystal structure of compound **(S,S)-2.20** there are two roughly identical molecules within the asymmetric unit, only one of them being represented in Figure 2. The poor quality of the data does not allow detailed discussion of the bonding parameters but clearly proves the molecular structure, confirming the spectral analyses. The distances between the O atoms suggest the presence of H-bonding.

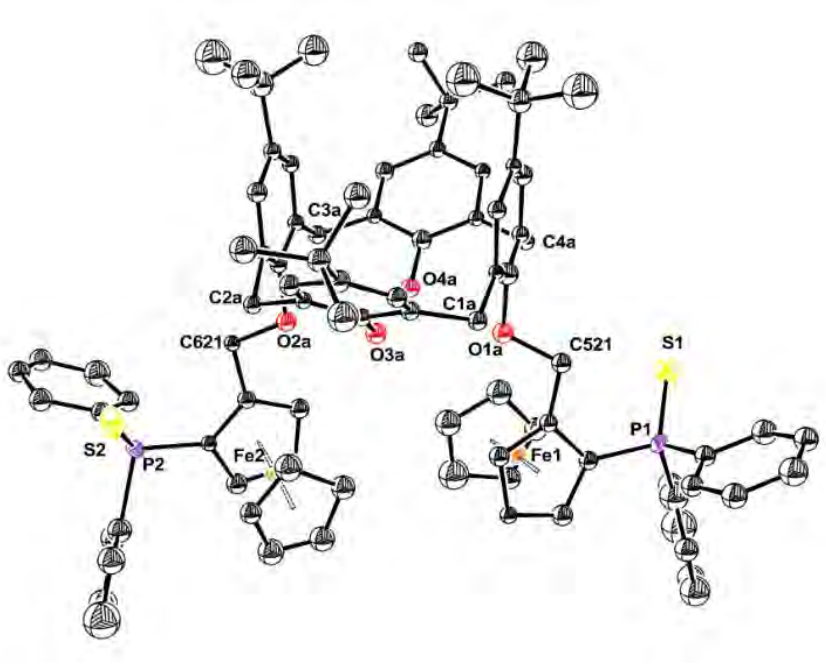
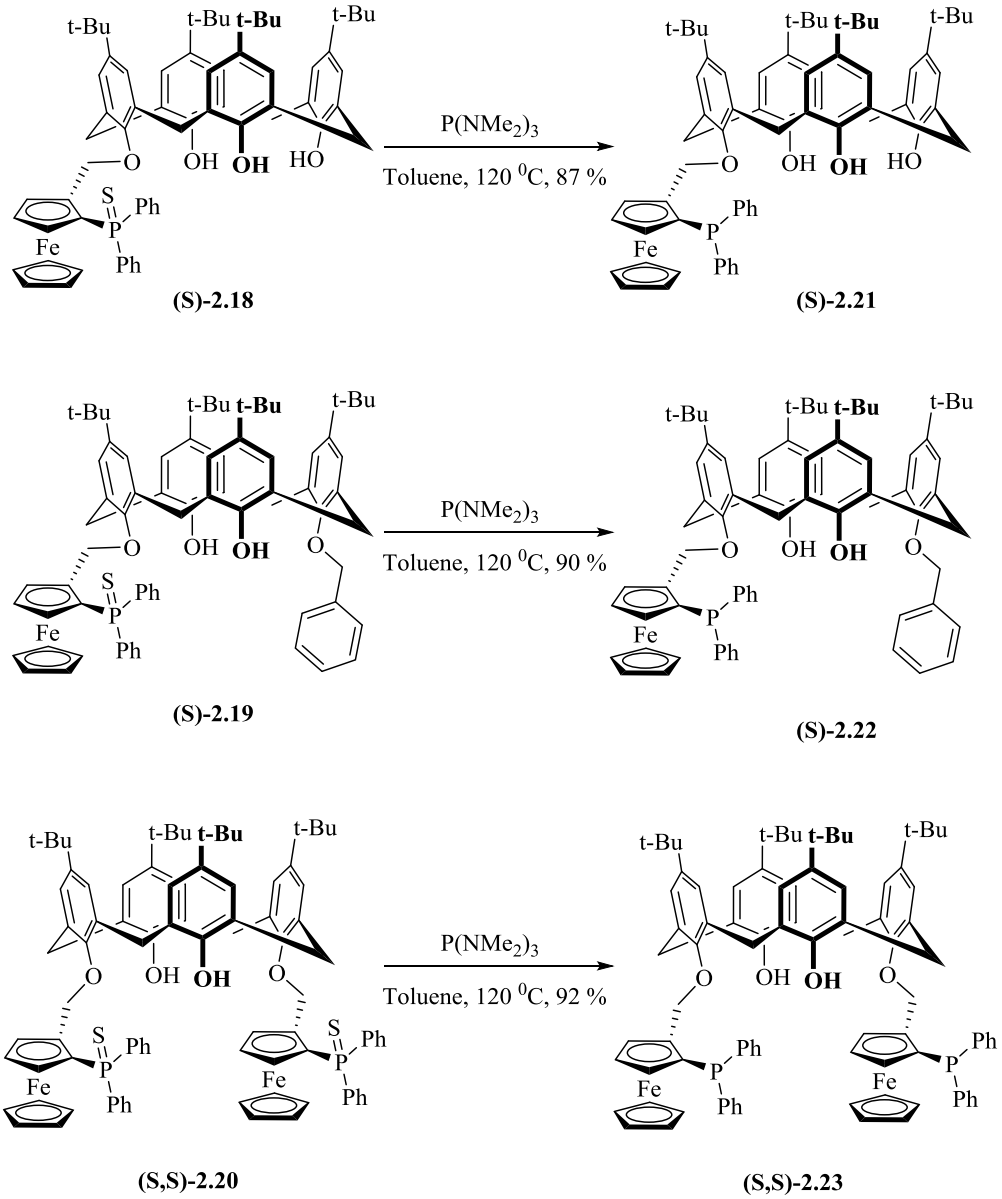


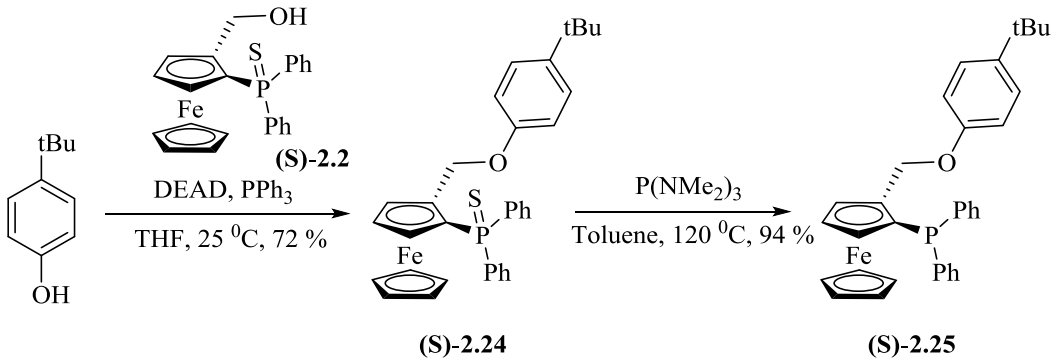
Figure. 2.6. Ortep view of compound **(S,S)-2.20** with the atom labeling scheme. Ellipsoids are drawn at the 30% probability level. H atoms attached have been omitted for the sake of clarity.

To remove sulfide protection from substituted phosphines exists several experimental approaches, including the use of Raney nickel or phosphines like $P(N(CH_3)_2)_3$. All attempts to provide desulfuration of **2.18** - **2.20** by Raney nickel action did not succeed but yield the original calix[4]arene **2.1** and (S)-(2-diphenylthiophosphinoferrocene) methanol **2.2**. The use of $P(N(CH_3)_2)_3$ in boiling toluene for 10 hours, gave free phosphines with yields of 87 - 92% (Scheme 2.7).



Scheme 2.7. Desulfuration of thiophosphines.

In order to be able to determine the influence of the calixarene moieties of the ligands **2.21** and **2.22** on theircatalytic properties, compound **2.24** was synthesized by a Mitsunobu reaction. After removing the sulfide protection enantiomerically pure ligand **2.25** was obtained (Scheme 2.8).

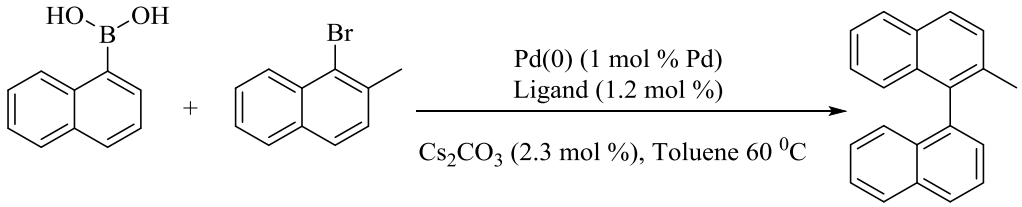


(S)-2.24 **(S)-2.25**

Scheme 2.8.

2.3. Catalytic properties of obtained phosphines

The catalytic efficiency of the chiral calixarene mono(ferrocenylphosphine) ligands **(S)-2.21** and **(S)-2.22** were tested in the palladium-catalyzed Suzuki-Miyaura cross-coupling reaction (Scheme 2.9) and that of the di(ferrocenylphosphine) ligand **(S,S)-2.23** in the Tsuji-Trost allylic substitution reactions.



Scheme 2.9. Suzuki-Miyaura cross-coupling reaction.

The asymmetric version of the well-known palladium-catalyzed Suzuki-Miyaura cross-coupling reaction has only been developed in the last fifteen years and is still largely challenging since no privileged ligands with broad substrate range have emerged. If efficient catalytic systems for Suzuki-Miyaura cross-coupling reaction with calixarene-based ligands have already been developed, [15, 61] no asymmetric versions have been published yet to the best of our knowledge. To check whether the calixarene macrocyclic frame could

influence the coupling reaction of 1-naphthaleneboronic acid and 1-bromo-2-methylnaphthalene, we compared **(S)-2.21** and **(S)-2.22** with modeling compound diphenylphosphino ferrocene **(S)-2.24** (see Table 2.2). Using bis(dibenzylideneacetone)palladium(0) (Pd(dba)2) as palladium precursor at 60 °C, the catalytic systems based on ligands **(S)-2.21** and **(S)-2.22** were really sluggish. However using allylpalladium chloride dimer, full conversions and good yields of the coupling products could be obtained after 24 h but the enantiomeric excesses of 2-methyl-1,1'-binaphtalene were very low (less than 5%), lower than the one we could obtain using other phosphine-ether ligand based on the same chiral scaffold **(S)-2.24**, bearing a 4-t-butylphenyl substituent, which can found also in ligands **2.21** and **2.22** (see Table 2.2). Contrary to expectations, the free hydroxy groups in the lower rim of the ligands do not have positive effects on catalysis by establishing hydrogen bonds with the incoming boronic acids. Possibly, these OH groups could enter the palladium coordination sphere giving rise to several coordination complexes with an overall lowering of the enantioselectivity.

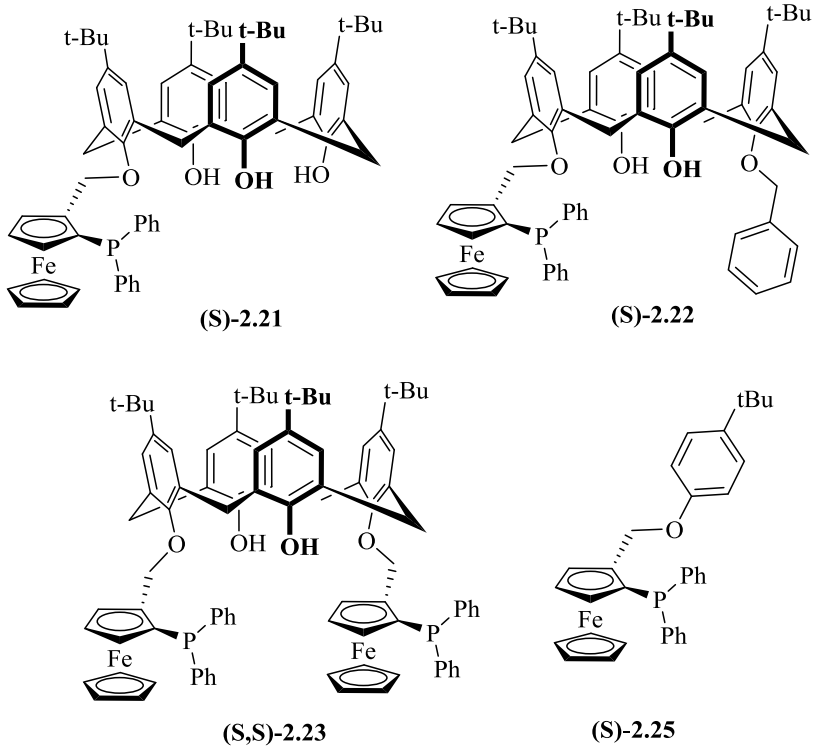


Figure. 2.7. Prepared phosphine ligands.

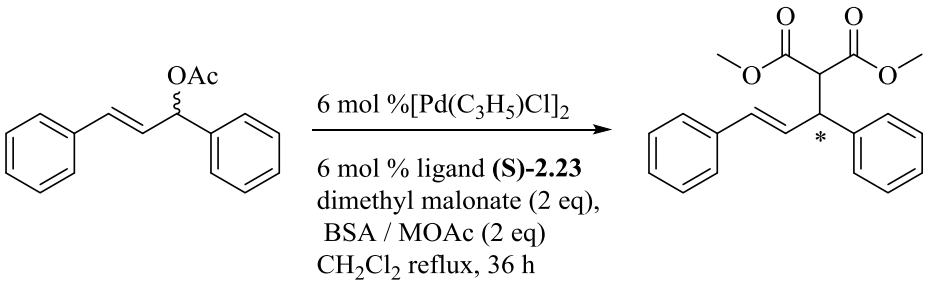
Table 2.2

Suzuki-Miyaura cross-coupling reaction results

№	Ligand	Palladium precursor	Yield, %	*ee*, %
1.	**(S)-2.21**	$Pd(dba)_2$	<5	-
2.	**(S)-2.22**	$Pd(dba)_2$	<5	-
3.	**(S)-2.21**	$[Pd(Cl(allyl)]_2$	66	<5
4.	**(S)-2.22**	$[Pd(Cl(allyl)]_2$	100	<5
5.	**(S)-2.25**	$[Pd(Cl(allyl)]_2$	82	34

Reactions carried out with ligand (0.012 mmol, 1.2 mol %), palladium precursor (1.1 mol % of palladium), 1-naphthaleneboronic acid (1.2 mmol), cesium carbonate (2.3 mol %), 1-bromo-2-methylnaphthalene (1.00 mmol) in 10 mL of toluene at 60°C during 24h.

We have also tested ligand **(S,S)-2.23** in the asymmetric allylic alkylation of 1,3-diphenylprop-2-enyl acetate by dimethylmalonate (see Table 2.3). Full conversion and good yields of malonate could be obtained whatever the acetate salt used with the N,O-bis(trimethylsilyl)acetamide (BSA) probase. However, the enantiomeric excess of the product depended strongly on the acetate alkaline cation, the best enantioselectivity being obtained with potassium (Table 3, entry 3). This 86% enantiomeric excess is, to the best of our knowledge, the best ones obtained in asymmetric allylic substitution using a calixarene-based ligand [38]. In the presence of the potassium cation, we can suppose that the dimethylmalonate anion interacts more strongly with the two hydroxyl groups of ligand **(S,S)-2.23**, directing the nucleophile more selectively toward one carbon of the π-allyl intermediate. This hypothesis is further supported by the fact that when the K^+-specific complexing agent 18-crown-6 crown ether was added to the reaction mixture, the ee of the product dropped (Table 3, entry 4).



Scheme 2.10. Asymmetric allylic alkylation reaction.

Table 2.3

*Asymmetric allylic alkylation in presence of the diphosphine ligand **(S,S)-2.23**.*

№	Base	Yield, %	*ee*, %
1.	CH_3COOLi/BSA	86	14
2.	CH_3COONa/BSA	76	25
3.	CH_3COOK/BSA	75	86
4.	CH_3COOK/BSA (+ 1.2 eq 18-Crown-6)	86	32
5.	CH_3COOCs/BSA	88	71

In conclusion, in this chapter, we described the synthesis of three new chiral enantiomerically pure phosphinoferrocenyl calixarene ligands. To the best of our knowledge, these compounds are the first calixarene derivatives bearing planar chiral ferrocenyl moieties. We have carried out preliminary catalytic tests with these ligands in two asymmetric reactions: the asymmetric Suzuki-Miyaura coupling reaction and the asymmetric Tsuji-Trost reaction. Although the enantioselectivities observed in the Suzuki-Miyaura reaction were disappointing, interesting enantiomeric excesses (ee up to 86%) were obtained with ligand **(S,S)-2.23** in the asymmetric allylic alkylation.

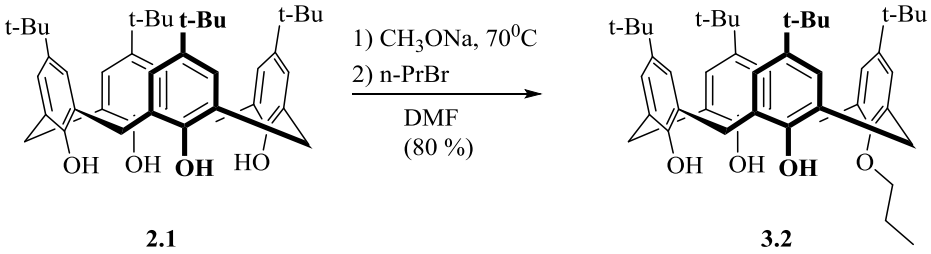
CHAPTER 3

CALIX[4]ARENES FUNCTIONALIZED WITH P(V)-GROUP (PHOSPHONIC ACIDS) SYNTHESIS AND CATALYTIC PROPERTIES

3.1. The synthesis of inherently chiral calix[4]arenes with ABHH type of substitution on the lower rim

The greatest practical interest are the inherently chiral calix[4]arenes, whose optical activity is due to the asymmetric position of achiral substituents on the macrocyclic platform. Although a great number of ‘‘inherently’’ chiral calixarenes have been described, most of them had been obtained as racemates or diastereomeric mixtures. Only a few of them had been resolved into individual isomers and characterized by X-ray structural analysis.

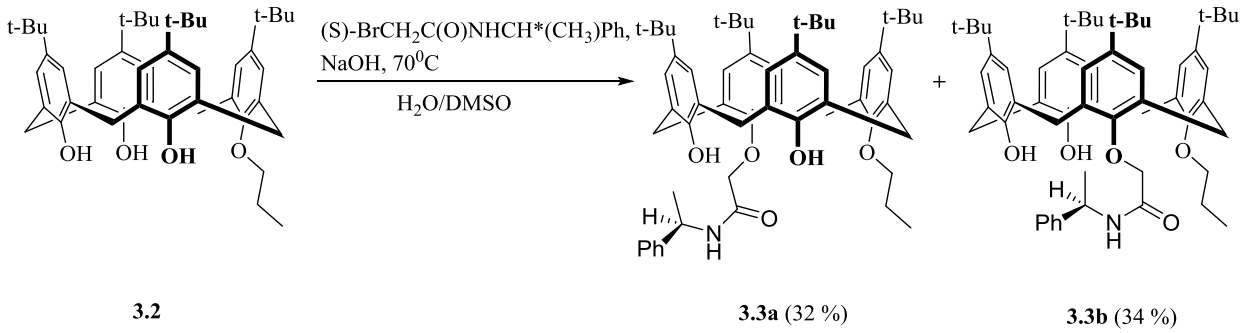
The optically pure inherently chiral tetra-p-tert-butylcalix[4]arene carboxylic acids **4a,b** were obtained from available monopropoxycalix[4]arene **3.2** in two steps.



2.1 **3.2**

Scheme 3.1. Synthesis of monopropoxycalix[4]arene **3.2.**

In the first step, the alkylation of monopropoxycalix[4]arene **3.2** with chiral (S)-N-(1-phenylethyl)bromoacetamide was carried out in NaOH/DMSO medium at 70–75 C. As known, the alkylation in such conditions proceeds regioselectively [112] and leads to 1:1 mixture of diastereomeric 1,2-heterosubstituted calix[4]arene **3.3a** and **3.3b** (Scheme 3.2). The two diactereomers pair was separated by column chromatography on silica gel (hexane/ethyl acetate 6:1).



3.2 **3.3a** (32 %) **3.3b** (34 %)

Scheme 3.2. Synthesis of diastereomeric pair **3.3a** and **3.3b**.

The absolute configuration of the molecule **3.3a** has been established by X-ray diffraction using the known absolute configuration of the asymmetric carbon atom in phenylethylamide group (Figure. 3.1). It was found that the substituents HO, HO, PrO, Ph(Me)CHNHC(O)CH_2O on the calixarene macrocycle are placed clockwise (view from above) and this isomer may be described as cS. Then in isomers **3.3b** these substituents are located counterclockwise and it has cR configuration [129].

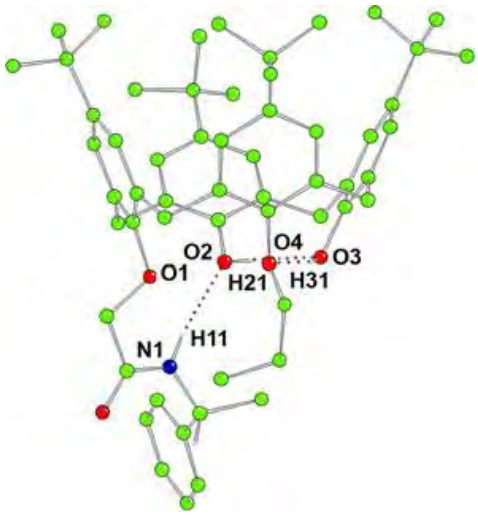
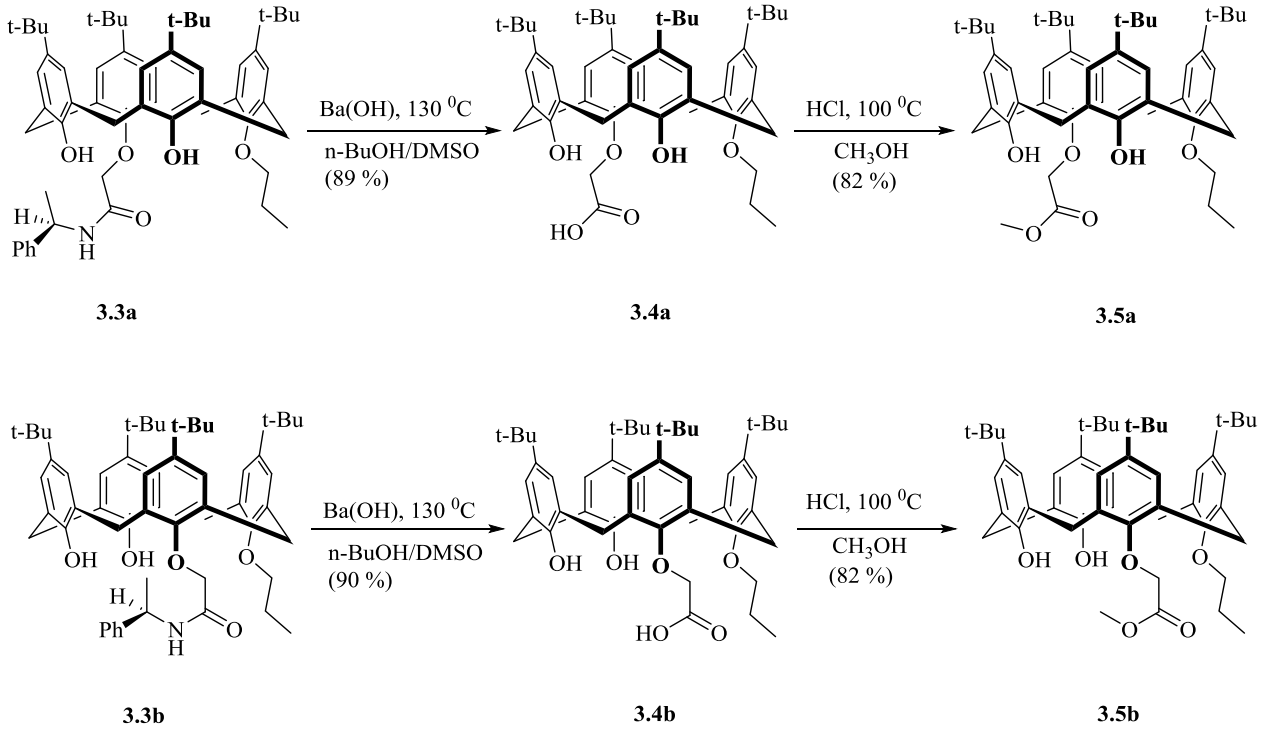


Figure. 3.1. Molecular structure of calixarene **3a**.

In the next step, the individual enantiomers of calix[4]arene carboxylic acids **3.4a-b** were obtained after hydrolytic removing of auxiliary phenylethylamide groups in compounds **3.3a** and **3.3b**, respectively. It should be noted that NH groups in calix[4]arenes **3.3a-b** are included in the system of intramolecular hydrogen bonds on the lower rim of macrocycle (Figure. 3.1). The consequences of this feature is a significant stabilisation of compounds **3.3a** and **3.3b** which makes more difficult both acid and alkaline hydrolysis. We found that chiral inductor can be removed only in boiling mixture of n-butanol/DMSO (20 : 1) in the presence of 10–12-fold excess of barium hydroxide for 3–4 h (Scheme 3.2). The yield of the target acids reached 89–90 %.

Previously, similar conditions, but with Ba(OH)2•8H2O, were used by Zhi-Tang Huang et all. to remove protective acrylic group in calixarenamides [113].



Scheme 3.3. Synthesis of calix[4]arene carboxylic acids **3.4a,b** and methyl

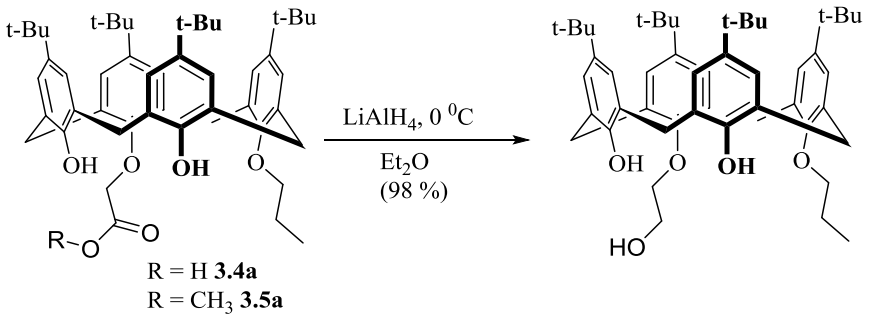
esters **3.5a,b**.

The acids **3.4a,b** reacts with alcohol under acid catalysis and form the corresponding esters. Thus, in boiling methanol in the presence of chlorhydric acid, methyl esters **3.5a,b** were obtained in 82 % yield after 30–40 min reaction (Scheme 3.2).

All compounds **3.3**–**3.5** adopt the cone conformation in solution. This fact is confirmed by NMR spectra. Thus, in ^{1}H NMR spectra AB-spin system is observed for $ArCH_2Ar$ methylene protons with an average coupling constants J_{HH}^{2} = 12.2–13.9 Hz and the difference between resonances of the axial and equatorial protons $\Delta\delta > 0.5$ ppm. In the ^{13}C NMR spectra all signals of bridges carbons are in the range 31–34 ppm. The very broad signal of carboxyl hydrogen (12.40–12.60 ppm) and the shift of the signals of phenolic hydrogens to weak field (10.10 and 10.33 ppm) in the acids **3.4a,b** indicates a strong hydrogen bonds between these groups.

In further studies, we used derivatives of the first isomer: acid **3.4a** and corresponding ester **3.5a**. However, it can be expected that the others enantiomers would react similarly.

The first step towards obtaining phosphonic acid based on already formed macrocycle was to reduce the carboxyl group in ester **3.5a**. Since, there are two acidic protons of phenolic OH groups in the compound, an 4-fold excess of lithium aluminum hydride was used. The reaction is carried out in diethyl ether at ice bath cooling (Scheme 3.4).



Scheme 3.4. Synthesis of enantiomerically pure calix[4]arene **3.6**.

After 1 hour reaction, work-up of the reaction mixture allow to isolated alcohol **3.6** with practically quantitative yield.

It was also shown that in these conditions acid **3.4** could be easily reduced, but a 5 eq. excess of lithium aluminum hydride should be used (Scheme 3.4). Alcohol is obtained with 95% purity (according to ^{1}H NMR data) and further used without purification. However, if necessary, the product can be purified additionally by column flash chromatography on silica using an hexane-ethyl acetate 3:1 mixture. The preservation of the chirality along the synthetic pathway from **3.4.** to **3.6.** was proved by a X-ray study on monocrystals of **3.6.** (Figure 3.2).

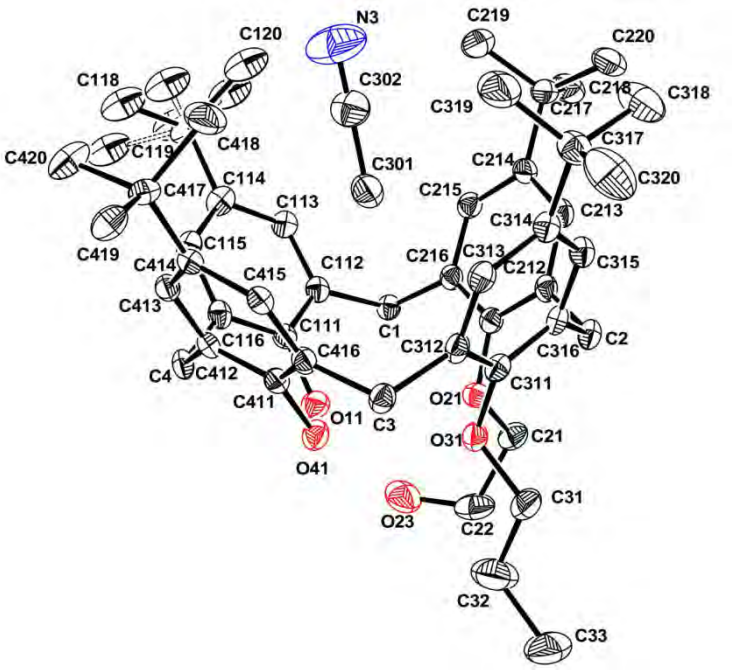


Figure. 3.2. Molecular structure of calix[4]arene **3.6**.

For further functionalization, halogen derivatives of calix[4]arenes are of particular interest, since such compounds can efficently react with nucleophiles. But attempts to synthesise chloro derivatives in classical way – through the reaction of alcohol **3.6** with thionyl chloride did not give in our hands the desired product: after boiling with thionyl chloride in chloroform no reaction was observed, and boiling in pure thionyl chloride yields a complex mixture of degradation products.

However, the use of Appel reaction (the reaction of alcohols with carbon tetrachloride in the presence of triphenylphosphine (Scheme 3.5)) was very successful. [114] The reaction proceeds by activation of the triphenylphosphine by reaction with the tetrahalomethane, followed by attack of the alcohol oxygen at phosphorus to generate an oxyphosphonium intermediate. The oxygen is then transformed into a leaving group, and an S_N2 displacement by halide takes place, proceeding with inversion of configuration if the carbon is asymmetric.

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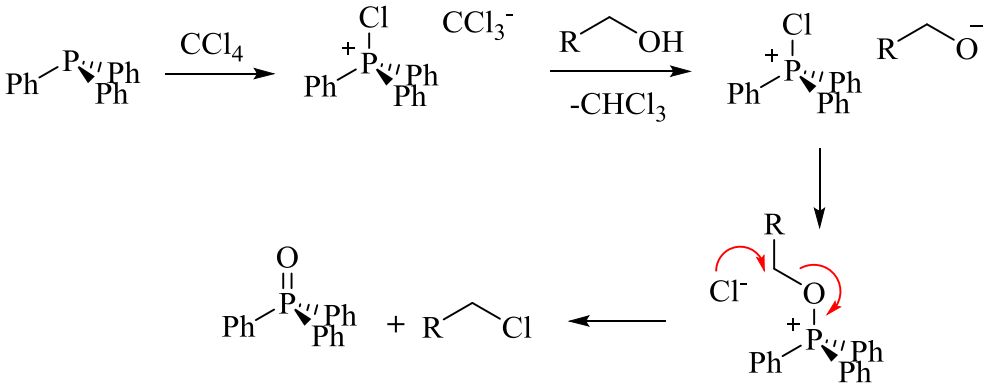
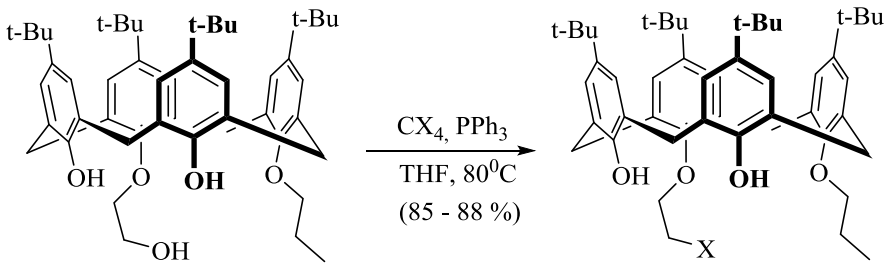


Scheme 3.5. Mechanism of the Appel Reaction**.**

First, reaction of alcohol **3.6** with triphenylphosphine was performed in pure carbon tetrachloride at various temperatures (from 0 °C to solvent boiling point) with control by TLC. But in such conditions no reaction was observed and starting material was recovered. A possible reason for this could be the insufficient solubility of triphenylphosphine in carbon tetrachloride. Therefore, we decided to use a mixture of carbon tetrachloride with another solvent with a higher boiling point. We tested a mixture of carbon tetrachloride-toluene, carbon tetrachloride-tetrahydrofuran and carbon tetrachloride-dimethylformamide. A positive result for the reaction was observed in the last two cases, the ratio of carbon tetrachloride and DMF 1: 5, and carbon tetrachloride, THF = 1: 4, but using THF allow to obtain product with higher yield. After boiling for 4-6 hours in this mixture, followed by solvent evaporation and purification of the products by flash column chromatography on silica gel (eluent - chloroform: hexane = 1: 1) to get the final product **3.7** as a white solid crystalline substance in good 85% yield (Scheme 3.6).

Similarly, bromide **3.8** can be prepared with slightly better yield with carbon tetrabromide (Scheme 3.6).

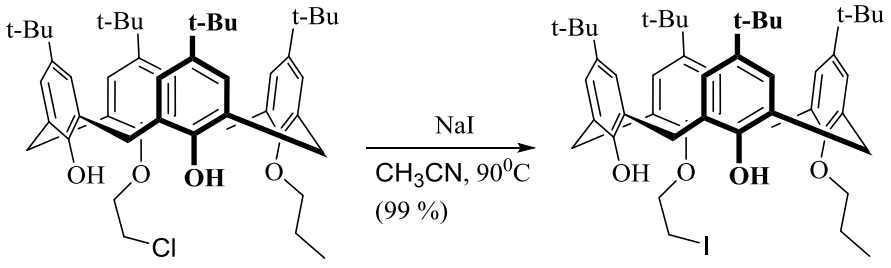


3.6

3.7 X = Cl
3.8 X = Br

Scheme 3.6. Synthesis of enantiomericaly pure calix[4]arenes halogen derivatives**.**

In order to increase the reactivity against nucleophiles, we tried to replace chlorine atoms by iodine. We then used classic conditions of Finkelstein reaction – reaction with sodium iodide in acetone [115]. Monitoring was carried out by TLC. However, even in boiling acetone, replacement did not occur. But, using acetonitrile with an higher boiling point instead of acetone, gave a positive result. After 120 hours at acetonitrile reflux in the presence of 25-fold excess of sodium iodide product, **3.9** was obtained quantitatively (Scheme 3.7).

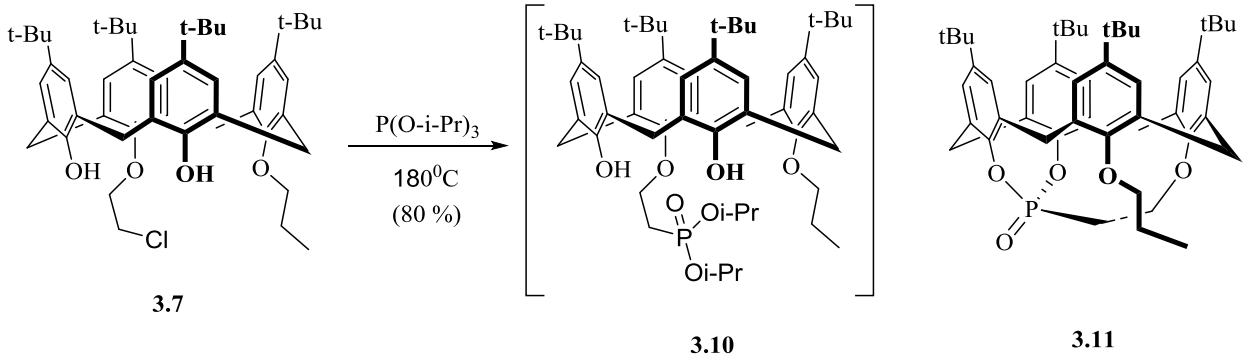


3.7 **3.9**

Scheme 3.7. Synthesis of enantiomericaly pure calix[4]arene **3.9.**

To introduce phosphoryl fragment in the synthesis of inherently chiral phosphorus-containing calix[4]arene with ABHH type of substitution was used Michaelis-Arbuzov reaction involving calix[4]arenes halides **3.7** – **3.9**. In classical conditions [76,77,78], boiling solution of the corresponding halide in

triisopropyl phosphite overnight, followed by removal of the remaining phosphite solvent in vacuo and chromatographic purification of the solid residue, yields the desired product. With compounds **3.7** – **3.9**, the only successful result was obtained with chloride **3.7**. A new product was obtained as a white solid. In the case of bromide **3.8** or iodide **3.9** after completion of the reaction a complex mixture of decomposition products was obtained in both cases. This result is explained by the hardness of the phosphite nucleophile (Scheme 3.8).



3.7 **3.10** **3.11**

Scheme 3.8. Synthesis of enantiomericaly pure calix[4]arene **3.11.**

However, the analysis of spectroscopic data of of product obtained from **3.7** showed that this new product is not the phosphonate **3.10** expected from Arbuzov reaction but a cyclic phosphonate **3.11** with a yield of 85-90% which can be obtained from **3.10** by transesterification (see scheme 3.8). The NMR data of **3.11** clearly proves the structure of the product, in particular the C-P coupligs of carbon atoms from phenolic rings that are bound to the phosphorus atom through a C-O-P connections. The structure of **3.11** was further established from X-ray study on monocrystals(Figure. 3.3).

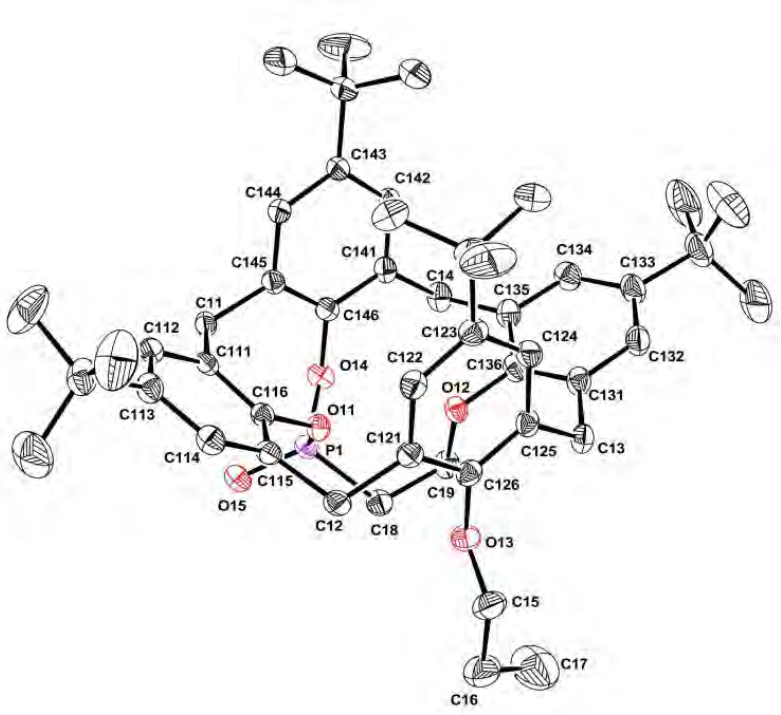


Figure. 3.3. Molecular structure of calix[4]arene **3.11.**

3.2. NMR studies of inherently chiral calix[4]arenes with ABHH type of substitution on the lower rim

For all obtained inherently chiral calix[4]arenes with ABHH type of substitution on the lower rim, a series of spectral studies was provided to confirm their structure. For convenience, the results are summarized in the tables below: ^{1}H NMR (Table 3.1) and ^{13}C NMR (Table 3.2).

Table 3.1

^{1}H NMR data for all obtained inherently chiral calix[4]arenes with ABHH type of substitution on the lower rim.

	3.6	**3.7**	**3.11**
$OCH_2CH_2C\underline{\boldsymbol{H}}_3$	1.16	1.06	1.11

C(C***H***$_3$)	1.17 1.20 1.23 1.31	0.99 1.17 1.21 1.21	0.58 1.00 1.34 1.36
OCH$_2$C***H***$_2$CH$_3$	2.08-2.25	1.98-2.22	1.80-1.96
Ar-C***H***$_2$-*eq*	3.37 3.43 3.44 3.45	3.32 3.35 3.41 3.46	3.19 3.24 3.36 3.48
OC***H***$_2$CH$_2$CH$_3$	3.86-3.94 4.02-4.08	3.80-3.90 4.07-4.17	3.68-3.89 4.18-423
OCH$_2$C***H***$_2$X	3.95-4.01 4.18-4.30	3.67-3.78 3.52-3.63	2.50-2.71 4.30-4.40
OC***H***$_2$CH$_2$X	4.18-4.30	4.07-4.17	3.68-3.89 4.30-4.40
Ar-C***H***$_2$-*ax*	4.19 4.30 4.50 4.60	4.10 4.12 4.40 4.50	4.35 4.39 4.49 4.70
OCH$_2$CH$_2$O***H***	5.23-5.21	—	—
Ar-***H***	6.94 6.96 7.08 7.09-7.11 (2H) 7.12 7.13-7.15 (2H)	6.86 (2H) 6.94 6.99 (2H) 7.03 (2H) 7.09	6.15 6.26 6.75 6.76 7.12 7.20 (2H) 7.22
O***H***	9.24	8.31	—

	9.66	8.94	—

The comparative table shows that a group of spatially distant from CH_2-group to which functional groups vary slightly influenced functional substituent – their signals virtually unchanged in several compounds **3.6**, **3.7**, **3.11**. The most informative is change of signal splitting and proton of CH_2-X groups. In this series of compounds going from X = OH to X = Cl and X = P, a shift in the signal position to strong field and an increase of the ^1H-^1H couplig constant growth were observed. In addition, the disappearance of phenolic hydroxyl signal in the compound **3.11** confirms phosphonate cyclic structure. The difference between the position of the last equatorial proton signal of bridging methylene groups and the first axial proton signal confirms that the compounds has a *cone* conformation. For *cone* result, the difference should bigger than 0.5, for *partial cone* or *alternate* the difference should be lower than 0.5. If the difference is closer to 0.5 but slightly higher, this indicates strongly *flattened cone* conformation [130]. In our case, the differences are: 0.74 for **3.6**, 0.64 for **3.7** and 0.87 for **3.11**, clearly indicating *cone* conformation.

Table 3.2

^{13}C NMR data for all obtained inherently chiral calix[4]arenes with ABHH type of substitution on the lower rim.

	3.6	**3.7**	**3.11**
(-C(***C***H_3)$_3$)	31.22 31.36 31.61 31.46	31.30 31.44 31.62 31.70	30.89 31.07 31.62 31.55
(***C***Me_3)	30.62	30.84	29.70

	32.73	32.65	29.70
	32.95	32.72	31.40
	33.18	33.77	32.09
$\underline{\boldsymbol{C}}^{Ph}$-*t*-Bu	142.70	141.96	144.94
	142.95	142.91	146.57
	146.61	145.90	146.81
	147.16	147.09	147.15
$\underline{\boldsymbol{C}}H^{Ph}$	124.97	124.83	124.03
	125.46	125.08	124.20
	125.46	125.19	125.05
	125.60	125.27	125.11
	125.80	125.47	125.51
	126.08	125.67	125.58
	126.46	126.63	125.96
	126.59	126.75	126.63
$\underline{\boldsymbol{C}}^{Ar}$-$CH_2$-$C^{Ar}$	126.94	127.88	128.33
	126.95	127.33	130.47
	127.97	128.56	130.88
	128.08	129.57	131.88
	130.11	132.18	132.31
	131.70	133.01	133.50
	133.87	133.03	135.31
	134.04	134.61	136.50
$\underline{\boldsymbol{C}}^{Ph}$-OH	148.28	148.13	146.28
$\underline{\boldsymbol{C}}^{Ph}$-OH	148.94	149.69	147.15
$\underline{\boldsymbol{C}}^{Ph}$-O-$CH_2$-	150.15	150.92	152.32
$\underline{\boldsymbol{C}}^{Ph}$-O-$CH_2$-	151.21	151.27	153.21
Ar-$\underline{\boldsymbol{C}}H_2$-Ar	33.90	33.97	33.42

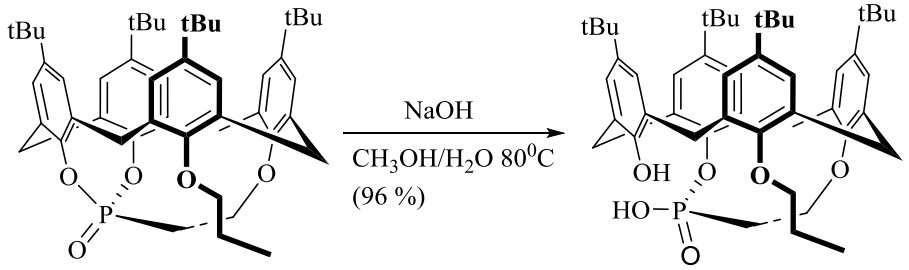
	33.97 34.12 34.13	34.04 34.07 34.27	33.82 34.22 34.33
O-***C***H_2-CH_2-CH_3	78.67	78.14	77.05
-***C***H_2-CH_3	23.15	23.32	23.60
-CH_2-***C***H_3	10.38	10.49	11.13
PhO-***C***H_2-CH_2-X	77.22	74.70	64.32
X-***C***H_2-CH_2-OPh	62.24	41.87	36.61

One could argue that due to its rigid structure compound **3.11** should have a *cone* conformation, which is another proof of the cycle phosphonate structure.

Comparison of ^{13}C NMR characteristics of the obtained compounds confirms the *cone* structure. For *cone* signals of bridging methylene groups carbon atoms are in the range of 29-34 ppm, *partial cone* or *alternate* - 35-37 ppm. Spectral data (Table 3.1 and Table 3.2) completely confirms proposed structure for compounds **3.6**, **3.7** and **3.11**.

3.3. Partial hydrolysis of cyclic phosphonate to obtain planar chiral phosphonic acid with ABCH type of substitution on the lower rim in enantiomerically pure form

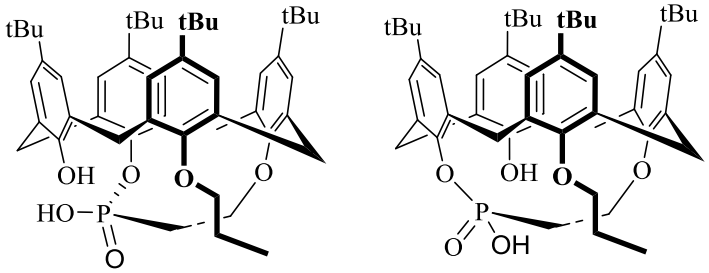
To obtain planar chiral phosphonic acid with ABCH type of substitution on the lower rim in enantiomerically pure form starting from cyclic phosphonate **3.11**, we used the classic hydrolysis conditions – refluxing ester in aqueous methanol solution of sodium hydroxide. This system allowed to obtain the product – phosphonic acid monoester, after saponification of only one C-O-P bond in quantitative yield (Figure 3.9).



3.11 **3.12**

Chart 3.9. Hydrolysis of enantiomericaly pure calix[4]arene phosphonate **3.11**.

Spectroscopic (^{1}H, ^{13}C and ^{31}P NMR studies) characteristics of product **3.12** fully proves that hydrolysis of only one of C-O-P bond takes place, indicating the presence of a single product of the hydrolysis, but does not allow to set regioselectivity of the process. Accordingly, there has been a possibility of formation of compound **3.12** and compound **3.12'** (Figure. 3.4), which is a geometric isomer of compound **3.12** and so should hypothetically have different spectroscopic properties. Thus, the presence of a mixture of hydrolysis products **3.12** and **3.12'** could probably be observed in the NMR spectra.



3.12 **3.12'**

Figure. 3.4. Isomer monophosphates 3.12 and 3.12'.

The X-ray diffraction analysis confirms the presence of a single stereoisomere. The results showed the hydrolysis of a distal C-O-P bond to phosphonate fragment, and the presence of a single form of the product – **3.12**

monoester of phosphonic acid that is enantiomerically pure compounds with ABCH planar chirality type. As expected, the spatial distribution of substituents on the lower rim remain unchanged.

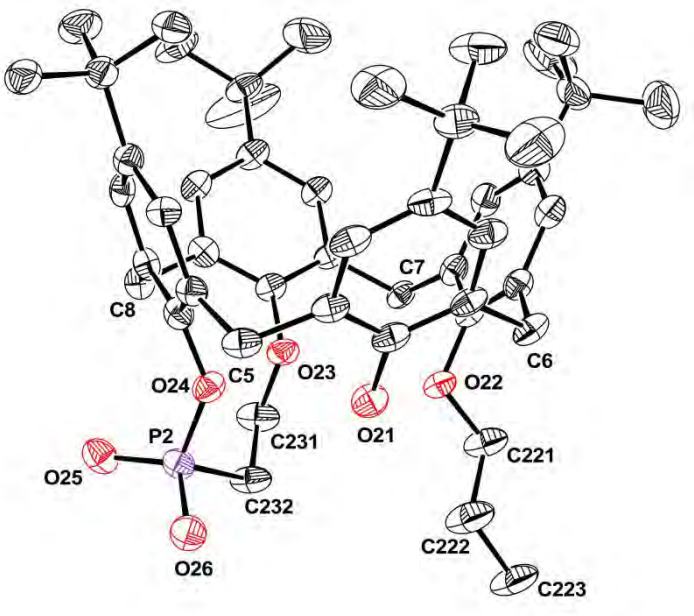
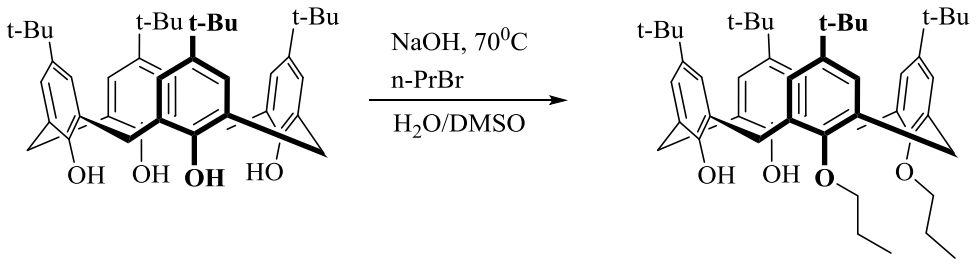


Figure. 3.5. The results of X-ray diffraction studies of monophosphate **3.12**.

3.4. The synthesis of inherently chiral calix[4]arenes with ABCH type of substitution on the lower rim

To obtain inherently chiral calix[4]arenes with ABCH type of substitution on the lower rim, we have developed preparative method for the synthesis of enantiomerically pure precursor carboxylic acid.

In the first stage by the distal alkylation of tetrahydroxy-tetra-para-tert-butylcalix[4]arene **2.1** in 40% aqueous sodium hydroxide and DMSO obtained 25,26-dipropoxycalix[4]arene **3.13** [112] (Scheme 3.10).

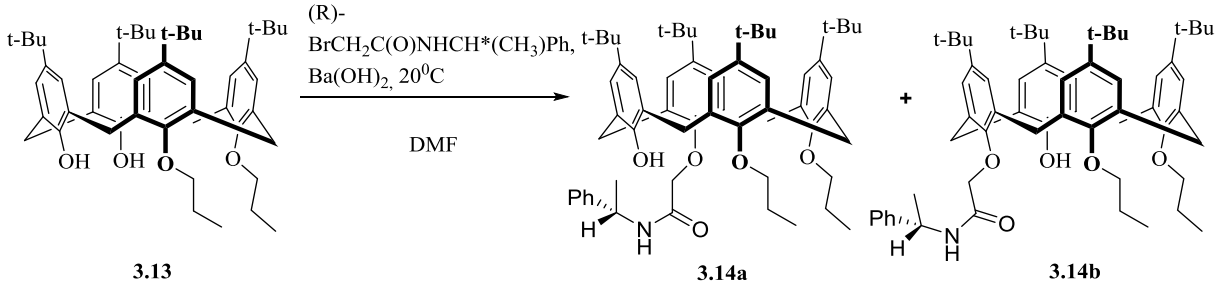


2.1 **3.13**

Scheme 3.10. Synthesis of 25,26-dypropoxycalix[4]arene **3.13**.

In the next step, the regioselective alkylation of the hydroxy group of dipropoxycalix[4]arene **3.13** was performed with chiral (S)- or (R)-N-(1-phenylethyl)bromoacetamide in dry DMF using anhydrous barium hydroxide as the base (Scheme 3.11). As known, the alkylation of tetrahydroxycalix[4]arene in the presence of $Ba(OH)_2$ leads exclusively to trisubstituted derivatives in a *cone* conformation [131].

The alkylation was carried out at 20–25 ˚C for 22–24 h, and the mixture of diastereomers **3.14a** and **3.14b** was isolated in 96% yield. The ratio of products was determined from the integration of the signals of the hydroxyl protons at 5.75 and 5.68 ppm, and found to be 2:1 (diastereomeric excess (de) of 33%).



3.13 **3.14a** **3.14b**

Scheme 3.11. Synthesis of diastereomers **3.14a** and **3.14b.**

The diastereomers had similar adsorption properties on silica, and were thus not separated by column chromatography. Due to different solubility in

acetonitrile, the disteroisomer **3.14a**, was isolated in almost diastereoisomerically pure but enantiomerically pure form after double crystallization of the resulting mixture. The yield was 40–41% (de=96–98% according to NMR spectra).

The diastereomers have two elements of chirality each: the asymmetric carbon atom of the phenylethylamide residue and the AABH asymmetrically substituted macrocyclic frame. Monocrystals suitable for X-ray diffraction analysis could be obtained for both diasteroisomers. Therefore, the structures of both compounds **3.14a** and **3.14b** could be determined by X-ray diffraction studies. The absolute configuration of molecules **3.14a** and **3.14b** were determined knowning the absolute configuration of the asymmetric carbon atom. We found that the substituents HO, PrO, PrO, and Ph(Me)CHNHC(O)CH_2O on the calixarene macrocycle in **3.14a** were placed clockwise (view from above), while in isomer **3.14b** these substituents were located counterclockwise (see Figures 3.6 and 3.7).

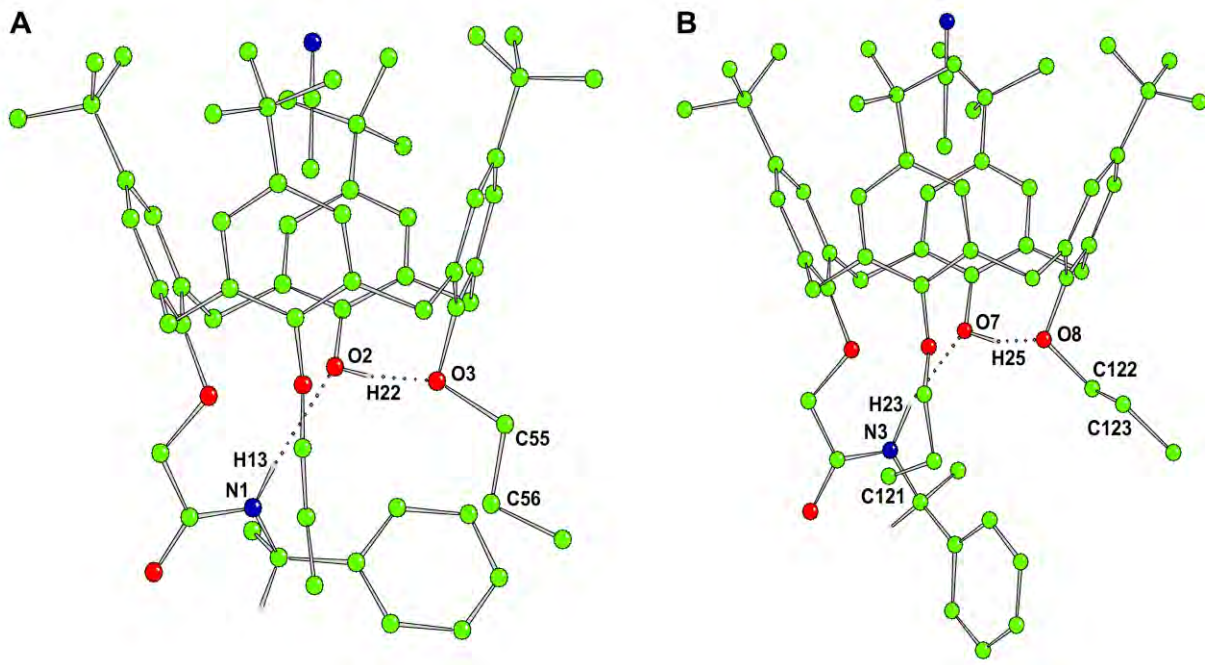


Figure. 3.6. X-ray molecular structure of conformers A and B of calixarene **3.14a.**

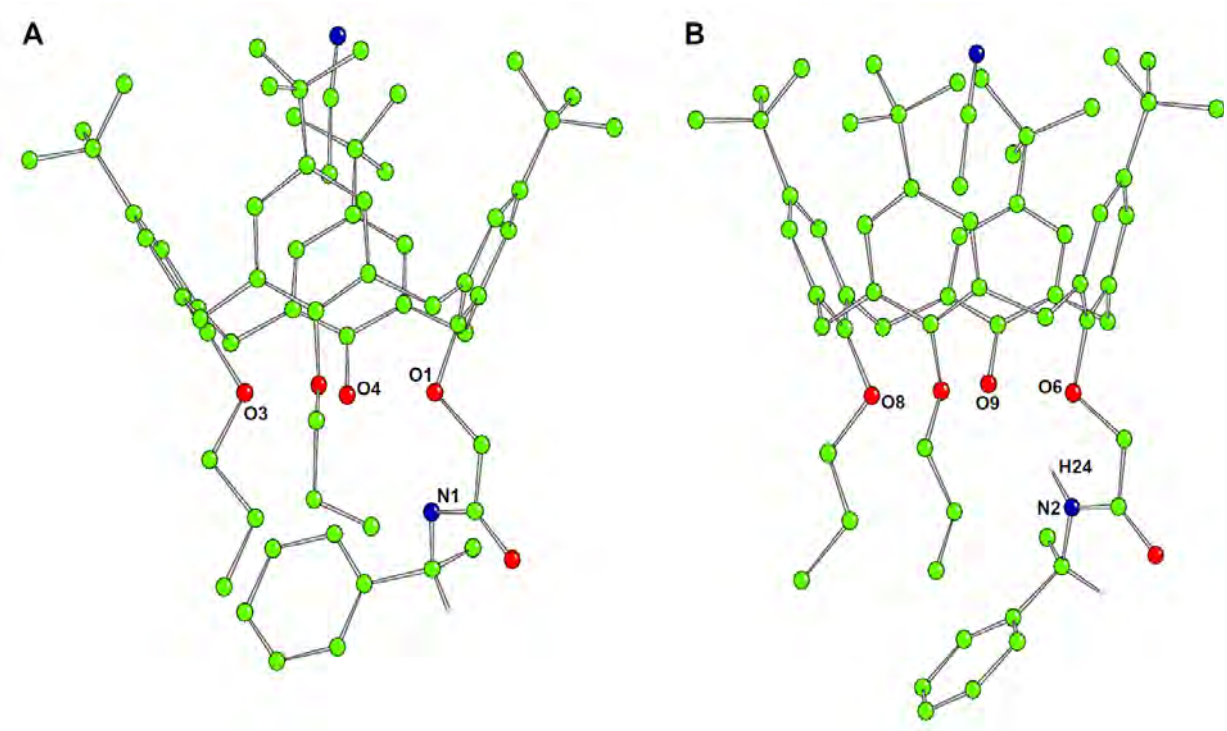


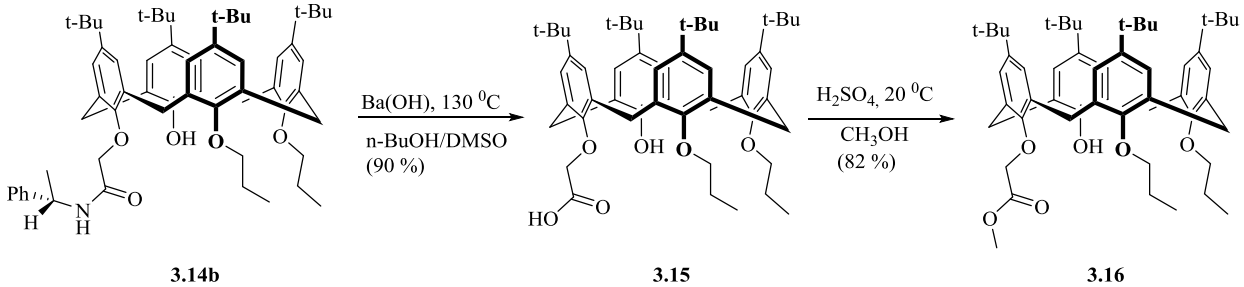
Figure. 3.7. X-ray molecular structure of conformers A and B of calixarene **3.14b.**

Molecules of both diastereoisomers adopt the distorted *cone* conformation. Asymmetric units of calixarenes **3.14a** and **3.14b** contain two symmetrical non-equivalent molecules with slightly different geometric parameters. The angles between least squares mean planes of opposite benzene rings of a macrocycle in **3.14a** (Figure. 3.6) are 70.04° and 40.44° (the conformer A), 57.16° and 51.06° (the conformer B). In the compound **3.14b** (Figure. 3.7) these angles are 63.28° and 46.18°, 60.53° and 43.53° respectively. One molecule of acetonitrile is located inside the cavity of each calixarene and is bonded with aromatic rings by C–H···π interactions. Besides that, other

molecules of acetonitrile are included in the crystal lattices of the both enantiomers; they are located in voids between the calixarenes.

Substituents at the lover rim of the calixarenes **3.14a** and **3.14b** form a system of intramolecular hydrogen bonds that stabilize positions of the substituents and the conformation of the molecule (**3.14a** A: N1–H13···O2 168°, H···O 2.144 Å, N···O 3.006 Å; O2–H22···O3 159°, H···O 2.038 Å, O···O 2.818 Å; **3.14a** B: N3–H23···O7 162.4°, H···O 1.980 Å, N···O 2.994 Å; O7–H25···O8 165°, H···O 1.763 Å, O···O 2.795 Å; **3.14b** A: N1···O1 2.716 Å, N1···O4 2.910 Å, O4···O1 2.829 Å, O4···O3 2.706 Å; **3.14b** B: N2–H24···O9 159°, H···O 2.268 Å; O9···O6 3.098 Å, O9···O8 2.737 Å).

The location of a phenylethylamid fragment noticeably differs among the conformers. Thus, in molecule **3.14a** A, phenyl moved aside of vertical axis of calixarene and turned by 63.25° relative to a main plane of the macrocycle that passes through methylene fragments. In conformer **3.14a** B, phenyl is located closely to the axis and almost parallel to it (the angle between the main plane of the macrocycle and the benzene ring is 84.05°). As to enantiomer **3.14b**, its conformers show similar difference. The phenyl of **3.14b** A is situated aside of the calixarene axis but the one of **3.14b** B lies nearer the axis. The angles between the benzene ring and the methylenes plane are 70.16° and 38.81° respectively.

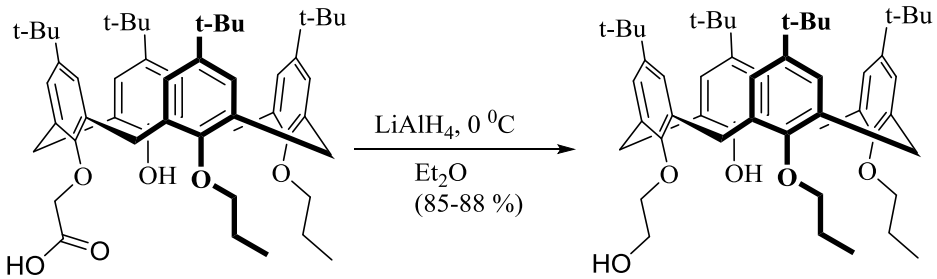


3.14b **3.15** **3.16**

Scheme 3.12. Synthesis of calix[4]arene **3.16.**

In the next step, the enantiomerically pure calix[4]arene carboxylic acid **3.15** were obtained in 82 % yield after hydrolysis of amides **3.14b**. The removal of chiral inductor was carried out in boiling mixture of n-butanol / DMSO in the presence of an excess of barium hydroxide for 10-12 h (Scheme 3.12).

Further functionalization of the trisubstituted compounds **3.15** was carried out using similar synthetic scheme the one for disubstituted dervivatives **3.4**. Reduction of ester **3.16** (Scheme 3.13) or acid **3.15** (Scheme 3.13) by lithium aluminum hydride yields alcohol **3.17** but slightly lower yields (85 % for ester, 88 % for acid).



R = H **3.15**
R = CH_3 **3.16**

3.17

Scheme 3.13. Synthesis of alcohol **3.17.**

An important factor in the whole process is to preserve the original structure of enantiomerically pure amide. Positions of groups on the lower rim in macrocyclic skeleton of alcohol **3.17**, was proved by X-ray diffraction analysis and showed the preservation of the original structure (Figure. 3.8).

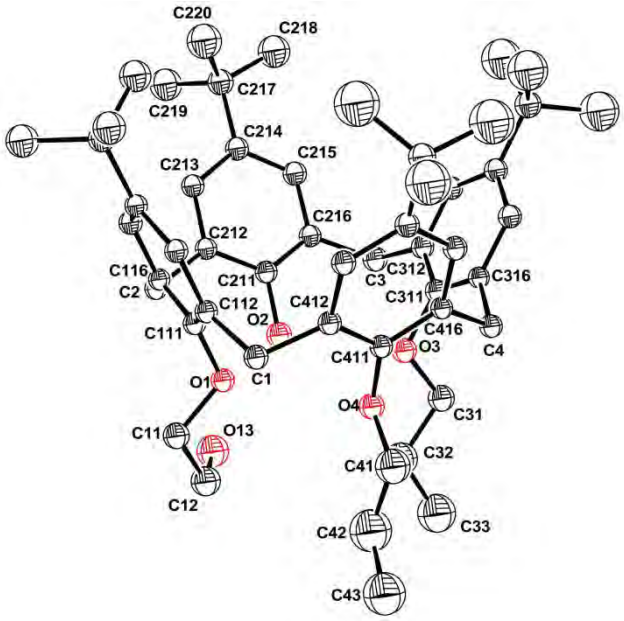
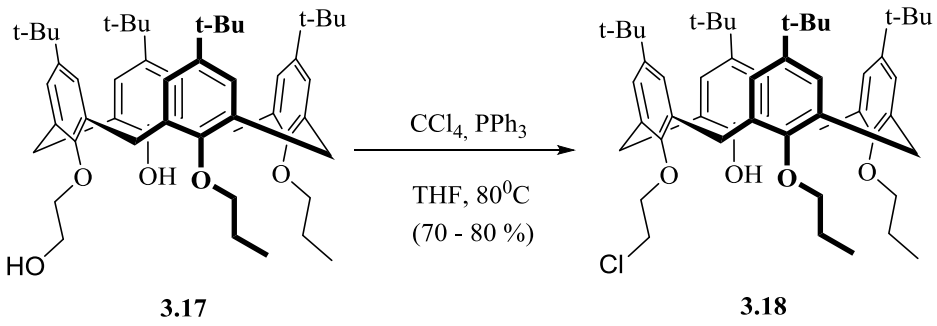


Figure. 3.8. X-ray molecular structure of **3.17.**

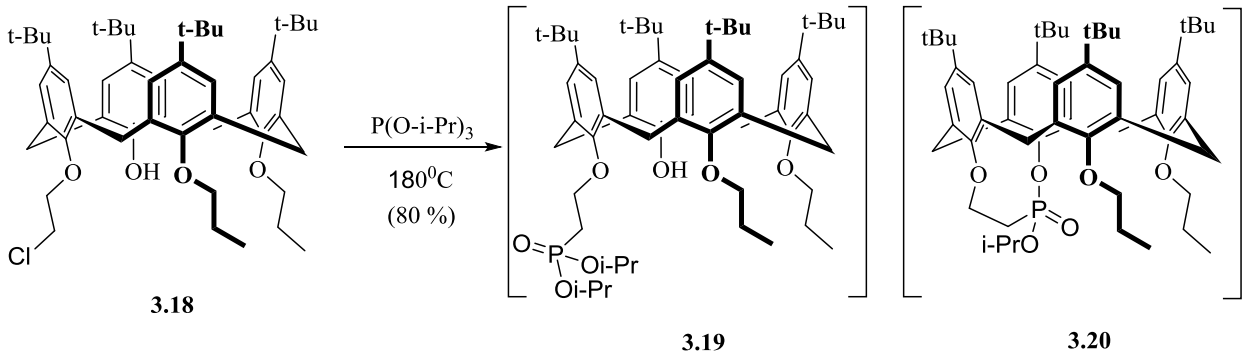
Halogenation of alcohol **3.17** was carried out by reaction with triphenylphosphine in a refluxing mixture of THF and carbon tetrachloride (1/5, v/v). After solvent removal and purification of the solid crude by column flash chromatography, pure halide **3.18** was obtained in 70-80% yield (Scheme 3.14).



3.17 **3.18**

Scheme 3.14. The synthesis of inherently chiral calix[4]arene chloride with ABCH type of substitution on the lower rim **3.18.**

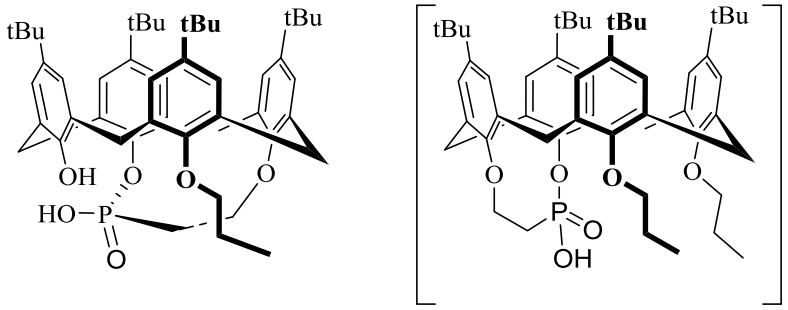
We then tried Michaelis-Arbuzov reaction on compound **3.18**. However, after refluxing of chloride **3.18** in triisopropyl phosphite overnight, phosphonate **3.19** or **3.20** could not be detected.



3.18 3.19 3.20

Scheme 3.15. Expected products of Michaelis-Arbuzov reaction with chloride **3.18.**

In order to favor Michaelis-Arbuzov reaction, an equimolar amount of sodium iodide, NaI, was added to the reaction mixture. However, after 24 hours of reflux, a complex mixture of decomposition products, which could be separated and identified, was obtained. The synthesis of analog **3.21** of acid **3.12** in enantiomerically pure form failed (Scheme. 3.9). **3.18** is probably too sterically crowed if you compare it with **3.7**, for an efficient Michaelis-Arbuzov reaction.



3.12 3.21

Figure. 3.9. Inherently chiral calix[4]arenes with ABCH (**3.12**) and AABC (**3.21**) type of substitution on the lower rim.

3.5. Spectroscopic properties of inherently chiral calix[4]arenes with AABH type of substitution on the lower rim

For all inherently chiral calix[4]arenes with AABH type of substitution on the lower rim, spectroscopic studies were carried out to confirm their structure. For convenience, the ^{13}C NMR data are summarized in the Table 3.3.

Table 3.3

^{13}C NMR data for all obtained inherently chiral calix[4]arenes with AABH type of substitution on the lower rim.

	3.17	**3.18**
(-C(***C***H$_3$)$_3$)	31.54	31.80
	31.40	31.72
	31.38	31.12
	31.31	31.09
(***C***Me$_3$)	30.92	31.04
	31.08	31.21
	31.54	31.29
	32.39	31.74
C^{Ph}-*t*-Bu	142.46	141.60
	145.14	145.18
	145.63	145.51
	146.10	145.55
CH^{Ph}	124.33	124.63
	124.95	124.71
	124.95	124.73
	125.11	125.00

	125.26	125.03
	125.45	125.20
	125.60	125.55
	125.84	125.67
$\underline{\boldsymbol{C}}^{Ar}$-$CH_2$-$C^{Ar}$	129.87	128.92
	130.65	130.03
	133.32	131.53
	133.52	132.00
	133.75	132.01
	133.87	132.57
	133.98	135.61
	134.12	135.92
$\underline{\boldsymbol{C}}^{Ph}$-OH	148.73	150.45
$\underline{\boldsymbol{C}}^{Ph}$-O-$CH_2$-	151.69	151.01
$\underline{\boldsymbol{C}}^{Ph}$-O-$CH_2$-	152.23	151.41
$\underline{\boldsymbol{C}}^{Ph}$-O-$CH_2$-	152.32	153.79
Ar-$\underline{\boldsymbol{C}}H_2$-Ar	33.82	33.68
	33.88	33.79
	33.95	33.90
	33.99	34.16
O-$\underline{\boldsymbol{C}}H_2$-$CH_2$-$CH_3$	78.26	78.17
O-CH_2-$\underline{\boldsymbol{C}}H_2$-$CH_3$	23.09	23.42
O-CH_2-CH_2-$\underline{\boldsymbol{C}}H_3$	10.39	10.81
PhO-$\underline{\boldsymbol{C}}H_2$-$CH_2$-X	76.64	75.07
X-$\underline{\boldsymbol{C}}H_2$-$CH_2$-OPh	62.25	42.53
O-$\underline{\boldsymbol{C}}H_2$-$CH_2$-$CH_3$	77.32	76.39
O-CH_2-$\underline{\boldsymbol{C}}H_2$-$CH_3$	22.89	22.69
O-CH_2-CH_2-$\underline{\boldsymbol{C}}H_3$	10.10	9.82

The resulting compounds are in the *cone* conformation, as evidenced by the position signals carbon atoms of methylene bridges in the range of 33-34 ppm, since ^{13}C NMR cone signals for bridging methylene groups are in the range of 29-34 ppm for *cone*, *partial cone* or *alternate* - 35-37 ppm [130].

Also characteristic is the shift in the strong field signal of methylene carbon atom in the transition from -CH_2-OH (62.25 ppm) to -CH_2-Cl (42.53 ppm). The remaining few signals change their position during the transition from alcohol **3.17** to halide **3.18**. NMR data fully confirm the proposed structure for compounds **3.17** and **3.18**.

3.6. Organocatalytic properties of inherently chiral calix[4]arene phosphonic acid with ABCH type of substitution on the lower rim

Over the past two decades, a number of chiral Brønsted phosphorus acids attracted the attention of many research groups. They are widely used in organocatalysis of large group of reactions and important processes of modern chemistry : activation of iminium ions and carboxyl compounds, Friedel-Crafts reaction, Mannich-type reaction, cycloaddition (including the Diels-Alder reaction) [116], asymmetric epoxides and aziridine ring oppening, different multicomponent conversion, and more. The results of research were published in over a hundred papers and a number of important reviews [117.118]. Good catalytic activities and high enantioselectivity could be obtained with chiral acids with axial (**A-C**, Figure. 3.10) or planar chirality (**D**, Figure. 3.10).

Acid **3.12** have similar structural features (Figure. 3.10), besides having a presence of supporting phenol functional group of different acidity that can affect the activity or selectivity of the substrate.

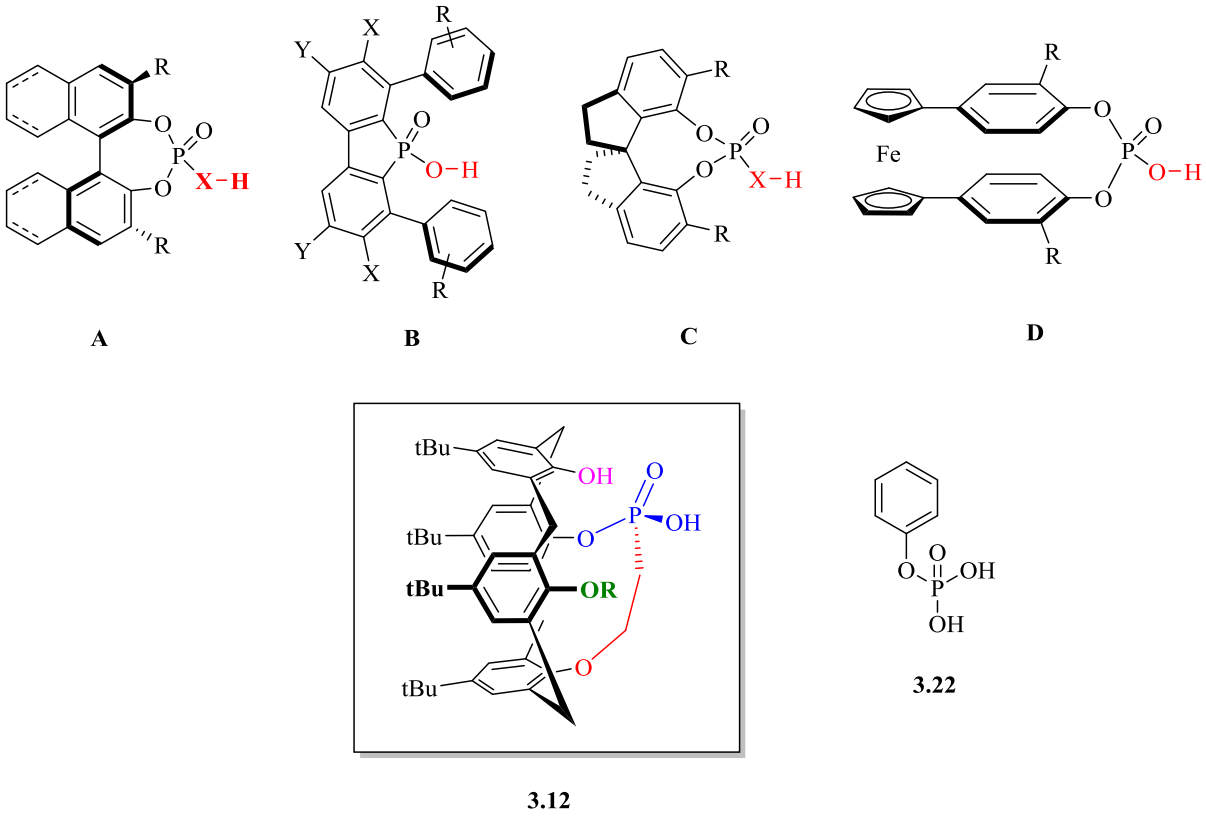
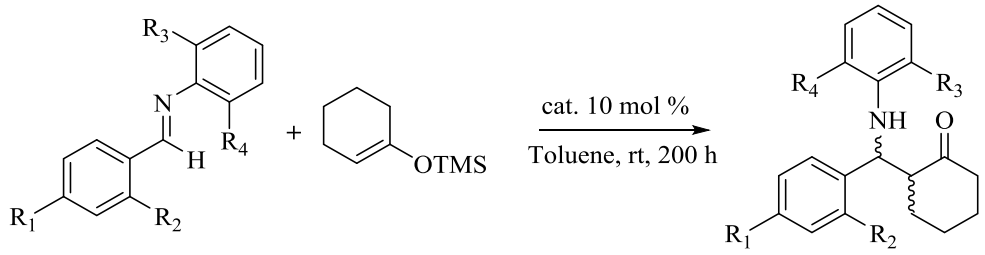


Figure. 3.10. Chiral Brønsted phosphorus acid**s.**

In order to study catalytic properties of inherently chiral calix[4]arene phosphonic acid with ABCH type of substitution on the lower rim, we had tested its activity in Mukaiyama aldol addition, aza-Diels-Alder reaction and in asymmetric epoxides ring opening.

3.6.1. Mukaiyama aldol addition

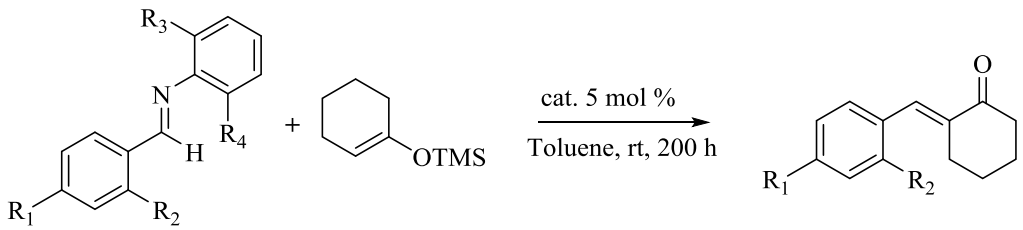
In 1973, a Japanese chemist Teruaki Mukaiyama proposed aldol condensation between silyl enolates as enol equivalent, and for activating the carbonyl component a Lewis acid, such as boron trifluoride or titanium chloride (IV) [119]. In this study, it was decided to use the analog carbonyl compounds – appropriate Schiff base (imines series was tested with different functional groups) and cyclohexene silyl enolate (Scheme 3.16).



Scheme 3.16. Aza-Mukaiyama aldol addition**.**

To optimize the reaction conditions model non-calix[4]arene-containing **3.22** acid was used as a catalyst (Figure. 3.10). The reaction was carried out with N-phenylbenzylideneimine and cyclohexene silyl enolate in toluene at room temperature. After the reaction is over, the β-amino carbonyl product, was isolated with 91% yield. ^{1}H NMR data have shown that the ratio of diastereomers *syn*: *anti* = 80 : 20 (corresponding spectral data are consistent with those described in the literature [120]).

However, when moving from model **3.22** to inherently chiral calix[4]arene phosphonic acid with ABCH type of substitution on the lower rim **3.12**, the reaction time increases 5 times, due to higher pKa value of phosphonic acid compared with phosphoric acid, and the only product of this reaction was (E)-2-phenyl methylidene cyclohexanone, crotonic condensation product (Chart 3.17).



Scheme 3.17. Aza-Mukaiyama crotonic condensation**.**

It is interesting that the *α, β*-unsaturated ketone is the only product proven in the case of all imines (Table 3.4). The only exceptions are strongly sterically hindered imine with diisopropyl groups, electron deficient nitro-containing

imine and salicylimine (Table 3.4, numbers 3, 5 and 6, respectively), for which no reactions were observed.

Table 3.4.

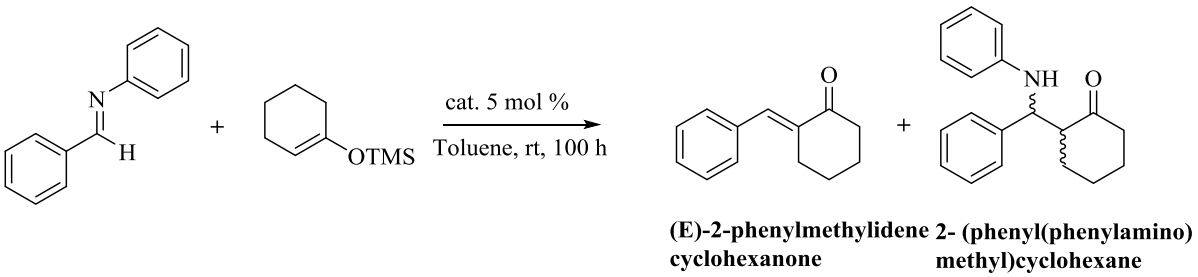
The results of catalytic Aza-Mukaiyama crotonic condensation (Figure 3.17).

№	**R_1**	**R_2**	**R_3**	**R_4**	**Yield, %**
1.	H	H	H	H	86
2.	Cl	H	H	H	78
3.	NO_2	H	H	H	-
4.	OCH_3	H	H	H	82
5.	H	OH	H	H	-
6.	H	H	i-Pr	i-Pr	-
7.	H	H	OH	H	88

Conditions: imine: cyclohexene silyl enolate=1:2, 5 mol % catalyst, toluene, 25 ˚C

We wanted to check if the desired aldol compounds were formed in the early stages of the reaction. For that, we reduced reaction time from 200h to 100h. In this case, the conversion of N-phenilbenzylideneimine was in complete: the conversion was 62% to yield a mixture of 2-(phenyl(phenylamino)methyl)cyclohexanone and (E)-2-phenylmethylidene cyclohexanone in 72:28 ratio. 2-(phenyl(phenylamino)methyl)cyclohexanone was obtained in 87:13 *syn* : *anti* ratio (Scheme 3.18). These data suggest that the first step is the formation of the expected 2-(phenyl(phenylamino)methyl)cyclohexanone from Mukaiyama aldol reaction and the second step its subsequent conversion to (E)-2-phenylmethylidene cyclohexanone (in the ^{1}H NMR spectra, no Z-product was observed) with

elimination of aniline, which was never reported previously, to the best of our knowledge.



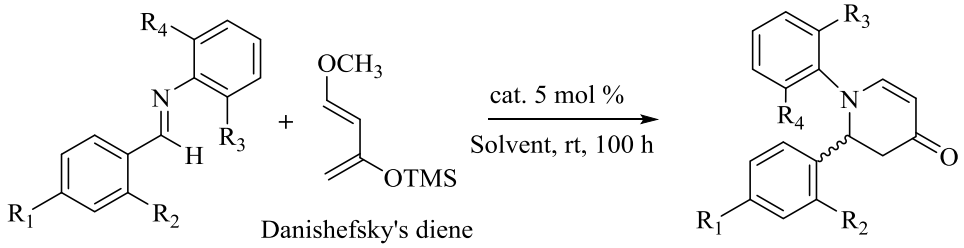
Scheme 3.18. Aza-Mukaiyama crotonic condensation**.**

The results suggest that this unusual behavior of inherently chiral calix[4]arene phosphonic acid with ABCH type of substitution on the lower rim **3.12** is a consequence of the presence of additional phenol functional groups in close proximity to the active site of the molecule.

3.6.2. Aza-Diels-Alder reaction

Aza-Diels-Alder reaction – is modified Diels-Alder reaction, an effective tool to synthesize various tetrahydropyridine derivatives. Nitrogen atom may be part of a diene or dienophile. In this area there are a number of synthetic developments both in its achiral version [121.122], and in stereoselective, products being obtained with good yields and ee in the 3 – 42 % range [116, 123].

Therefore, we also chose this reaction with a series of substituted imines with a diene with strong donor properties – E-1-methoxy-3-trimethylsilyloxy-1,3-butadiene (Danishefsky's diene) (see Scheme 3.19).



Scheme 3.19. Aza-Diels-Alder reaction**.**

Various imines have been selected as substrates with electron-withdrawing or electron donor substituents, with hydroxyl group in different positions (see Table 3.5). For all susbtrates, good yields could be obtained (up to 95% yield) but the enantiomeric excesses of the products were always low (up to 21%, see entry7, table 3.5).

Table 3.5.

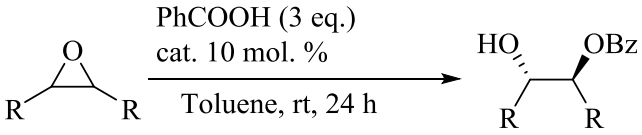
The results of catalytic reaction aza-Diels-Alder type, in presence of inherently chiral calix[4]arenes phosphoric acid ***3.12*** *(Scheme 3.19).*

№	***Solvent***	**R_1**	**R_2**	**R_3**	**R_4**	**Yield, %**	**ee, %**
1.	*CH_3CN*	H	H	H	H	83	<5
2.	*CH_3CN*	Cl	H	H	H	83	<5
3.	*CH_3CN*	NO_2	H	H	H	88	<5
4.	*CH_3CN*	OCH_3	H	H	H	85	5
5.	*CH_3CN*	H	OH	H	H	95	9
6.	*CH_3CN*	H	H	i-Pr	i-Pr	-	-
7.	*Toluene*	H	H	H	H	72	21
8.	*Toluene*	Cl	H	H	H	81	11
9.	*Toluene*	NO_2	H	H	H	74	<5
10.	*Toluene*	OCH_3	H	H	H	56	<5
11.	*Toluene*	H	OH	H	H	69	<5
12.	*Toluene*	H	H	i-Pr	i-Pr	-	-

13.	*Toluene*	H	H	OH	H	76	10

3.6.3. Asymmetric epoxides ring opening

Asymmetric epoxide ring openning is an important synthetic transformation and is widely industrially used. First version of this reaction using chiral phosphoric acid in heterodimers with benzoic acid was described by the List group [124]. The proposed methodology mimics enzymatic mechanism. They showed that the acid is an effective catalyst that yield products with 55 – 86 % yields and ee up to 93%.

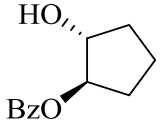


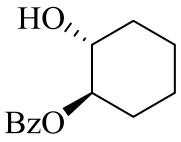
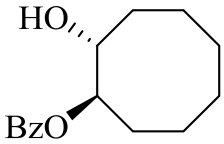
Scheme 3.20. Asymmetric epoxides ring opening**.**

In the present investigation a series of cyclic epoxides was tested. Cyclohexene and cyclopentene oxide could be opened in good yields (66 – 92 %) but cyclooctene oxide found to be poorly reactive with conversions of less than 10 % (se table 3.6). However, in all cases, enantioselectivties wer low (ee up to 18%).

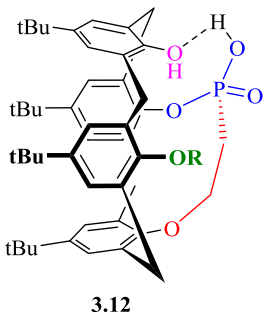
Table 3.6.

The results of catalytic asymmetric epoxide ring opening at the presence of inherently chiral acid ***3.12*** *(Scheme 3.20).*

№	**Product**	**Yield, %**	**ee, %**
1.		75	11

2.		71	18
3.		8	-

In all tested reactions, poor selectivity and moderate activity were observed. A possible reason could be the involvement of catalytic site – P(O)OH into strong intramolecular hydrogen bond (see Figure 3.11). Thus, additional hydroxyl group and close intramolecular hydrogen bond system could inhibit activity of the acid. It then could be of interest to synthesize analoguesof **3.12** with OR groups with R substituents of various steric hindrance instead of OH group.



3.12

Figure. 3.11. Chiral Brønsted phosphorus acids in “closed” conformation**.**

CHAPTER 4

CALIX[4]ARENES FUNCTIONALIZED WITH P(V)-GROUP (PHOSPHORIC ACID) : SYNTHESIS AND CATALYTIC PROPERTIES

4.1. Synthesis of inherently chiral calix[4]arenes carboxylic acids with ABCH type of substitution on the lower rim

A possible reason for the low selectivity of acid **3.12** could be the pKa value for phosphonic acid. In order to provide more interaction at the transition complex substrate-catalyst, it was decided to synthesize a series of enantiomerically pure phosphoric acids with the possibility to vary the amphiphilic properties by variation of the number and position of substituents on the lower rim of macrocyclic frame (Fig. 4.1).

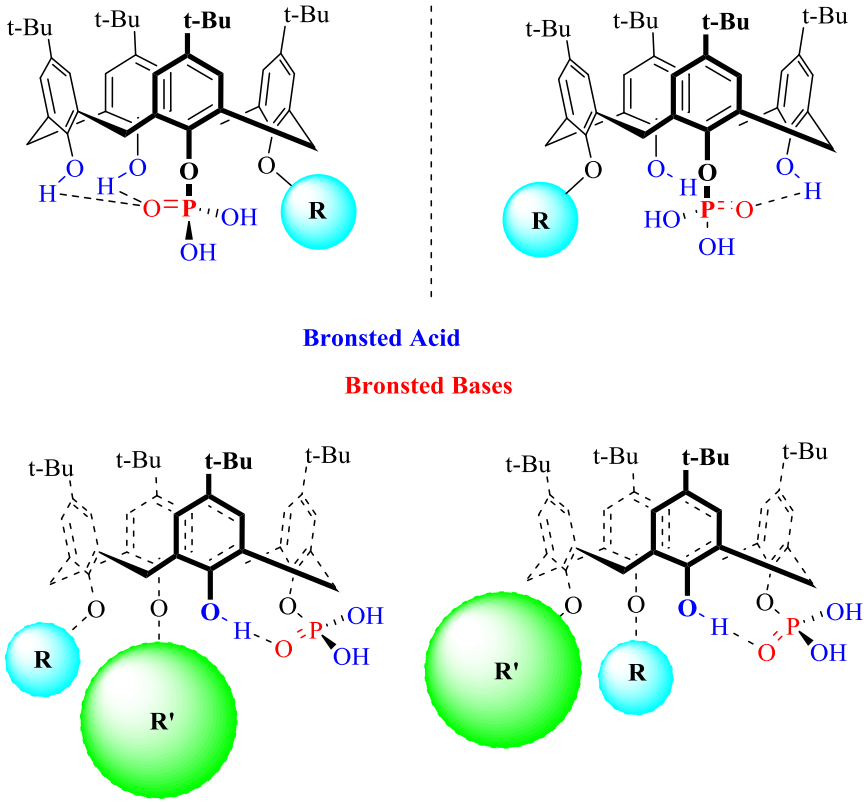
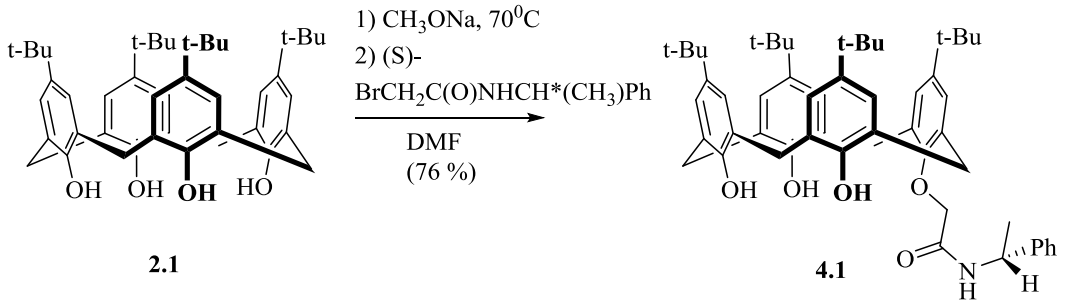


Fig. 4.1. General view of the target phosphoric acid with the possibility to vary the amphiphilic properties.

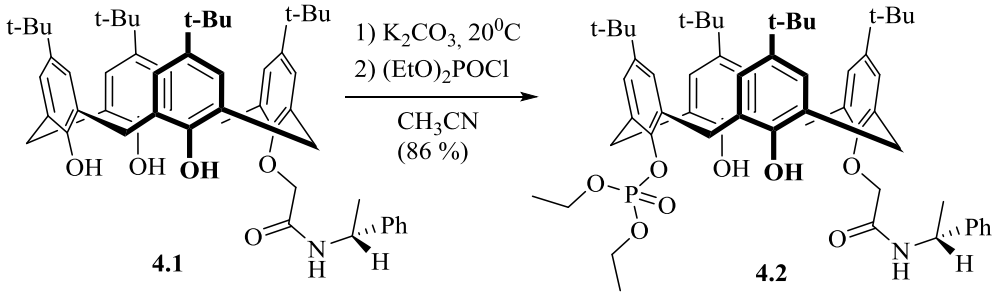
Synthetic strategy starts with the alkylation of 4-tert-butyltetrahydroxycalix[4]arene **2.1** by optically pure (S)- N-(1-phenylethyl)bromoacetamide using known procedure [111] (Figure 4.1). This procedure allows to obtain target monosubstituted product **4.1** with relatively high yield 76%.



2.1 **4.1**

Scheme 4.1. The synthesis of amide **4.1.**

The next step was the phosphorylation of monosubstituted calix[4]arene **4.1** by treatment with diethyl chlorophosphate in dry acetonitrile at the presence of a base K_2CO_3. This mild conditions allows obtaining selectively only distally disubstituted product **4.2** (Scheme 4.2).



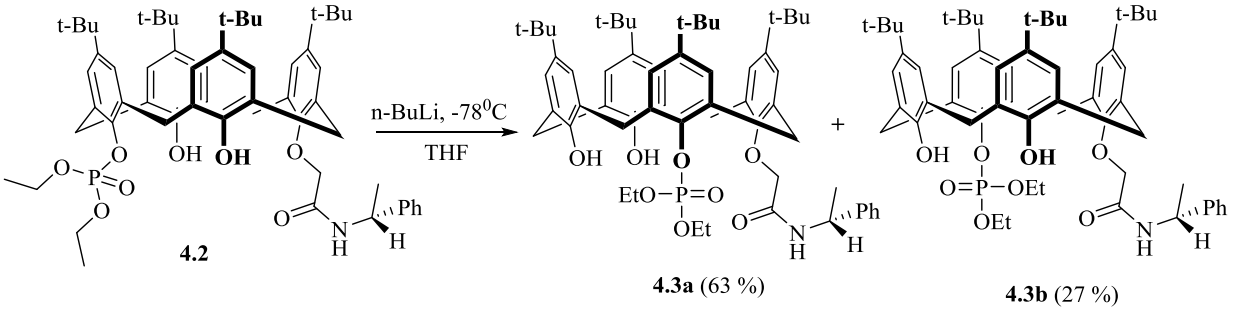
4.1 **4.2**

Scheme 4.2. Synthesis of distal phosphate **4.2**.

The resulting phosphonate **4.2** can be easily purified by a simple filtration through silica gel.

It is known that distal disubstituted phosphonates are capable to rearrange under the influence of strong bases [79]. The compound **4.2** is not an exception.

Treatment of **4.2** solution in THF with n-BuLi at -78˚C yields a diastereomeric mixture with a 2.5:1 diasteroisomeric ratio(Scheme 4.3). Products could be easily separated by flash-chromatography on silica.



Scheme 4.3. Phosphotropic rearrangement of distal phosphonate **4.2**.

Suitable crystals of the compound **4.3b** for X-ray analysis was obtained by slow evaporation of the solvent (acetonitrile) from its solution (Fig. 4.2). The stucture of **4.3b** obtained by X-ray diffraction analysis clearly shows the relative disposition of substituents on the lower rim of the macrocycle. Compound **4.3a** is the other diatereoisomer with miror arangement of substituents.

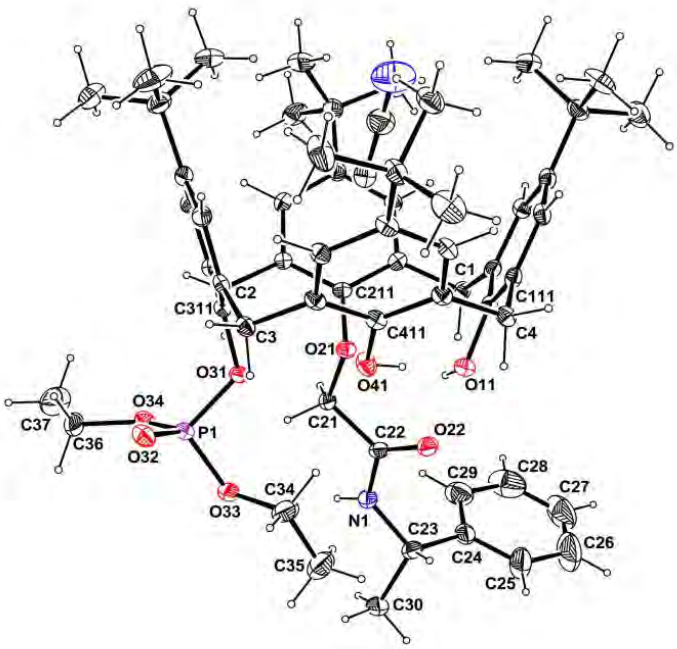
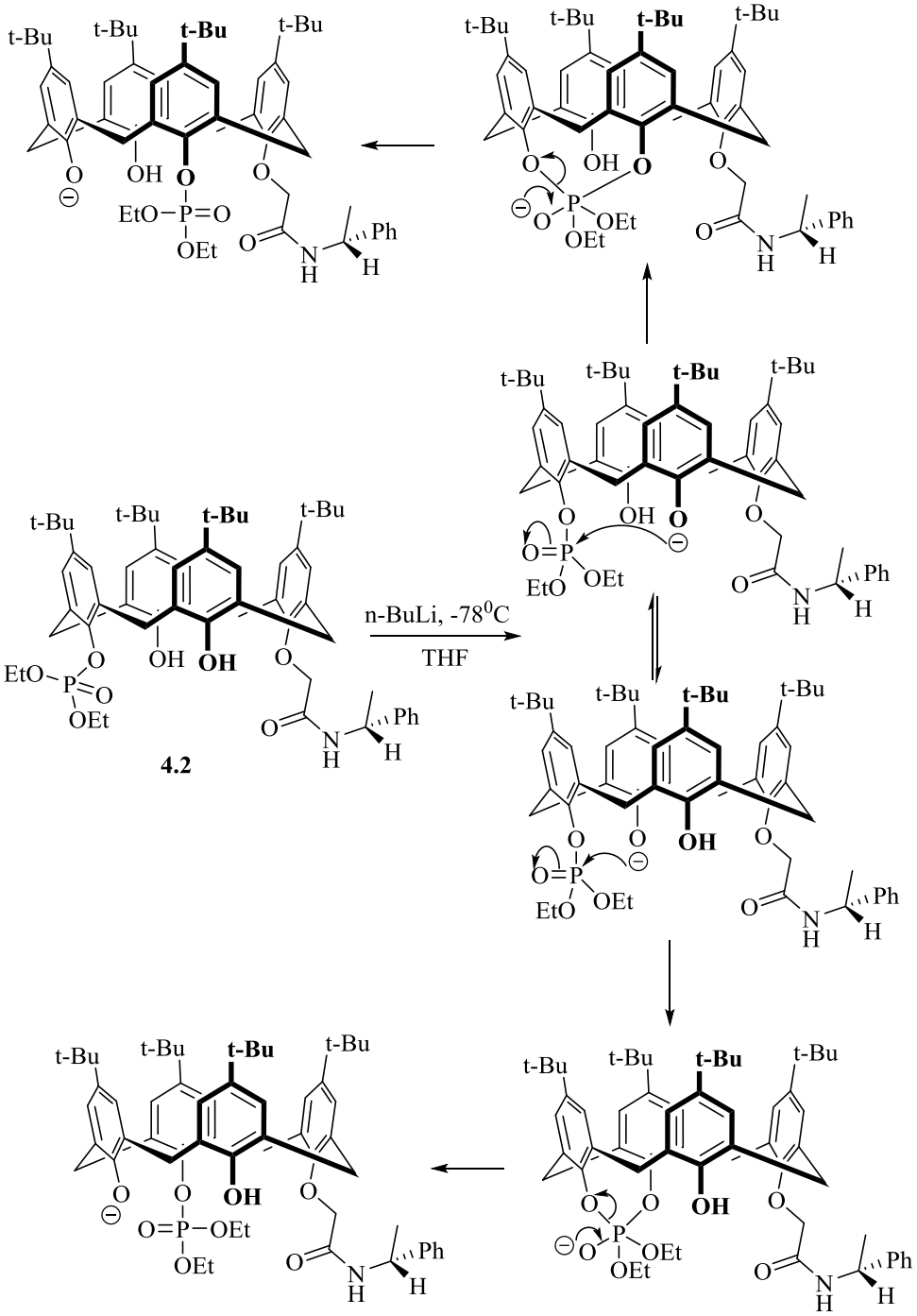


Fig. 4.2. Molecular view of **4.3b**.

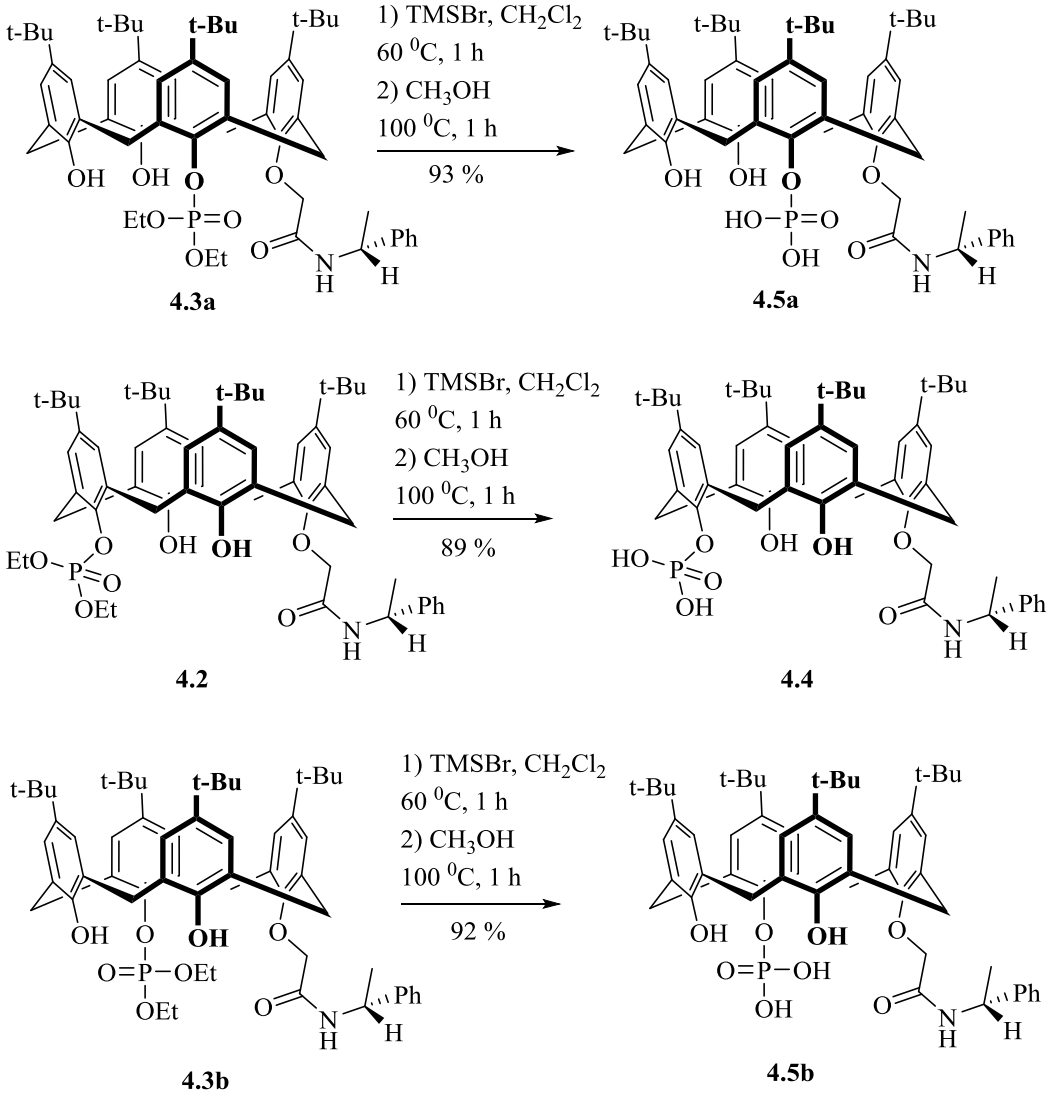
Reasonable mechanism of the phosphotropic rearrangement was proposed by Kalchenko *et al.* [125], and includes nucleophilic attack of generated phenolate anion to the phosphorus atom with subsequent rearrangement of the resulting pentacoordinated intermediate (Scheme 4.4.).



Scheme 4.4. The proposed mechanism of phospotropic rearrangement.

The mechanism was established by NMR : carrying out experiment in NMR tube under argon atmosphere in THF-d8 allow to observe ^{13}P NMR signal as broad peak at -4.7, which corresponds to transition pentacoordinated intermediate.

Diastereoselectivity of reaction is the result of the influence of chiral inductor - amide fragment in enantiomerically pure form. Amide fragment takes part in stabilization of transition state, yielding **4.3a** (Scheme 4.4., top).



Scheme 4.5. Partial hydrolysis of phosphates to phosphoric acids **4.4**, **4.5a-b**.

The mixture of diastereomeric phosphonates could be separated by flash column chromatography on silica gel using the eluent - mixture of hexane / ethyl acetate = 3/1.

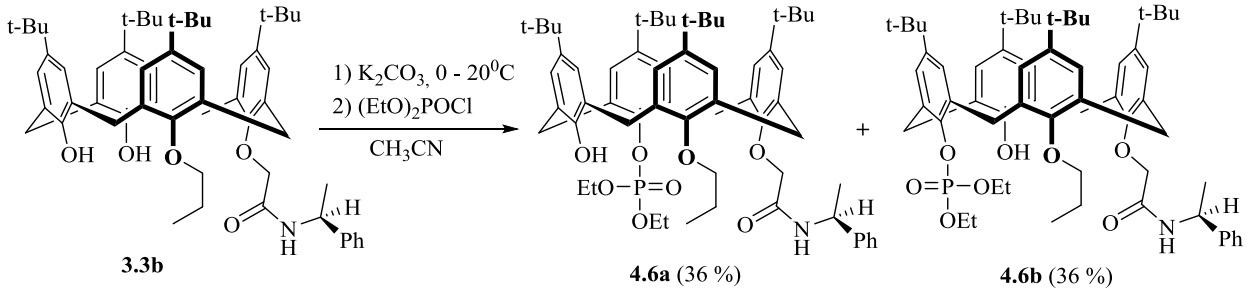
For the selective hydrolysis of alkyl esters of phosphoric acid preserving aryl substituent was used a method developed by Ukrainian chemists [125].

Phosphates (**4.2**, **4.3a-b**) were refluxed for an hour in DCM at the presence of TMSBr (Scheme 4.5). After stripping volatile components, the solid residue was dissolved in methanol and refluxed for an hour, to destroy formed silyl esters. Further removing of the solvent in vacuo provides a product with 95% purity.

For additional purification, the compounds may be crystallysed from aqueous ethanol. In addition , for further catalytic tests, an important criterion was the absence of even trace amounts of water or proton-active impurities. Thus, products phosphoric acid were precipitated by adding hexane to ether solutions and further dried under vacuum at 50 ˚C during 20 hours.

4.2. Synthesis of inherently chiral calix[4]arenes phosphoric acids with ABCH type of substitution at the lower rim

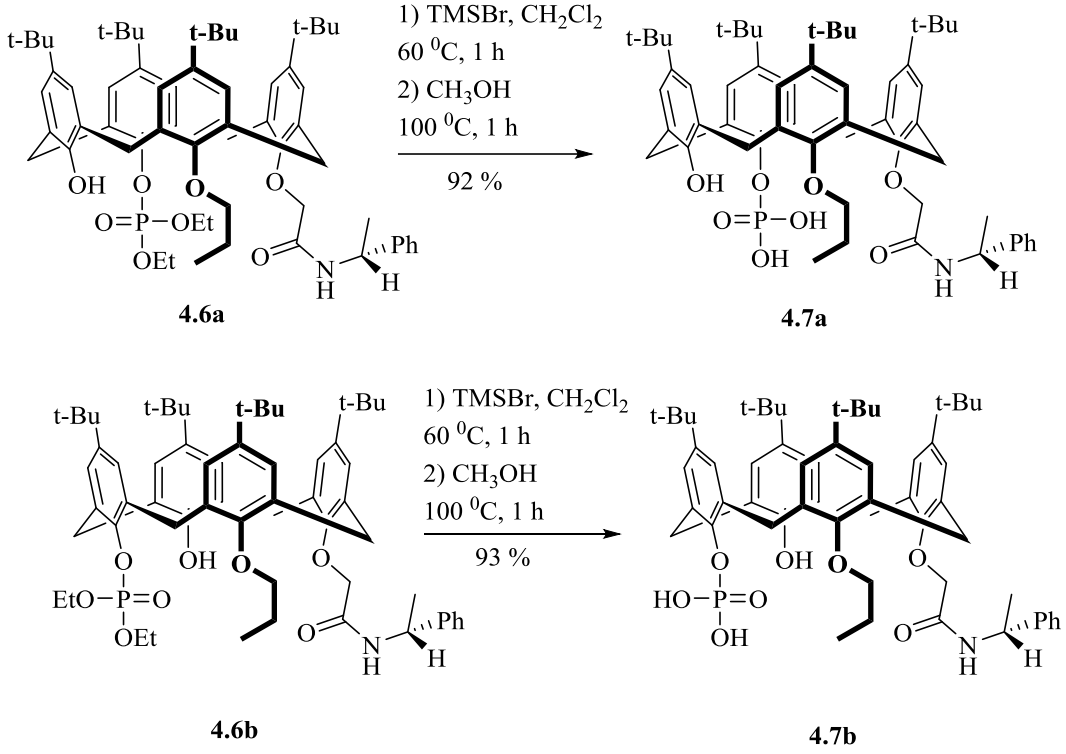
For inherently chiral phosphonates with ABCH type of substitution at the lower rim of macrocycle, synthesis starts with optically pure amide **3.3b**.



Scheme 4.6. Phosphorylation of amide **3.3b**.

Phosphorylation of amide **3.3b** in acetonitrile at room temperature at the presence of a base - K_2CO_3, provides a mixture of diastereomers **4.6a-b** with relatively good yield (Scheme 4.6). The products can be separated by flash column chromatography on silica gel using the eluent - mixture of hexane / ethyl acetate = 2/1. Such mild conditions totally prevent the synthesis of the tetrasubstituted product.

Resulting phosphates **4.6a-b** could be easily convert into corresponding acid in the same way as **4.2** and **4.3a-b**, with conservation of P-O-C^{Ar} bond. Such simple two-step methodology is convenient to obtain inherently chiral calix[4]arenes phosphoric acid with programed ABCH type of substitution at the lower rim.



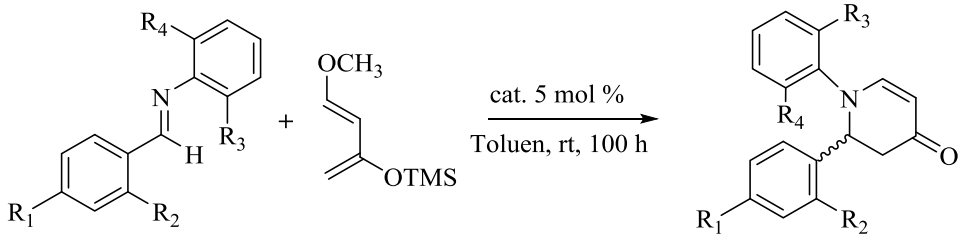
Scheme 4.7. Partial hydrolysis of phosphates **4.6a-b**.

4.3. Organocatalytic properties of inherently chiral calix[4]arenes phosphoric acid with ABHH and ABCH type of substitution at the lower rim

4.3.1. Aza-Diels-Alder reaction

Aza-Diels-Alder reaction is an effective tool to synthesize various tetrahydropyridine derivatives. Nitrogen atom may be part of a diene or a

dienophile. In this area there are a number of synthetic developments both in its achiral version [121.122], and in stereoselective, products obtained with good yields but moderate enantioselectivities (ee in the range 3 – 42 %) [116, 123].



Scheme 4.8. Aza-Diels-Alder reaction.

Therefore, we also chose this reaction of series of substituted imines with diene with strong donor properties – E-1-methoxy-3-trimethylsilyloxy-1,3-butadiene (Danishefsky's diene). With the selected N-benzylideneaniline imines, yields were good using **4.4**, **4.5a** or **4.5b** but ee were very low again (up to 16%) (see table 4.1), **4.4** being realy poorly active and **4.5a** being a little be more active and more enantioselective catalyst than **4.5b**.

Table 4.1.

*Catalyzed aza-Diels-Alder reactions in presence of inherently chiral calix[4]arenes phosphoric acids **4.5a-b** (Scheme 4.8).*

№	**R_1**	**R_2**	**R_3**	**R_4**	***4.5a***		***4.5b***	
					Yield, %	**ee, %**	**Yield, %**	**ee, %**
1.	H	H	H	H	74	6	71	5
2.	Cl	H	H	H	86	<5	90	<5
3.	NO_2	H	H	H	80	16	81	8
4.	OCH_3	H	H	H	81	16	75	11
5.	H	OH	H	H	84	<5	63	<5

6.	H	H	i-Pr	i-Pr	-	-	-	-
7.	H	H	OH	H	70	6	68	<5

The same substrates were also tested with phosphoric acids **4.7a** or **4.7b** (see table 4.2). Again, yields were good but the ee were very low again (up to 27%), with **4.7a** being significantly more enantioselective than **4.7b** in some cases (see table 4.2, entries 1 and 4).

Table 4.2.

*Catalyzed aza-Diels-Alder reactions in presence of inherently chiral calix[4]arenes phosphoric acids **4.7a-b** (Scheme 4.8).*

№	**R_1**	**R_2**	**R_3**	**R_4**	***4.7a***		***4.7b***	
					Yield, %	**ee, %**	**Yield, %**	**ee, %**
1.	H	H	H	H	57	27	81	<5
2.	Cl	H	H	H	76	5	91	5
3.	NO_2	H	H	H	82	<5	83	<5
4.	OCH_3	H	H	H	82	12	65	<5
5.	H	OH	H	H	84	<5	83	11
6.	H	H	i-Pr	i-Pr	-	-	-	-
7.	H	H	OH	H	71	<5	62	<5

3.6.3. Asymmetric epoxide ring opening

Some cyclic epoxides was tested were also tested in presence of phosphoric acids **4.4**, **4.5a,b** and **4.7a,b**. Cyclohexene and cyclopentene oxide yieldrelatively high yields 66 – 92 %, but cyclooctene oxide was found again to

be poorly reactive, with conversion lower than 10 % (see tables 4.3 and 4.4). Ee were again low (up to 25%, see table 4.4, entry 1).

Table 4.3.

*Catalytic asymmetric epoxide ring opening in the presence of inherently chiral acids **4.4-4.5** (Scheme 4.9).*

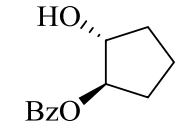
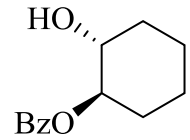
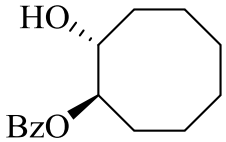
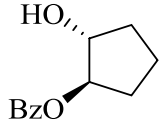
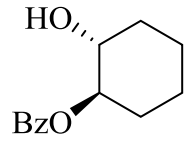
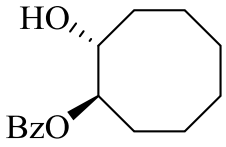
№	Product	*4.4*		*4.5a*		*4.5b*	
		Yield, %	**ee, %**	**Yield, %**	**ee, %**	**Yield, %**	**ee, %**
1.		74	<5	89	<5	91	<5
2.		66	<5	90	<5	92	<5
3.		Conv. 7 %	-	Conv. 9 %	-	Conv. 4 %	-

Table 4.4.

*Catalytic asymmetric epoxide ring opening in the presence of inherently chiral acids **4.7a-b** (Scheme 4.9).*

№	Product	*4.7a*		*4.7b*	
		Yield, %	**ee, %**	**Yield, %**	**ee, %**
1.		53	25	59	5

2.		67	<5	65	<5
3.		Conv. 6 %	-	Conv. 7 %	-

In all tested reactions, poor selectivities and rather low activities were observed. A possible reason is that the catalytic site – P(O)OH is involved into strong intramolecular hydrogen bond like exemplified in figure 4.3 for acid **4.4** . Thus, additional hydroxyl groups and close intramolecular hydrogen bond system could inhibit activity of the acid.

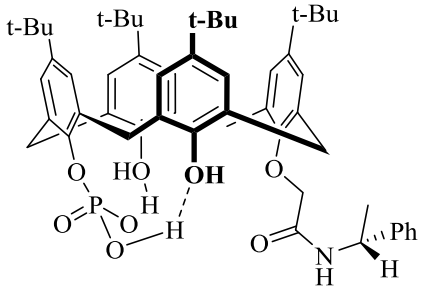


Fig. 4.3. “Closed” structure of acid **4.4**.

In conclusion, it is certainly of interest to synthesize analogues of chiral calixarene phosphoric acids with **no** free hydroxyl group and to test them as chiral Bronsted acid catalysts.

CHAPTER 5

EXPERIMENTAL PART

All reactions were carried out under an argon atmosphere using standard Schlenk techniques. Solvents were carefully dried by conventional methods and distilled under argon before use. ^{1}H, $^{13}C\{^{1}H\}$ and $^{31}P\{^{1}H\}$ NMR spectra of compounds were recorded with a Bruker Avance 500 FT-NMR spectrometer. The resonances were calibrated relative to the residual solvent peaks and are reported with positive values downfield from TMS. For all characterized compounds, the peak assignments in the ^{1}H and ^{13}C NMR spectra were based on COSY, HSQC and HMBC 2D experiments. HRMS were obtained from dichloromethane solutions with a Xevo G2 Q TOF spectrometer by the electrospray method.

General procedure to obtain ligands 2.3 - 2.7.

In a Schlenk tube, 2-thiodiphenyl phosphino (hydroxymethyl) ferrocene **2.1** (0.200 g, 0.46 mmol) was dissolved in 20 mL of dry dichloromethane. A 54% solution of tetrafluoroboric acid in ether (200µL, 1.45 mmol, 3.15 eq.) was then added. After 1 min stirring, nucleophile (22.7 mol, 50eq) was added. After 1 min of stirring, the crude materials were filtered on silica gel with ether as an eluent. After solvent evaporation desired product was obtained as orange solid.

*2-thiodiphenylphosphino (n-hexylaminomethyl) ferrocene **2.3***. Yield 95 %.

^{1}H NMR (δ (ppm), $CDCl_3$): 0.86 (t, 3H, CH_3), 1.15 (m, 8H, CH_2, n-Hexyl), 1.80 (s, 1H, NH), 2.36 (m, 2H, NHC***H***$_2CH_2$), 3.50 (d, 1H, J_{HH} = 13.3 Hz, AB system, CH_2), 3.76 (m, 1H, subst. Cp), 4.30 (d, 1H, J_{HH} = 13.4 Hz, AB system, CH_2), 4.61 (m, 1H, subst. Cp), 4.32 (s, 5H, Cp), 7.47 (m, 6H, PPH_2), 7.70 (dd, 2H, PPH_2), 7.83 (dd, 2H, PPH_2).

$^{13}C\{^{1}H\}$ NMR (δ (ppm), $CDCl_3$): 14.1 (***C***H_3), 22.6 (***C***H_2, n-Hexyl), 26.8 (***C***H_2, n-Hexyl), 29.7 (***C***H_2, n-Hexyl), 31.7 (***C***H_2, n-Hexyl), 47.3 (NH***C***H_2), 49.2

(fc-***C***H_2-NH), 70.6 (Cp), 74.6 (d, J_{PC} = 12.3 Hz: subst. Cp), 74.6 (d, J_{PC} = 95.4 Hz, Cp), 74.7 (d, J_{PC} = 9.6 Hz, subst. Cp), 90.8 (d, J_{PC} = 12.4 Hz, Cp), 128.1 (d, J_{PC} = 12.0 Hz, PPH_2), 128.4 (d, J_{PC} = 12.1 Hz, PPH_2), 131.3 (d, J_{PC} = 2.9 Hz, PPH_2), 131.4 (d, J_{PC} = 3.0 Hz, PPH_2), 131.6 (d, J_{PC} = 10.5 Hz, PPH_2), 132.0 (d, J_{PC} = 10.5 Hz, PPH_2), 133.4 (d, J_{PC} = 86.4 Hz, PPH_2), 134.9 (d, J_{PC} = 85.4 Hz, PPH_2).

$^{31}P\{^1H\}$ NMR (δ (ppm), $CDCl_3$): 43.6.

HRMS (ESI) m/z: 516.1578 (100%, 516.1577 for $C_{29}H_{34}FeNPS$ ($M+H^+$)).

2-thiodiphenylphosphino (t-butyloxycarbonylaminomethyl) ferrocene ***2.4***. Yield 85 %.

^1H NMR (δ (ppm), $CDCl_3$): 1.34 (s, 9H, CH_3), 3.74 (m, 1H, Cp), 4.15 (dd, 1H, CH_2), 4.30 (s, 6H, Cp), 4.54 (dd,1H, CH_2), 4.68 (m, 1H, Cp), 5.06 (m, 1H, NH), 7.49 (m, 8H, PPH2), 7.83 (m, 2H, PPH_2).

$^{13}C\{^1H\}$ NMR (δ (ppm), $CDCl_3$): 28.3 (***C***H_3), 38.2 (***C***$(CH_3)_3$), 70.5 (s, Cp), 74.3 (d, J_{PC} = 12.3 Hz, Cp), 74.5 (d, J_{PC} = 95.4 Hz, quat. Cp), 74.9 (d, J_{PC} = 9.5 Hz, Cp), 78.7 (O***C***$(CH_3)_3$), 90.7 (d, J_{PC} = 12.2 Hz, quat. Cp), 128.1 (d, J_{PC} = 12.5 Hz, PPH_2), 128.5 (d, J_{PC} = 12.7 Hz, PPH_2), 131.3 (d, J_{PC} = 2.9 Hz, PPH_2), 131.4 (d, J_{PC} = 3.1 Hz, PPH_2), 131.6 (d, J_{PC} = 10.5 Hz, PPH_2), 132.0 (d, J_{PC} = 11.1 Hz, PPH_2), 133.0 (d, J_{PC} = 84.6 Hz, quat. PPH_2), 134.9 (d, J_{PC} = 86.3 Hz, quat. PPH_2), 155.6 (HN***C***O).

$^{31}P\{^1H\}$ NMR (δ (ppm), $CDCl_3$): 41.6.

HRMS (ESI) m/z: 554.0982 (70%, 554.0982 for $C_{28}H_{30}FeNO_2PS$ ($M+Na^+$)).

2-thiodiphenylphosphino (bromoacetamidomethyl) ferrocene ***2.5***. Yield 61 %.

^1H NMR (δ (ppm), $CDCl_3$): 7.83 (m, 2H, PPH_2), 7.52 (m, 8H, PPH2), 7.03 (s, NH), 4.78 (dd, 1H, CH_2), 4.69 (m, 1H, Cp), 4.36 (dd, 1H, CH_2), 4.32 (s, 6H,

Cp), 3.77 (m, 1H, Cp), 3.52 (d, 2H, AB system, J_{HH} = 13.4 Hz, CH_2), 3.38 (d, 2H, AB system, J_{HH} = 13.9 Hz, CH_2).

$^{13}C\{^1H\}$ NMR (δ (ppm), $CDCl_3$): 164.8 (HN***C***O), 134.9 (d, J_{PC} = 86.5 Hz, quat. PPH_2), 132.7 (d, J_{PC} = 86.5 Hz, quat. PPH_2), 132.0 (d, J_{PC} = 10.9 Hz, PPH_2), 131.8 (d, J_{PC} = 10.5 Hz, PPH_2), 131.6 (d, J_{PC} = 3.0 Hz, PPH_2), 131.3 (d, J_{PC} = 2.9 Hz, PPH_2), 128.6 (d, J_{PC} = 12.7 Hz, PPH_2), 128.2 (d, J_{PC} = 12.5 Hz, PPH_2), 88.7 (d, J_{PC} = 12.5 Hz, Cp), 75.2 (d, J_{PC} = 9.4 Hz, Cp), 74.5 (Cp), 69.3 (d, J_{PC} = 10.2 Hz, Cp), 38.1 (***C***H_2), 28.7 (***C***H_2).

$^{31}P\{^1H\}$ NMR (δ (ppm), $CDCl_3$): 41.4.

HRMS (ESI) m/z: 550.9771 (50%, 550.9771 for $C_{25}H_{23}BrFeNOPS$ (M)).

(2-thiodiphenylphosphino (2-bromoethyloxymethyl) ***2.6***. Yield 92 %.

^1H NMR (δ (ppm), $CDCl_3$): 7.83 (dd, 2H, PPH_2), 7.67 (dd, 2H, PPH_2), 7.46 (m, 6H, PPH_2), 4.96 (d, 1H, J_{HH} = 11.3 Hz, AB system, CH_2), 4.65 (m, 1H, Cp), 4.47 (d, 1H, J_{HH} = 10.9 Hz, AB system, CH_2), 4.35 (s, 6H), 3.81 (m, 1H Cp), 3.54 (m, 2H, CH_2), 3.01 (m, 2H, CH_2).

$^{13}C\{^1H\}$ NMR (δ (ppm), $CDCl_3$): 134.8 (d, J_{PC} = 87.9 Hz, quat. PPH_2), 133.4 (d, J_{PC} = 86.5 Hz, quat. PPH_2), 132.1 (d, J_{PC} = 10.9 Hz, PPH_2), 132.0 (d, J_{PC} = 10.7 Hz, PPH_2), 131.3 (d, J_{PC} = 3.0 Hz, PPH_2), 131.2 (d, J_{PC} = 2.9 Hz, PPH_2), 128.1 (d, J_{PC} = 4.1 Hz, PPH_2), 128.0 (d, J_{PC} = 4.7 Hz, PPH_2), 87.7 (d, J_{PC} = 11.8 Hz, quat. Cp), 75.3 (d, J_{PC} = 12.3 Hz, Cp), 74.6 (d, J_{PC} = 94.3 Hz, quat. Cp), 74.3 (d, J_{PC} = 9.2 Hz, Cp), 70.7 (Cp), 70.1 (***C***H_2), 69.4 (d, J_{PC} = 10.5 Hz, quat. Cp), 67.3 (***C***H_2), 30.0 (***C***H_2).

$^{31}P\{^1H\}$ NMR (δ (ppm), $CDCl_3$): 41.7.

HRMS (ESI) m/z: 562.9925 (34%, 562.9695 for $C_{25}H_{24}BrFeOPS$ ($M+Na^+$)).

2-thiodiphenylphosphino (3- bromo- n-propyloxymethyl) ***2.7***. Yield 82 %.

^{1}H NMR (δ (ppm), $CDCl_3$): 7.82 (dd, 2H, PPH_2), 7.67 (dd, 2H, PPH_2), 7.46 (m, 6H, PPH_2), 4.94 (d, 1H, J_{HH} = 10.8 Hz, AB system, CH_2), 4.63 (m, 1H, Cp), 4.34 (s, 7H, Cp), 3.81 (m, 1H, Cp), 3.39 (m, 2H, CH_2), 3.07 (m, 2H, CH_2), 1.76 (m, 2H, CH_2).

^{13}C{^{1}H} NMR (δ (ppm), $CDCl_3$): 134.9 (d, J_{PC} = 87.9 Hz, quat. PPH_2), 133.6 (d, J_{PC} = 85.9 Hz, quat. PPH_2), 132.3 (d, J_{PC} = 9.6 Hz, PPH_2), 132.0 (d, J_{PC} = 9.8 Hz, PPH_2), 131.2 (d, J_{PC} = 3.0 Hz, PPH_2), 131.2 (d, J_{PC} = 2.9 Hz, PPH_2), 128.1 (d, J_{PC} = 7.2 Hz, PPH_2), 128.0 (d, J_{PC} = 7.0 Hz, PPH_2), 88.0 (d, J_{PC} = 12.0 Hz, quat. Cp), 75.3 (d, J_{PC} = 12.2 Hz, Cp), 74.6 (d, J_{PC} = 94.9 Hz, quat. Cp), 74.4 (d, J_{PC} = 9.8 Hz, Cp), 70.6 (Cp), 69.4 (d, J_{PC} = 9.7 Hz, quat. Cp), 68.0 (***C***H_2), 67.3 (***C***H_2), 32.9 (***C***H_2), 30.8 (***C***H_2).

^{31}P{^{1}H} NMR (δ (ppm), $CDCl_3$): 41.7.

HRMS (ESI) m/z: 576.9863 (38%, 576.9852 for $C_{26}H_{26}BrFeOPS$ ($M+Na^+$)).

Synthesis of 5,11,17,23-Tetra-tert-butyl-25-(S)-(2-diphenylthiophosphinoferrocenyl)methoxy-26,27,28-calix[4]arene **(S)-2.18**.

In a Schlenk tube under argon, a mixture of 4-tert-butylcalix[4]arene (**2.1**, 0.308 mmol), triphenylphosphine (0.496 mmol), and (S)-(2-diphenylthiophosphinoferrocenyl) methanol [**(S)-2.2**, 0.694 mmol] was dissolved in THF (48 mL) and then cooled in an ice bath. At this temperature, diethyl diazodicarboxylate (40 % in toluene, 0.659 mmol) was added dropwise. The resulting mixture was stirred at room temperature for 24 h, and the solvent was removed in vacuo. Purification by flash chromatography on a silica gel column (EtOAc/hexanes, 1:20) gave an orange solid. Yield 72%.

$[\alpha]_D^{20}$ = +28.8 ($CHCl_3$, c = 0.5).

^{1}H NMR (δ (ppm), $CDCl_3$): 10.17 (s, 1H, OH), 9.55 (s, 1H, OH), 9.33 (s, 1H, OH), 7.91 (m, 2H, Ar), 7.78 (m, 2H, Ar), 7.56 (m, 3H, Ar), 7.3-6.9 (m, 11H, Ar), 5.76 (s, 1H, Cp), 5.49 (d, 1H, J_{HH} = 11.6 Hz, AB system, CH_2), 5.32 (d, 1H,

J_{HH} = 11.6 Hz, AB system, CH_2), 4.70 (d, 1H, J_{HH} = 12.6 Hz, AB system, CH_2), 4.66 (s, 1H, Cp), 4.47 (s, 5H, Cp), 4.35 (d, 1H, J_{HH} = 13.5 Hz, AB system, CH_2), 4.20 (d, 1H, J_{HH} = 13.7 Hz, AB system, CH_2), 3.94 (s, 1H, Cp), 3.51 (m, 4H, CH_2), 2.97 (d, 1H, J_{HH} = 13.5 Hz, AB system, CH_2), 1.25 (s, 27H, tBu), 1.19 (s, 9H, tBu).

$^{13}C\{^1H\}$ NMR (δ (ppm), $CDCl_3$): 148.9 (^{Ar}***C***-OH), 148.8 (^{Ar}***C***-OCH_2), 148.0; 147.6 (^{Ar}***C***-OH), 143.7 (^{Ar}***C***-tBu), 143.1 (^{Ar}***C***-tBu), 142.9 (^{Ar}***C***-tBu), 134.2 (d, J_{PC} = 86.5 Hz, ^{PH}***C***), 134.0 (^{Ar}***C***-CH_2), 133.2 (d, J_{PC} = 86.0 Hz, ***C***^{PH}), 132.6 (^{Ar}***C***-CH_2), 132.1 (d, J_{PC} = 10.9 Hz, ***C***H^{Ar}), 131.8 (d, J_{PC} = 10.6 Hz, ***C***H^{Ar}), 131.4 (d, J_{PC} = 2.7 Hz, ***C***H^{Ar}), 131.1 (d, J_{PC} = 2.8 Hz, ***C***H^{Ar}), 129.2 (^{Ar}***C***-CH_2), 128.7 (^{Ar}***C***-CH_2), 128.4 (d, J_{PC} = 12.5 Hz, ***C***H^{Ar}), 128.1 (d, J_{PC} = 12.4 Hz, ***C***H^{Ar}), 127.7 (^{Ar}***C***-CH_2), 127.5 (^{Ar}***C***-CH_2), 127.4 (^{Ar}***C***-CH_2), 126.75 (^{Ar}***C***-CH_2), 126.74 (^{Ar}***C***H), 126.1 (^{Ar}***C***H), 125.8 (^{Ar}***C***H), 125.61 (^{Ar}***C***H), 125.55 (^{Ar}***C***H), 125.49 (^{Ar}***C***H), 83.5 (d, J_{PC} = 12.0 Hz, Cp), 74.70 (d, J_{PC} = 8.9 Hz, Cp), 74.66 (d, J_{PC} = 12.1 Hz, Cp), 74.0 (***C***H_2), 71.2 (Cp), 73.8 (d, J_{PC} = 94.8 Hz, Cp), 70.7 (d, J_{PC} = 10.2 Hz, Cp), 34.21 (***C***$(CH_3)_3$), 34.04 (***C***$(CH_3)_3$), 33.92 (***C***$(CH_3)_3$), 33.90 (***C***$(CH_3)_3$), 33.15 (***C***H_2), 33.10 (***C***H_2), 32.10 (***C***H_2), 31.59 (***C***H_3), 31.56 (***C***H_3), 31.49 (***C***H_3), 31.45 (***C***H_2), 31.2 (***C***H_3).

$^{31}P\{^1H\}$ NMR (δ (ppm), $CDCl_3$): 40.9.

HRMS (ESI) m/z: 1061.4397 (100%, 1061.4397 for $C_{67}H_{75}FeO_4PS$: M-H).

Synthesis of 5,11,17,23-Tetra-tert-butyl-25-(S)-(2-diphenylthiophosphinoferrocenyl) methoxy-27-benzyloxy-26,28-calix[4]arene **(S)-2.19**.

To a mixture of 5,11,17,23-tetra-tert-butyl-25-(S)-(2-diphenylthiophosphinoferrocenyl)methoxy-26,27,28-calix[4]arene [**(S)-2.18**, 0.100 mmol] and potassium carbonate (0.500 mmol) in dry acetonitrile (10 mL) in a Schlenk tube at room temperature under argon was added benzyl bromide

(0.250 mmol) dropwise. The resulting mixture was stirred at room temperature for 12 h and then diluted with HCl (2 M). The resulting mixture was extracted with CH_2Cl_2. The organic phase was washed with distilled water (2 × 15 mL) and brine and then dried with Na_2SO_4. The solvent was removed in vacuo, and the crude product was purified by flash chromatography on a silica gel column (EtOAc/hexanes, 1:25), to give an orange solid. Yield 90%.

$[\alpha]_D^{20}$ = +15.4 ($CHCl_3$, c = 0.5).

^{1}H NMR (δ (ppm), $CDCl_3$): 7.83 (m, 2H, Ar), 7.72 (m, 2H, Ar), 7.62 (m, 4H, Ar), 7.47 (m, 6H, ArH), 7.34 (m, 4H, Ar OH), 7.15 (s, 1H, OH), 7.14 (s, 1H, Ar), 7.12 (d, J_{HH} = 2.2 Hz, 1H, Ar), 7.10 (d, J_{HH} = 2.2 Hz, 1H, Ar), 7.03 (d, J_{HH} = 2.2 Hz, 1H, Ar), 6.79 (s, 1H, Ar), 6.77 (s, 1H, Ar), 6.75 (s, 1H, Ar), 6.68 (d, J_{HH} = 2.1 Hz, 1H, Ar), 5.63 (d (AB system), J_{HH} = 12.4 Hz, 1H, CH_2), 5.46 (s, 1H, Cp), 5.07 (dd, (AB system), J = 11.4 Hz, 2H, PHC***H***$_2$O), 4.52 (d, (AB system), J_{HH} = 12.8 Hz, 1H, CH_2), 4.52 (d, (AB system), J_{HH} = 12.9 Hz, 1H, CH_2), 4.44 (m, 5H, Cp + 1H, CH_2), 4.58 (d, 1H, CH_2), 4.40 (d (AB system), J_{HH} = 13.6 Hz, 1H, CH_2), 4.35 (s, 1H, Cp), 4.00 (d (AB system), J_{HH} = 13.1 Hz, 1H, CH_2), 3.79 (s, 1H, Cp), 3.45 (d (AB system), J_{HH} = 13.6 Hz, 1H, CH_2), 3.36 (d (AB system), J_{HH} = 13.1 Hz, 1H, CH_2), 3.34 (d, (AB system), J_{HH} = 13.1 Hz, 1H, CH_2), 3.08 (d (AB system), J = 13.4 Hz, 1H, CH_2), 1.36 (s, 9H, tBu), 1.34 (s, 9H, tBu), 0.93 (s, 9H, tBu), 0.92 (s, 9H, tBu).

^{13}C{^{1}H} NMR (δ (ppm), $CDCl_3$): 150.9 (^{Ar}***C***-CH_2), 150.8 (^{Ar}***C***-CH_2), 149.9 (^{Ar}***C***-OCH_2), 149.5 (^{Ar}***C***-OH), 147.0 (^{Ar}***C***-tBu), 146.9 (^{Ar}***C***-tBu), 141.4 (^{Ar}***C***-tBu), 141.3 (^{Ar}***C***-tBu), 137.3 (^{Ar}***C***-OCH_2), 134.5 (d, J_{PC} = 86.5 Hz, ***C***^{PH}), 133.4 (d, J_{PC} = 86.0 Hz, ***C***^{PH}), 132.6 (^{Ar}***C***-CH_2), 132.4 (^{Ar}***C***-CH_2), 132.2 (^{Ar}***C***-CH_2), 132.1 (^{Ar}***C***-CH_2), 132.08 (^{Ar}***C***H), 131.97 (^{Ar}***C***H), 131.77 (^{Ar}***C***H), 131.66 (^{Ar}***C***H), 131.25 (d, J_{PC} = 2.9 Hz, ^{Ar}***C***H), 131.18 (d, J_{PC} = 2.9 Hz, ^{Ar}***C***H), 128.62 (^{Ar}***C***H), 128.4 (d, J_{PC} = 12.6 Hz, ^{Ar}***C***H), 128.1 (d, J_{PC} = 12.3 Hz, ^{Ar}***C***H), 127.9 (^{Ar}***C***H), 127.83 (^{Ar}***C***-CH_2), 127.80 (^{Ar}***C***-CH_2), 127.76 (^{Ar}***C***H), 127.62 (^{Ar}***C***-CH_2), 127.53 (^{Ar}***C***-CH_2), 125.6 (^{Ar}***C***H), 125.5 (^{Ar}***C***H), 125.3 (^{Ar}***C***H), 125.2 (^{Ar}***C***H), 125.1 (^{Ar}***C***H), 125.0

(^{Ar}***C***H), 124.9 (^{Ar}***C***H), 124.8 (^{Ar}***C***H), 88.9 (d, J_{PC} = 11.6 Hz, Cp), 78.2 (PH***C***H_2O), 74.2 (d, J_{PC} = 12.1 Hz, Cp), 73.5 (d, J_{PC} = 95.2 Hz, Cp), 72.7 (***C***H_2), 72.1 (d, J_{PC} = 9.0 Hz, Cp), 71.1 (5C, CH Cp), 69.4 (d, J_{PC} = 10.2 Hz, Cp), 33.90 (***C***$(CH_3)_3$), 33.86 (***C***$(CH_3)_3$), 33.84 (***C***$(CH_3)_3$), 31.77 (***C***H_3), 31.75 (***C***H_3 + ***C***H_2), 33.65 (***C***H_2), 31.48 (***C***H_2), 31.24 (***C***H_2), 30.97 (***C***H_3).

^{31}P{^{1}H} NMR (δ (ppm), $CDCl_3$): 41.5.

HRMS (ESI) m/z: 1152.4923 (100%, 1152.4943 for $C_{74}H_{81}FeO_4PS$: M).

Synthesis of 5,11,17,23-Tetra-tert-butyl-25,27-bis[(S)-(2-diphenylthiophosphinoferrocenyl)methoxy]-26,28-calix[4]arene **(S,S)-2.20**.

In a Schlenk tube under argon, a mixture of 4-tert-butylcalix[4]arene (**2.1**, 0.308 mmol), triphenylphosphine (0.992 mmol), and (S)-(2-diphenylthiophosphinoferrocenyl)methanol [**(S)-2.2**, 0.992 mmol] was dissolved in THF (48 mL) and then cooled in an ice bath. At this temperature, diethyl diazodicarboxylate (40 % in toluene, 1.317 mmol) was added dropwise. The resulting mixture was stirred at room temperature for 35 h, and the solvent was then removed in vacuo. The crude product was purified by flash chromatography on a silica gel column (EtOAc/hexanes, 1:15) to give an orange solid. Yield 68%.

$[\alpha]_D^{20}$ = +15.0 ($CHCl_3$, c = 0.5).

^{1}H NMR (δ (ppm), $CDCl_3$): 7.82 (dd, 4H, Ar), 7.64 (dd, 4H, Ar), 7.51 (m, 6H, Ar), 7.32 (m, 6H, Ar), 7.14 (d, J_{HH} = 2.5 Hz, 2H, Ar), 7.01 (d, J_{HH} = 2.2 Hz, 2H, Ar), 6.94 (c, 2H, OH), 6.66 (d, J_{HH} = 2.2 Hz, 2H, Ar), 6.60 (d, J_{HH} = 2.3 Hz, 2H, Ar), 5.53 (m, 2H, Cp + (AB system), J_{HH} = 11.9 Hz, 2H, CH_2), 4.64 (d (AB system), J_{HH} = 12.4 Hz, 2H, CH_2), 4.52 (m, 10H, Cp + 2H, CH_2), 4.44 (m, 2H, Cp), 3.92 (d (AB system), J_{HH} = 13.1 Hz, 2H, CH_2), 3.80 (m, 2H, Cp), 3.45 (d (AB system), J_{HH} = 13.1 Hz, 2H, CH_2), 3.02 (d (AB system), J_{HH} = 13.1 Hz, 2H, CH_2), 1.35 (s, 18H, tBu), 0.85 (s, 18H, tBu).

$^{13}C\{^1H\}$ NMR (δ (ppm), $CDCl_3$): 150.7 ($^{Ar}\boldsymbol{C}$-CH_2), 149.6 ($^{Ar}\boldsymbol{C}$-OH), 146.8 ($^{Ar}\boldsymbol{C}$-tBu), 141.3 ($^{Ar}\boldsymbol{C}$-tBu), 134.3 (d, J_{PC} = 86.4 Hz, $^{Ar}\boldsymbol{C}$), 133.3 (d, J_{PC} = 85.4 Hz, $^{Ar}\boldsymbol{C}$), 132.11 ($^{Ar}\boldsymbol{C}$-CH_2), 132.11 ($^{Ar}\boldsymbol{C}$H), 131.99 ($^{Ar}\boldsymbol{C}$H), 131.91 ($^{Ar}\boldsymbol{C}$H), 131.67 (d, J_{PC} = 10.8 Hz, $^{Ar}\boldsymbol{C}$H), 131.3 (d, J_{PC} = 2.7 Hz, $^{Ar}\boldsymbol{C}$H), 128.45 (d, J_{PC} = 12.2 Hz, $^{Ar}\boldsymbol{C}$H), 128.1 (d, J_{PC} = 12.2 Hz, $^{Ar}\boldsymbol{C}$H), 127.96 ($^{Ar}\boldsymbol{C}$-CH_2), 127.75 ($^{Ar}\boldsymbol{C}$H), 125.25 ($^{Ar}\boldsymbol{C}$-CH_2), 125.19 ($^{Ar}\boldsymbol{C}$H), 124.9 ($^{Ar}\boldsymbol{C}$H), 88.84 (d, J_{PC} = 11.5 Hz, Cp), 74.2 (d, J_{PC} = 12.3 Hz, Cp), 74.07 (d, J_{PC} = 94.9 Hz, $^{Cp}\boldsymbol{C}$-PPH_2), 72.82 ($\boldsymbol{C}H_2$), 72.57 (d, J_{PC} = 9.1 Hz, Cp), 71.22 (Cp), 71.16 (Cp), 69.21 (d, J_{PC} = 9.9 Hz, Cp), 33.84 ($\boldsymbol{C}(CH_3)_3$), 33.78 ($\boldsymbol{C}(CH_3)_3$), 31.77 ($\boldsymbol{C}H_3$), 31.45 ($\boldsymbol{C}H_2$), 30.99 ($\boldsymbol{C}H_2$), 30.90 ($\boldsymbol{C}H_3$).

$^{31}P\{^1H\}$ NMR (δ (ppm), $CDCl_3$): 41.3.

HRMS (ESI) m/z: 1475.4397 (100%, 1475.4765 for $C_{90}H_{93}Fe_2O_4P_2S_2$: M-H).

Synthesis of (4-tert-Butylphenyl) (S)-[(2-Diphenylthiophosphinoferrocenyl)methyl] Oxide **(S)-2.24**.

In a Schlenk tube under argon, a mixture of 4-tert-butylphenol (0.616 mmol), triphenylphosphine (0.992 mmol), and (S)-(2-diphenylthiophosphinoferrocenyl)methanol (0.308 mmol) was dissolved in THF (48 mL) and then cooled in an ice bath. At this temperature, diethyl diazodicarboxylate (40 % in toluene, 1.317 mmol) was added dropwise, and the resulting mixture was stirred at room temperature for 12 h. The solvent was removed in vacuo, and the crude product was purified by flash chromatography on a silica gel column (EtOAc/hexanes, 1:10) to give the product as an orange solid. Yield 82%.

$[\alpha]_D^{20}$ = +36.1 ($CHCl_3$, c = 0.5).

^1H NMR (δ (ppm), $CDCl_3$): 7.85 (m, 2H, PPH_2); 7.66 (m, 2H, PPH_2); 7.49 (m, 2H, PPH_2); 7.34 (m, 4H, PPH_2); 7.21 (m, 2H, O-C_6H_4-*p*-tBu); 6.64 (m, 2H, O-C_6H_4-*p*-tBu); 5.05 (d (AB system), J_{HH} = 11.1 Hz, 1H, CH_2), 5.02 (d (AB

system), J_{HH} = 11.1 Hz, 1H, CH_2); 4.75 (s, 1H, Cp), 4.40 (s, 1H, Cp), 4.39 (s, 5H, Cp), 3.95 (s, 1H, Cp), 1.29 (s, 9H, C(C***H***$_3$)$_3$).

^{13}C{^{1}H} NMR (δ (ppm), $CDCl_3$): 159.3 (^{Ar}***C***-O-CH_2), 143.2 (^{Ar}***C***-O-tBu), 133.8 (d, $^1J_{PC}$ = 19.4 Hz, ^{Ar}***C***-P); 132.2 (d, $^3J_{PC}$ = 10.8 Hz, PHH); 132.0 (d, $^3J_{PC}$ = 10.7 Hz, PHH); 131.3 (d, $^4J_{PC}$ = 2.9 Hz, PHH); 131.1 (d, $^4J_{PC}$ = 2.9 Hz, PHH); 128.2 (d, $^2J_{PC}$ = 11.2 Hz, PHH); 128.0 (d, $^2J_{PC}$ = 11.2 Hz, PHH); 125.9 (ArH); 114.1 (ArH); 87.5 (d, J_{PC} = 11.7 Hz, Cp); 75.11 (d, J_{PC} = 12.6 Hz, Cp); 73.78 (d, J_{PC} = 9.2 Hz, Cp); 70.8 (Cp); 75.0 (d, J_{PC} = 94.6 Hz, Cp), 69.7 (d, J_{PC} = 10.4 Hz, Cp); 64.7 (***C***H_2); 34.0 (***C***$(CH_3)_3$); 31.5 (C(***C***$H_3)_3$).

^{31}P{^{1}H} NMR (δ (ppm), $CDCl_3$): 41.7

HRMS (ESI) m/z: 587.1245 (25%, 587.1237 for $C_{33}H_{33}FeOPSNa$: M+Na); 415.0378 (100%, 415.0373 for $C_{23}H_{20}FePS$: M-(OAr).

General Procedure of Desulfuration of the Thiophosphines.

In a Schlenk tube, the thiophosphine derivative (0.115 mmol) was dissolved in toluene (5 mL) along with tris(dimethylamino)phosphine (0.2 mL) under argon. The resulting solution was heated at reflux overnight. After the mixture was cooled to room temp., the solvent was removed in vacuo. The crude product was purified by flash chromatography under argon on a silica gel column (CH_2Cl_2) to give the product as an orange solid.

5,11,17,23-Tetra-tert-butyl-25-(S)-(2-diphenylphosphinoferrocenyl)methoxy-26,27,28-calix[4]arene **(S)-2.21**. Yield 90%.

^{1}H NMR (δ (ppm), $CDCl_3$): 7.50 (m, 2H, Ar), 7.36 (m, 3H, 2OH, Ar), 7.30 (m, 2H, Ar), 7.26 (m, 1H, Ar), 7.18 (m, 2H, Ar), 7.15 (m, 1H, Ar), 7.10 (m, 1H, Ar), 7.08 (m, 1H, Ar), 7.05 (m, 1H, Ar), 7.00 (m, 3H, Ar), 7.00 (s, 1H, OH), 6.87 (m, 1H, Ar), 6.77 (m, 2H, Ar), 4.69 (d (AB system), J_{HH} = 14.6Hz, 1H, CH_2), 4.62 (m, 2H, CH_2), 4.58 (m, 1H, Cp), 4.31 (td (AB system), J_{HH} = 12.6

Hz, 3H, CH_2), 4.23 (m, 2H, CH_2), 3.94 (s, 5H, Cp), 3.66 (d (AB system), J_{HH} = 14.5Hz, 2H, CH_2), 3.65 (d (AB system), J_{HH} = 14.4Hz, 1H, CH_2), 3.61 (s, 1H, Cp), 1.42 (s, 9H, tBu), 1.39 (s, 9H, tBu), 1.29 (s, 9H, tBu), 1.17 (s, 9H, tBu).

$^{13}C\{^1H\}$ NMR (δ (ppm), $CDCl_3$): 154.8 (^{Ar}***C***-OH), 147.08 (^{Ar}***C***-OCH_2), 147.05 (^{Ar}***C***-OH+^{Ar}***C***-tBu), 147.6 (^{Ar}***C***-OH), 146.5 (^{Ar}***C***-tBu), 146.2 (^{Ar}***C***-tBu), 145.9 (^{Ar}***C***-tBu), 144.4 (^{Ar}***C***H), 138.9 (d, J_{PC} = 8.8 Hz, ^{Ar}***C***), 137.4 (d, J_{PC} = 8.8 Hz, ^{Ar}***C***), 135.3 (^{Ar}***C***H), 135.1 (^{Ar}***C***H), 134.9 (d, J_{PC} = 3.7 Hz, ^{Ar}***C***H), 134.8 (d, J_{PC} = 3.7 Hz, ^{Ar}***C***H), 133.3 (^{Ar}***C***-CH_2), 133.28 (^{Ar}***C***H), 133.22 (^{Ar}***C***-CH_2), 132.94 (^{Ar}***C***-CH_2), 132.91 (^{Ar}***C***-CH_2), 131.8 (^{Ar}***C***H), 131.6 (^{Ar}***C***H), 130.4 (d, J_{PC} = 2.9 Hz, ^{Ar}***C***H), 131.4 (d, J_{PC} = 2.9 Hz, ^{Ar}***C***H), 129.02 (^{Ar}***C***H), 128.1 (^{Ar}***C***H), 128.0 (^{Ar}***C***H), 127. 8 (^{Ar}***C***H), 127.7 (^{Ar}***C***H), 127.1 (^{Ar}***C***H), 126.3 (^{Ar}***C***H), 126.25 (^{Ar}***C***H), 126.12 (^{Ar}***C***H), 125.8 (^{Ar}***C***H), 125.6 (^{Ar}***C***H), 125.5 (^{Ar}***C***H), 89.00 (d, J_{PC} = 24.2 Hz, Cp), 72.4 (d, J_{PC} = 3.7 Hz, Cp), 71.3 (d, J_{PC} = 3.7 Hz, Cp), 70.9 (d, J_{PC} = 11.2 Hz, ***C***H_2), 70.7 (Cp), 69.7 (Cp), 69.6 (Cp), 34.4 (***C***$(CH_3)_3$), 34.3 (***C***$(CH_3)_3$), 34.2 (***C***H_2), 34.0 (***C***H_2), 33.6 (***C***H_2), 31.7 (C(***C***$H_3)_3$), 31.6 (C(***C***$H_3)_3$), 31.5 (C(***C***$H_3)_3$).

$^{31}P\{^1H\}$ NMR (δ (ppm), $CDCl_3$): -22.2.

5,11,17,23-Tetra-tert-butyl-25-(S)-(2-diphenylphosphinoferrocenyl)methoxy-27-benzyloxy-26,28-calix[4]arene **(S)-2.22**. Yield 87%.

^1H NMR (δ (ppm), $CDCl_3$): 7.69 (m, 2H, Ar), 7.55 (m, 3H, Ar), 7.4 (m, 6H, ArH, 2 OH), 7.14 (m, 8H, ArH), 7.03 (m, 2H, Ar), 6.77 (m, 3H, Ar), 6.70 (s, 1H, Ar), 5.23 (s, 1H, Cp), 5.17 (d, (AB system), J_{HH} = 11.8 Hz, 1H, CH_2), 5.06 (dd, (AB system), J_{HH} = 11.4 Hz, 2H, PHC***H***$_2$O), 4.52 (d, (AB system), J_{HH} = 12.8 Hz, 1H, CH_2), 4.52 (d, (AB system), J_{HH} = 12.9 Hz, 1H, CH_2), 4.40 (s, 1H, Cp), 4.38 (d, J_{HH} = 13.5 Hz, 2H, CH_2), 4.36 (s, 1H, Cp), 4.19 (s, 5H, Cp), 4.16 (d (AB system), J_{HH} = 13.3 Hz, 1H, CH_2), 3.43 (d (AB system), J_{HH} = 13.6 Hz, 1H,

CH_2), 3.36 (d (AB system), J_{HH} = 13.8 Hz, 1H, CH_2), 3.34 (d, (AB system), J_{HH} = 13.8 Hz, 1H, CH_2), 3.14 (d (AB system), J_{HH} = 13.2 Hz, 1H, CH_2), 1.35 (s, 9H, tBu), 1.33 (s, 9H, tBu), 0.94 (s, 9H, tBu), 0.92 (s, 9H, tBu).

$^{13}C\{^1H\}$ NMR (δ (ppm), $CDCl_3$): 150.9 (^{Ar}C-CH_2), 150.8 (^{Ar}C-CH_2), 149.9 (^{Ar}C-OCH_2), 149.8 (^{Ar}C-OH), 146.9 (^{Ar}C-tBu), 146.8 (^{Ar}C-tBu), 141.3 (^{Ar}C-tBu), 141.2 (^{Ar}C-tBu), 137.2 (^{Ar}C-OCH_2), 134.9 (d, J_{PC} = 20.5 Hz, ^{Ar}C), 132.4 (d, J_{PC} = 24.3 Hz, ^{Ar}CH), 129.2 (^{Ar}C-CH_2), 129.1 (^{Ar}C-CH_2), 128.9 (^{Ar}C-CH_2), 128.6 (^{Ar}CH), 128.3 (^{Ar}CH), 128.2 (^{Ar}CH), 128.1 (^{Ar}CH), 127.92 (^{Ar}CH), 127.89 (^{Ar}CH), 127.85 (^{Ar}C-CH_2), 127.78 (^{Ar}C-CH_2), 127.77 (^{Ar}CH), 127.59 (^{Ar}C-CH_2), 127.43 (^{Ar}C-CH_2), 125.5 (^{Ar}CH), 125.46 (^{Ar}CH), 125.3 (^{Ar}CH), 125.2 (^{Ar}CH), 125.05 (^{Ar}CH), 125.02 (^{Ar}CH), 124.99 (^{Ar}CH), 124.86 (^{Ar}CH), 89.68 (d, J_{PC} = 22.7 Hz, Cp), 78.3 (PHCH$_2$O), 73.5 (d, J_{PC} = 12.5 Hz, Cp), 70.95 (d, J_{PC} = 3.7 Hz, Cp), 70.2 (d, J_{PC} = 3.7 Hz, Cp), 70.0 (5C, CH^{Cp}), 69.7 (Cp), 69.6 (CH$_2$), 53.4 (CH$_2$), 33.90 (C(CH$_3$)$_3$), 33.86 (C(CH$_3$)$_3$), 33.83 (C(CH$_3$)$_3$), 31.77 (CH$_3$), 31.75 (CH$_3$ + CH$_2$), 31.50 (CH$_2$), 31.48 (CH$_2$), 31.24 (CH$_2$), 30.98 (CH$_3$), 30.96 (CH$_3$).

$^{31}P\{^1H\}$ NMR (δ (ppm), $CDCl_3$): -23.0.

5,11,17,23-Tetra-tert-butyl-25,27-bis[(S)-(2-diphenylphosphinoferrocenyl)methoxy]-26,28-calix[4]arene **(S)-2.23**. Yield 92%.

^1H NMR (δ (ppm), $CDCl_3$): 7.56 (m, 4H, Ar), 7.40 (m, 6H, Ar), 7.22-7.06 (m, 12H, Ar), 7.00 (d, J_{HH} = 2.2 Hz, 2H, Ar), 6.97 (s, 2H, OH), 6.69 (d, J_{HH} = 2.2 Hz, 2H, Ar), 6.62 (d, J_{HH} = 2.2 Hz, 2H, Ar), 5.25 (s, 2H, Cp), 5.49 (d (AB system), J_{HH} = 11.9 Hz, 2H, CH_2), 4.62 (d (AB system), J_{HH} = 11.3 Hz, 2H, CH_2), 4.55 (d (AB system), J_{HH} = 12.6 Hz, 2H, CH_2), 4.39 (m, 2H, Cp), 4.24 (s, 10H, Cp), 4.05 (d (AB system), J_{HH} = 13.1 Hz, 2H, CH_2), 3.77 (m, 2H, Cp), 3.42 (d (AB system), J_{HH} = 13.0 Hz, 2H, CH_2), 3.07 (d (AB system), J_{HH} = 13.2 Hz, 2H, CH_2), 1.35 (s, 18H, tBu), 0.86 (s, 18H, tBu).

$^{13}C\{^1H\}$ NMR (δ (ppm), $CDCl_3$): 150.8 (^{Ar}C-OCH_2), 149.9 (^{Ar}C-OH), 146.7 (^{Ar}C-tBu), 141.1 (^{Ar}C-tBu), 139.1 (d, J_{PC} = 9.8 Hz, ^{Ar}C), 137.1 (d, J_{PC} = 9.2 Hz, ^{Ar}C), 135.1 (^{Ar}CH), 134.9 (^{Ar}CH), 132.23 (^{Ar}C-CH_2), 132.21 (^{Ar}CH), 132.03 (^{Ar}C-CH_2), 132.01 (^{Ar}C-CH_2), 129.1 (^{Ar}CH), 128.7 (d, J_{PC} = 86.0 Hz, ^{Ar}C), 128.24 (d, J_{PC} = 9.8 Hz, ^{Ar}CH), 128.17 (d, J_{PC} = 11.4 Hz, ^{Ar}CH), 127.9 (^{Ar}C-CH_2), 127.7 (d, J_{PC} = 22.8 Hz, ^{Ar}CH), 125.29 (^{Ar}CH), 125.18 (^{Ar}C-CH_2), 124.98 (^{Ar}CH), 124.89 (^{Ar}CH), 89.47 (d, J_{PC} = 23.2 Hz, Cp), 74.63 (d, J_{PC} = 7.4 Hz, Cp), 73.72 (CH$_2$), 73.60 (CH$_2$), 71.08 (d, J_{PC} = 3.4 Hz, Cp), 70.91 (d, J_{PC} = 3.5 Hz, Cp), 70.06 (Cp), 69.66 (Cp), 33.82 (C(CH$_3$)$_3$), 33.78 (C(CH$_3$)$_3$), 31.77 (CH$_3$), 31.62 (CH$_2$), 31.23 (CH$_2$), 30.92 (CH$_3$).

$^{31}P\{^1H\}$ NMR (δ (ppm), $CDCl_3$): -23.0.

((4-tert-Butylphenyl)[(2-Diphenylphosphinoferrocenyl)methyl]Oxide **(S)-2.24**. Yield 93%.

^1H NMR (δ (ppm), $CDCl_3$): 7.61 (m, 2H, PPH_2); 7.40 (m, 8H, PPH_2); 7.24 (m, 2H, O-C_6H_4-*p*-tBu); 6.71 (m, 2H, O-C_6H_4-*p*-tBu); 4.98 (dd, (AB system), J_{HH} = 10.6 Hz, J_{HH} = 2.1 Hz, 1H, CH_2), 4.92 (d (AB system), J_{HH} = 10.6 Hz, 1H, CH_2); 4.65 (s, 1H, Cp), 4.37 (s, 1H, Cp), 4.11 (s, 5H, Cp), 3.86 (s, 1H, Cp), 1.31 (s, 9H, C(CH$_3$)$_3$).

$^{13}C\{^1H\}$ NMR (δ (ppm), $CDCl_3$): 156.6 (^{Ar}C-O-CH_2), 143.2 (^{Ar}C-tBu), 139.8 (d, $^1J_{PC}$ = 9.5 Hz, ^{Ar}C-P); 137.5 (d, $^1J_{PC}$ = 9.5 Hz, ^{Ar}C-P); 135.2 (d, $^2J_{PC}$ = 21.1 Hz, ^{Ar}CH); 133.8 (d, $^3J_{PC}$ = 19.4 Hz, ^{Ar}CH); 132.3 (d, $^3J_{PC}$ = 17.7 Hz, ^{Ar}CH); 126.0 (^{Ar}CH); 114.1 (^{Ar}CH); 88.5 (d, J_{PC} = 23.9 Hz, Cp); 72.0 (d, J_{PC} = 17.4 Hz, Cp); 72.1 (d, J_{PC} = 17.2 Hz, Cp); 69.7 (s, Cp); 65.5 (d, J_{PC} = 10.5 Hz, quat. Cp), 55.8 (s, CH_2); 34.0 (C(CH$_3$)$_3$); 31.5 (C(CH$_3$)$_3$).

$^{31}P\{^1H\}$ NMR (δ (ppm), $CDCl_3$): -22.5.

General Procedure for Asymmetric Suzuki–Miyaura Coupling Reaction.

The ligand (0.012 mmol, 1.2 mol-%), $[Pd(C_3H_5)Cl]_2$ (1.8 mg, 0.005 mmol, 1.1 mol-%), 1-naphthaleneboronic acid (1.2 mmol), cesium carbonate (750 mg, 2.030 mmol, 2.3 mol-%), and 1-bromo-2-methylnaphthalene (1.00 mmol) were introduced, under an argon stream, into a Schlenk tube that contained toluene (10 mL). The reaction mixture was stirred at 60 °C for 24 h under Ar. The mixture was cooled to room temp., and then acidified water (1 mol L–1 HCl water solution) was added. The resulting mixture was extracted with diethyl ether, and the organic phase was then filtered through silica. The solvent was removed under reduced pressure to give the product. The enantiomeric excess value was determined by supercritical fluid chromatography (SFC)-HPLC [Chiralcel OJ column; CO_2/iPrOH, 9:1; flow rate: 4 mL min^{-1}]: tR = 5.04 min (R isomer) and 8.68 min (S isomer).

General Procedure for Asymmetric Allylic Substitution.

A mixture of calixarene ligand (S,S)-8 (0.003 mmol), 1,3-diphenylprop-2-enyl acetate (0.126 g, 0.5 mmol), and [Pd(C3H5)Cl]2 (5.3 mg, 0.0015 mmol) was dissolved in dry dichloromethane (20 mL). Dimethyl malonate (0.115 mL, 1 mmol), the acetate salt (1 mmol), and BSA (0.250 mL, 1 mmol) were then added to the resulting solution. The reaction was heated at reflux, and the progress of the reaction was monitored by TLC analysis. After 36 h, the mixture was quenched by the addition of a saturated aqueous solution of ammonium chloride (20 mL). The aqueous phase was extracted with dichloromethane, and the combined organic layers were dried with magnesium sulfate and filtered. The solvent was evaporated. The conversion was calculated by using the integration of signals of the ^1H NMR spectra for the crude reaction mixture. Subsequent purification by chromatography on silica (dichloromethane/pentane, 1:1) afforded the product as a colorless oil. The enantiomeric excess value was determined by ^1H NMR spectroscopy using the chiral shift reagent (+)-$Eu(hfc)_3$ [hfc = (heptafluoropropylhydroxymethylene)-camphorate].

Monopropoxy-p-tert-butylcalix[4]arene **3.2** was obtained according to the literature [111].

The alkylation of compound **3.2** was carried out by the method described in reference [112]. The mixture of monopropoxycalix[4]arenes 1 (1.0 mmol), sodium hydroxide (40 % water solution, 3.53 mL, 50.05 mmol), and DMSO (25 mL) was warmed to 60 ˚C. Then (R)-N-(1-phenylethyl)bromoacetamide (2.0 mmol) was added and the mixture was stirred under inert atmosphere at 60 ˚C for 6 h. After cooling to room temperature the reaction mixture was acidified with 10 % hydrochloric acid to pH = 4–5; then the mixture was extracted with $CHCl_3$ (50 mL). The organic phase was washed with water (2 x 30 mL), dried over Na_2SO_4 and concentrated. The residue of diastereomeric mixture **3a, b** were separated by column chromatography on silica gel (hexane/ethyl acetate 6:1).

Amide hydrolysis. A mixture of amide **3.3a** or **3.3b** (0.50 g, 0.559 mmol) and $Ba(OH)_2$ (0.96 g, 5.614 mmol) in n-butanol (20 mL)/DMSO (1 mL) was stirred at 130 ˚C for 4 h. The solvents were removed in vacuo. Then water (20 mL) and 30 % HCl (to pH = 4–5) were added to the remaining solid. The product was extracted with $CHCl_3$ (3 x 5 mL), washed with water (10 mL), brine (10 mL), and dried over Na_2SO_4. The solvent was removed in vacuo. The solid residue was boiled with hexane (5 mL) and left at 5–10 ˚C for 15 h. The hexane solution was decanted and the solvent was removed in vacuo. The spectroscopically pure acid was obtained.

(cS)-5,11,17,23-Tetra-tert-butyl-25,26-dihydroxy-27-propoxy-28-carboxylmethoxycalix[4]arene **3.4a** or *(cR)-5,11,17,23-Tetra-tert-butyl-25,26-dihydroxy-27-carboxylmethoxy-28-propoxycalix[4]arene* **3.4b**. M.p. 145 ^oC

(acetonitrile). $[\alpha]_D^{20}$ -7.53 (c 0.014 M, $CHCl_3$) for **3.4a,** -16.04 (c 0.016 M, $CHCl_3$) for **3.4b**. IR (KBr): 3480-3250 (OH), 1740 (C=O).

^{1}H NMR (δ (ppm), $CDCl_3$): 1.15 (s, 9H, t-Bu), 1.17 (t, 3H, $OCH_2CH_2C\boldsymbol{H_3}$, $J^3_{H\text{-}H}$ = 7.5 Hz), 1.20 (s, 18H, t-Bu), 1.24 (s, 9H, t-Bu), 1.98-2.18 (m, 2H, $OCH_2C\boldsymbol{H_2}CH_3$), 3.36 (d, 1H, Ar-C$\boldsymbol{H_2}$-eq, $J^2_{H\text{-}H}$ = 12.7 Hz), 3.43 (d, 1H, Ar-C$\boldsymbol{H_2}$-eq, $J^2_{H\text{-}H}$ = 13.7 Hz), 3.44 (d, 1H, Ar-C$\boldsymbol{H_2}$-eq, $J^2_{H\text{-}H}$ = 12.2 Hz), 3.52 (d, 1H, Ar-C$\boldsymbol{H_2}$-eq, $J^2_{H\text{-}H}$ = 13.7 Hz), 3.87-3.96 (m, 1H, OC$\boldsymbol{H_2}CH_2CH_3$), 4.01 (d, 1H, Ar-C$\boldsymbol{H_2}$-ax, $J^2_{H\text{-}H}$ = 13.7 Hz), 4.05 -4.13 (m, 1H, OC$\boldsymbol{H_2}CH_2CH_3$), 4.16 (d, 1H, Ar-C$\boldsymbol{H_2}$-ax, $J^2_{H\text{-}H}$ = 12.7 Hz), 4.23 (d, 1H, O-C$\boldsymbol{H_2}$-CO, $J^2_{H\text{-}H}$ = 15.7 Hz), 4.26 (d, 1H, Ar-C$\boldsymbol{H_2}$-ax, $J^2_{H\text{-}H}$ = 13.7 Hz), 4.32 (d, 1H, Ar-C$\boldsymbol{H_2}$-ax, $J^2_{H\text{-}H}$ = 12.2 Hz), 4.87 (d, 1H, O-C$\boldsymbol{H_2}$-CO, $J^2_{H\text{-}H}$ = 15.7 Hz), 6.95 (d, 1H, Ar-***H***, $J^4_{H\text{-}H}$ = 2.4 Hz), 7.05 (c, 2H, Ar-***H***), 7.08 (d, 1H, Ar-***H***, $J^4_{H\text{-}H}$ = 2.2 Hz), 7.11 (d, 1H, Ar-***H***, $J^4_{H\text{-}H}$ = 2.2 Hz), 7.24 (d, 1H, Ar-***H***, $J^4_{H\text{-}H}$ = 2.4 Hz), 10.09 (s, 1H, O***H***), 10.31 (s, 1H, O***H***), 12.03-12.56 (шир.с., 1H, COO***H***).

^{13}C{^{1}H} NMR (δ (ppm), $CDCl_3$): 10.63 (-CH_2-***C***H_3), 23.42 (-***C***H_2-CH_3), 30.71 (***C***Me_3), 31.27 (-C(***C***$H_3)_3$), 31.38 (-C(***C***$H_3)_3$), 31.58 (-C(***C***$H_3)_3$), 31.61 (-C(***C***$H_3)_3$), 33.27 (***C***Me_3), 33.37 (***C***Me_3), 33.60 (***C***Me_3), 34.03 (Ar-***C***H_2-Ar), 34.14 (Ar-***C***H_2-Ar), 34.26 (Ar-***C***H_2-Ar), 34.37 (Ar-***C***H_2-Ar), 72.63 (O-***C***H_2-CO), 79.16 (O-***C***H_2-CH_2), 125.44, 125.46, 125.72, 125.76, 125.92 (***C***^{PH}-H), 126.16 (***C***^{PH}-*t*-Bu), 126.50, 126.99, 127.06 (***C***^{PH}-H), 127.17 (***C***^{PH}-*t*-Bu), 128.00 (***C***^{PH}-*t*-Bu), 129.16 (***C***^{PH}-*t*-Bu), 131.39, 132.55, 133.45, 134.41, 143.13, 143.47, 147.51, 147.88 (***C***^{PH}-CH_2), 148.22, 148.47 (***C***^{PH}-OH), 149.26, 150.20 (***C***^{PH}-O-CH_2-), 170.37 (***C***OOH).

Elementary Analysis : Found, %: C 78.03; H 8.87. Calculated $C_{49}H_{64}O_6$, %: C 78.57; H 8.61.

Synthesis of methyl esters of monopropoxy-p-tertbutylcalix[4]arene carboxilyc acids. To solution of acid **3.4a** or **3.4b** (0.50 g, 0.632 mmol) in methanol (5 mL), conc. H_2SO_4 (2–3 drops) was added and the mixture was

boiled for 1 h. The solution was cooled and white precipitate of methyl ester **3.5a** or **3.5b** was filtered off. Yield 76-80 %.

(cS)-5,11,17,23-Tetra-tert-butyl-25,26-dihydroxy-27-propoxy-28-methoxycarbonylmethoxycalix[4]arene **3.5a** or *(cR)-5,11,17,23-Tetra-tert-butyl-25,26-dihydroxy-27-methoxycarbonylmethoxy-28-propoxycalix[4]arene* **3.5b**. M.p. 173-174 ^{0}C.

$[\alpha]_D^{20}$ - 7.04 (c 1.197 g/100 mL, $CHCl_3$) for **5a,** + 6.83 (c 1.347 g/100 mL, $CHCl_3$) for **5b**. IR (KBr), ν, см$^{-1}$: 3370 (br) (OH...O=C), 1760 (C=O).

^{1}H NMR (δ (ppm), $CDCl_3$): 1.06 (s, 9H, t-Bu), 1.14 (t, 3H, $OCH_2CH_2C\boldsymbol{H_3}$, $J^3_{H\text{-}H}$ = 7.4 Hz), 1.16 (s, 9H, t-Bu), 1.18 (s, 9H, t-Bu), 1.29 (s, 9H, t-Bu), 2.01-2.15 (m, 2H, $OCH_2C\boldsymbol{H_2}CH_3$), 3.34 (d, 1H, Ar-C$\boldsymbol{H_2}$-eq, $J^2_{H\text{-}H}$ = 12.7 Hz), 3.35 (d, 1H, Ar-C$\boldsymbol{H_2}$-eq, $J^2_{H\text{-}H}$ = 13.9 Hz), 3.38 (d, 1H, Ar-C$\boldsymbol{H_2}$-eq, $J^2_{H\text{-}H}$ = 13.1 Hz), 3.40 (d, 1H, Ar-C$\boldsymbol{H_2}$-eq, $J^2_{H\text{-}H}$ = 13.4 Hz), 3.84-3.92 (m, 1H, $OC\boldsymbol{H_2}CH_2CH_3$), 3.85 (s, 3H, $OC\boldsymbol{H_3}$), 4.15-4.21 (m, 1H, $OC\boldsymbol{H_2}CH_2CH_3$), 4.24 (d, 1H, Ar-C$\boldsymbol{H_2}$-ax, $J^2_{H\text{-}H}$ = 13.4 Hz), 4.33 (d, 1H, Ar-C$\boldsymbol{H_2}$-ax, $J^2_{H\text{-}H}$ = 13.4 Hz), 4.58 (d, 1H, Ar-C$\boldsymbol{H_2}$-ax, $J^2_{H\text{-}H}$ = 12.9 Hz), 4.74 (d, 1H, Ar-C$\boldsymbol{H_2}$-ax, $J^2_{H\text{-}H}$ = 12.8 Hz), 4.80 (d, 1H, OC$\boldsymbol{H_2}$-C(O)OMe, $J^2_{H\text{-}H}$ = 15.1 Hz), 4.96 (d, 1H, OC$\boldsymbol{H_2}$-C(O)OMe, $J^2_{H\text{-}H}$ = 16.1 Hz), 6.83 (d, 1H, Ar-***H***, $J^4_{H\text{-}H}$ = 2.4 Hz), 6.88 (d, 1H, Ar-***H***, $J^4_{H\text{-}H}$ = 2.4 Hz), 6.93 (d, 1H, Ar-***H***, $J^4_{H\text{-}H}$ = 2.4 Hz), 6.97 (d, 1H, Ar-***H***, $J^4_{H\text{-}H}$ = 2.4 Hz), 7.01 (d, 1H, Ar-***H***, $J^4_{H\text{-}H}$ = 2.4 Hz), 7.03 (d, 1H, Ar-***H***, $J^4_{H\text{-}H}$ = 2.4 Hz), 7.06 (d, 1H, Ar-***H***, $J^4_{H\text{-}H}$ = 2.4 Hz), 7.07 (d, 1H, Ar-***H***, $J^4_{H\text{-}H}$ = 2.4 Hz), 8.66 (s, 1H, O***H***), 9.04 (s, 1H, O***H***).

^{13}C{^{1}H} NMR (δ (ppm), $CDCl_3$): 10.28 (-CH_2-***C***H_3), 23.05 (-***C***H_2-CH_3), 31.01 (***C***Me_3), 31.10 (-C(***C***H_3)$_3$), 31.12 (-C(***C***H_3)$_3$), 31.24 (-C(***C***H_3)$_3$), 31.42 (-C(***C***H_3)$_3$), 32.04 (***C***Me_3), 32.29 (***C***Me_3), 32.31 (***C***Me_3), 33.58 (Ar-***C***H_2-Ar), 33.70 (Ar-***C***H_2-Ar), 33.75 (Ar-***C***H_2-Ar), 33.83 (Ar-***C***H_2-Ar), 51.83 (O-***C***H_3), 71.67 (O-***C***H_2-CO), 77.81 (O-***C***H_2-CH_2), 124.56 (2C), 124.79, 125.13, 125.27, 125.52, 125.65, 125.88 (***C***^{PH}-H), 127.19 (***C***^{PH}-*t*-Bu), 127.54 (***C***^{PH}-*t*-Bu), 127.94 (***C***^{PH}-*t*-Bu), 128.53 (***C***^{PH}-*t*-Bu), 132.06, 132.96 (2C), 133.06, 141.76, 141.79,

145.93, 146.01, (***C***^{PH}-CH_2), 148.07, 148.84 (***C***^{PH}-OH), 150.20, 152.34 (***C***^{PH}-O-CH_2-), 170.83 (***C***OOH).

Elementary Analysis : Founded, %: C 78.83; H 8.56. Calculated $C_{50}H_{66}O_6$, %: C 78.70; H 8.72.

25,26-Dipropoxy-p-tert-butylcalix[4]arene **3.13** was obtained according to the literature [128].

Synthesis of amides of dipropoxycalix[4]arene carboxylic acids.

A mixture of 25,26-dipropoxycalix[4]arene **3.13** (0.50 g, 0.682 mmol) and $Ba(OH)_2$ (0.15 g, 0.875 mmol) in dry DMF (7 mL) was stirred at 40 ˚C for 30 min. After cooling to room temperature, the (S)- or (R)-form of N-(1-phenylethyl)bromoacetamide (0.2 g, 0.826 mmol) was added and the mixture was stirred at 20–25 ˚C for 24 h. Next, water (10 mL) and 30% HCl (1 mL) were added to the reaction mixture and products were extracted with $CHCl_3$ (3 x 5 mL). The organic phase was washed with water (5 mL), washed with brine (5 mL), and dried over Na_2SO_4. After removal of the solvent and double recrystallization from acetonitrile (9 and 4 mL, respectively), the enantiomerically pure compound **3.14a** or **3.14b** was obtained.

(cS)-5,11,17,23-Tetra-p-tert-butyl-27,28-dipropoxy-25-hydroxy-26-(S)-N-(10-phenylethyl-) aminocarbonylmethoxycalix[4]aren **3.14a**. R_f = 0.16. M.p. 107 ^{o}C (acetonitryl). IR (KBr): 3350 (OH...OAlk), 3530 (NH), 1680 (C=O).

$[\alpha]_D^{20}$ -9.22 (*c* = 0.015 M, $CHCl_3$).

^{1}H NMR (δ (ppm), $CDCl_3$): 0.58 (t, 3H, $OCH_2CH_2C\boldsymbol{H_3}$, $J^3_{H\text{-}H}$ = 7.8 Hz), 0.86 (s, 9H, t-Bu), 0.91 (s, 9H, t-Bu), 0.98 (t, 3H, $OCH_2CH_2C\boldsymbol{H_3}$, $J^3_{H\text{-}H}$ = 7.5 Hz), 1.27 (s, 9H, t-Bu), 1.32 (s, 9H, t-Bu), 1.55 (d, 3H, $CHC\boldsymbol{H_3}$, $J^3_{H\text{-}H}$ = 7.2 Hz), 1.73-1.91 (m, 4H, $OCH_2C\boldsymbol{H_2}CH_3$), 3.17 (d, 2H, Ar-$C\boldsymbol{H_2}$-eq, $J^2_{H\text{-}H}$ = 12.4 Hz), 3.22 (d, 1H, Ar-$C\boldsymbol{H_2}$-eq, $J^2_{H\text{-}H}$ = 12.9 Hz), 3.37 (d, 1H, Ar-$C\boldsymbol{H_2}$-eq, $J^2_{H\text{-}H}$ = 13.4

Hz), 3.71-3.91 (m, 4H, OC***H₂***CH_2CH_3), 4.08 (d, 1H, O-C***H₂***-CO, J^2_{H-H} = 16.0 Hz), 4.16 (d, 1H, Ar-C***H₂***-ax, J^2_{H-H} = 13.4 Hz), 4.31 (d, 1H, Ar-C***H₂***-ax, J^2_{H-H} = 12.9 Hz), 4.33 (d, 2H, Ar-C***H₂***-ax, J^2_{H-H} = 12.4 Hz), 4.73 (d, 1H, O-C***H₂***-CO, J^2_{H-H} = 16.0 Hz), 5.23-5.34 (m, 1H, C***H***), 5.75 (s, 1H, O***H***), 6.59 (d, 1H, Ar-***H***, J^4_{H-H} = 2.4 Hz), 6.61 (d, 1H, Ar-***H***, J^4_{H-H} = 2.4 Hz), 6.67 (d, 1H, Ar-***H***, J^4_{H-H} = 2.4 Hz), 6.71 (d, 1H, Ar-***H***, J^4_{H-H} = 2.4 Hz), 7.08 (s, 2H, Ar-***H***), 7.09 (d, 1H, Ar-***H***, J^4_{H-H} = 2.4 Hz), 7.11 (d, 1H, Ar-***H***, J^4_{H-H} = 2.4 Hz), 7.26-7.31 (m, 1H, Ar-***H***), 7.33-7.40 (m, 2H, Ar-***H***), 7.49 (d, 2H, Ar-***H***), 8.68 (d, 1H, N***H***, J^3_{H-H} = 7.5 Hz).

$^{13}C\{^1H\}$ NMR (δ (ppm), $CDCl_3$): 9.73 (-CH_2-***C***H_3), 10.68 (-CH_2-***C***H_3), 22.31 (CH-***C***H_3), 23.04 (-***C***H_2-CH_3), 23.37 (-***C***H_2-CH_3), 31.09, 31.11, 31.42, 31.45, 31.73, 31.79, 33.77 (Ar-***C***H_2-Ar), 33.88 (Ar-***C***H_2-Ar), 34.02 (Ar-***C***H_2-Ar), 34.19 (Ar-***C***H_2-Ar), 48.86 (***C***H-CH_3), 74.08 (O-***C***H_2-CO), 76.23 (O-***C***H_2-CH_2), 78.31 (O-***C***H_2-CH_2), 124.60, 124.67, 124.88, 125.26, 125.38, 125.40, 125.43, 125.53, 126.50, 126.97, 128.36, 128.93, 130.39, 131.14, 131.42, 132.32, 132.88, 135.10, 135.54, 142.52, 143.26, 145.38, 145.54, 146.12, 149.76 (***C***^{PH}-O-CH_2-), 150.08 (***C***^{PH}-O-CH_2-), 151.52 (***C***^{PH}-O-CH_2-), 153.17 (***C***^{PH}-OH), 168.99 (O-CH_2-***C***O).

Elementary Analysis : Founded, %: C 79.16; H 8.81; N 3.66. Calculated $C_{60}H_{79}NO_5$. CH_3CN , %: C 79.44; H 8.60; N 3.29.

(cR)-5,11,17,23-Tetra-p-tert-butyl-26,27-dipropoxy-25-hydroxy-28-(S)-N-(10-phenylethyl-)-aminocarbonylmethoxycalix[4]arene **3.14b**. R_f = 0.14. M.p. 103-104 °C (acetonitryl). IR (KBr): 3350 (OH...OAlk), 3530 (NH), 1680 (C=O).

$[\alpha]_D^{20}$ +9.49 (*c* =0.015 M, $CHCl_3$).

^1H NMR (δ (ppm), $CDCl_3$): 0.86 (s, 9H, t-Bu), 0.90 (s, 9H, t-Bu), 0.96 (t, 3H, OCH_2CH_2C***H₃***, J^3_{H-H} = 7.6 Hz), 1.11 (t, 3H, OCH_2CH_2C***H₃***, J^3_{H-H} = 7.5 Hz), 1.32 (s, 9H, t-Bu), 1.34 (s, 9H, t-Bu), 1.66 (d, 3H, CHC***H₃***, J^3_{H-H} = 7.1 Hz), 1.89-2.05 (m, 2H, OCH_2C***H₂***CH_3), 2.07-2.19 (m, 2H, OCH_2C***H₂***CH_3), 3.05 (d, 1H, Ar-C***H₂***-eq, J^2_{H-H} = 12.9 Hz), 3.22 (d, 1H, Ar-C***H₂***-eq, J^2_{H-H} = 12.4 Hz), 3.24 (d,

1H, Ar-C***H₂***-eq, $J^2_{H\text{-}H}$ = 12.4 Hz), 3.37 (d, 1H, Ar-C***H₂***-eq, $J^2_{H\text{-}H}$ = 13.4 Hz), 3.74-3.82 (m, 1H, OC***H₂***CH_2CH_3), 3.86-3.97 (m, 2H, OC***H₂***CH_2CH_3), 3.99-4.08 (m, 1H, OC***H₂***CH_2CH_3), 4.03 (d, 1H, O-C***H₂***-CO, $J^2_{H\text{-}H}$ = 16.0 Hz), 4.11 (d, 1H, Ar-C***H₂***-ax, $J^2_{H\text{-}H}$ = 12.9 Hz), 4.19 (d, 1H, Ar-C***H₂***-ax, $J^2_{H\text{-}H}$ = 13.4 Hz), 4.37 (d, 1H, Ar-C***H₂***-ax, $J^2_{H\text{-}H}$ = 12.4 Hz), 4.41 (d, 1H, Ar-C***H₂***-ax, $J^2_{H\text{-}H}$ = 12.4 Hz), 4.71 (d, 1H, O-C***H₂***-CO, $J^2_{H\text{-}H}$ = 16.0 Hz), 5.26-6.35 (m, 1H, C***H***), 5.68 (s, 1H, O***H***), 6.57 (d, 1H, Ar-***H***, $J^4_{H\text{-}H}$ = 2.4 Hz), 6.60 (d, 1H, Ar-***H***, $J^4_{H\text{-}H}$ = 2.4 Hz), 6.64 (d, 1H, Ar-***H***, $J^4_{H\text{-}H}$ = 2.4 Hz), 6.71 (d, 1H, Ar-***H***, $J^4_{H\text{-}H}$ = 2.4 Hz), 7.03 (d, 1H, Ar-***H***, $J^4_{H\text{-}H}$ = 2.4 Hz), 7.04-7.10 (m, 4H, Ar-***H***), 7.13 (d, 1H, Ar-***H***, $J^4_{H\text{-}H}$ = 2.4 Hz), 7.14 (d, 1H, Ar-***H***, $J^4_{H\text{-}H}$ = 2.4 Hz), 7.32-7.36 (m, 2H, Ar-***H***), 8.81 (d, 1H, N***H***, $J^3_{H\text{-}H}$ = 8.5 Hz).

(cR)-5,11,17,23-Tetra-p-tert-butyl-26,27-dipropoxy-25-hydroxy-28-carboxymethoxy-calix[4]arene **3.15a** or *(cS)-5,11,17,23-Tetra-p-tert-butyl-26,27-dipropoxy-25-hydroxy-28-carboxymethoxy-calix[4]arene* **3.15b**. M.p. 116-117 °C (acetonitryl). IR (KBr): 3530 (OH), 3320 (COOH), 1740 i 1760 (br, C=O); (CH_2Cl_2): 3690 (COOH), 3270 (CHOH), 1750 (C=O).

^{1}H NMR (δ (ppm), $CDCl_3$): 0.98 (s, 9H, t-Bu), 0.99 (t, 3H, OCH_2CH_2C***H₃***, $J^3_{H\text{-}H}$ = 7.3 Hz), 1.07 (t, 3H, OCH_2CH_2C***H₃***, $J^3_{H\text{-}H}$ = 7.4 Hz), 1.16 (s, 18H, t-Bu), 1.18 (s, 9H, t-Bu), 1.87-2.00 (m, 2H, OCH_2C***H₂***CH_3), 2.01-2.14 (m, 2H, OCH_2C***H₂***CH_3), 3.25 (d, 1H, Ar-C***H₂***-eq, $J^2_{H\text{-}H}$ = 13.2 Hz), 3.30 (d, 2H, Ar-C***H₂***-eq, $J^2_{H\text{-}H}$ = 12.5 Hz), 3.38 (d, 1H, Ar-C***H₂***-eq, $J^2_{H\text{-}H}$ = 13.4 Hz), 3.76-3.93 (m, 3H, OC***H₂***CH_2CH_3), 4.12 -4.20 (m, 1H, OC***H₂***CH_2CH_3), 4.13 (d, 1H, Ar-C***H₂***-ax, $J^2_{H\text{-}H}$ = 13.4 Hz), 4.20 (d, 1H, Ar-C***H₂***-ax, $J^2_{H\text{-}H}$ = 13.2 Hz), 4.31 (d, 1H, Ar-C***H₂***-ax, $J^2_{H\text{-}H}$ = 12.5 Hz), 4.44 (d, 1H, Ar-C***H₂***-ax, $J^2_{H\text{-}H}$ = 12.5 Hz), 4.50 (d, 1H, O-C***H₂***-CO, $J^2_{H\text{-}H}$ = 15.8 Hz), 4.76 (d, 1H, O-C***H₂***-CO, $J^2_{H\text{-}H}$ = 15.8 Hz), 6.80 (dd, 2H, Ar-***H***), 6.90 (d, 1H, Ar-***H***, $J^4_{H\text{-}H}$ = 2.4 Hz), 6.96-6.98 (m, 3H, Ar-***H***), 7.03 (d, 1H, Ar-***H***, $J^4_{H\text{-}H}$ = 2.4 Hz), 7.11 (d, 1H, Ar-***H***, $J^4_{H\text{-}H}$ = 2.4 Hz), 8.27 (s, 1H, O***H***), 11.78-12.10 (s, 1H, COO***H***).

$^{13}C\{^1H\}$ NMR (δ (ppm), $CDCl_3$): 10.34 (-CH_2-***C***H_3), 10.36 (-CH_2-***C***H_3), 22.98 (-***C***H_2-CH_3), 23.30 (-***C***H_2-CH_3), 30.74 (***C***Me_3), 31.26 (-C(***C***$H_3)_3$), 31.41 (-C(***C***$H_3)_3$), 31.46 (-C(***C***$H_3)_3$), 31.54 (-C(***C***$H_3)_3$), 31.66 (***C***Me_3), 32.60 (***C***Me_3), 33.13 (***C***Me_3), 33.92 (Ar-***C***H_2-Ar), 33.98 (Ar-***C***H_2-Ar), 34.14 (Ar-***C***H_2-Ar), 34.22 (Ar-***C***H_2-Ar), 71.40 (O-***C***H_2-CO), 76.94 (O-***C***H_2-CH_2), 78.83 (O-***C***H_2-CH_2), 124.87, 125.33 (***C***^{PH}-*t*-Bu), 125.35 (***C***^{PH}-*t*-Bu), 125.36 (***C***^{PH}-*t*-Bu), 125.38 (***C***^{PH}-*t*-Bu), 125.49, 125.97, 126.40, 128.22, 129.01, 132.67, 132.77, 132.93, 133.20, 134.45, 134.48, 142.46, 145.48, 146.83, 146.96, 148.73 (***C***^{PH}-OH), 150.68 (***C***^{PH}-O-CH_2-), 150.94 (***C***^{PH}-O-CH_2-), 151.46 (***C***^{PH}-O-CH_2-), 170.65 (***C***OOH).

Elementary Analysis : Founded, %: C 79.03; H 8.87. Calculated $C_{52}H_{70}O_6$, %: C 78.95; H 8.92.

Synthesis of methyl esters of dipropoxycalix[4]arene carboxylic acids. To a solution of acid **3.15a** or **3.15b** (0.50 g, 0.632 mmol) in methanol (5 mL) conc. H_2SO_4 (2–3 drops) was added and the mixture was boiled for 1 h. The solvent was evaporated in vacuo and the product was crystallized from acetonitrile (5 mL)., Yield 80-82 %.

(cS)-5,11,17,23-Tetra-p-tert-butyl-27,28-dipropoxy-25-hydroxy-26-methoxycarbonylmethoxy-calix[4]arene ***3.16*****a** or *(cR)-5,11,17,23-Tetra-p-tert-butyl-27,28-dipropoxy-25-hydroxy-26-methoxycarbonylmethoxy-calix[4]arene* **3.16b**. M.p. 73-74 ^{0}C (acetonitryl). IR (KBr), ν, см$^{-1}$: 3530 (OH...O=C), 1755 (br) (C=O).

^1H NMR (δ (ppm), $CDCl_3$): 0.76 (s, 9H, t-Bu), 0.88 (s, 9H, t-Bu), 0.95 (t, 3H, OCH_2CH_2C***H₃***, $J^3_{H\text{-}H}$ = 7.3 Hz), 1.08 (t, 3H, OCH_2CH_2C***H₃***, $J^3_{H\text{-}H}$ = 7.3 Hz), 1.30 (s, 9H, t-Bu), 1.31 (s, 9H, t-Bu), 1.83-2.03 (m, 2H, -C***H₂***-), 2.13-2.25 (m, 1H, -C***H₂***-), 2.25-2.38 (m, 1H, -C***H₂***-), 2.80 (d, 1H, Ar-C***H₂***-eq, $J^2_{H\text{-}H}$ = 12.4 Hz), 2.81 (d, 1H, Ar-C***H₂***-eq, $J^2_{H\text{-}H}$ = 13.0 Hz), 2.85 (d, 1H, Ar-C***H₂***-eq, $J^2_{H\text{-}H}$ = 13.3

Hz), 2.90 (d, 1H, Ar-C***H₂***-eq, $J^2_{H\text{-}H}$ = 13.3 Hz), 3.33-3.48 (m, 2H, OC***H₂***), 3.42 (s, 3H, OC***H₃***), 3.51 (t, 2H, OC***H₂***, $J^3_{H\text{-}H}$ = 8.3 Hz), 3.85 (d, 1H, Ar-C***H₂***-ax, $J^2_{H\text{-}H}$ = 13.3 Hz), 3.98 (d, 1H, Ar-C***H₂***-ax, $J^2_{H\text{-}H}$ = 12.4 Hz), 4.07 (d, 1H, Ar-C***H₂***-ax, $J^2_{H\text{-}H}$ = 13.0 Hz), 4.08 (d, 1H, OC***H₂***-C(O)OMe, $J^2_{H\text{-}H}$ = 15.5 Hz), 4.16 (d, 1H, Ar-C***H₂***-ax, $J^2_{H\text{-}H}$ = 13.3 Hz), 4.19 (d, 1H, OC***H₂***-C(O)OMe, $J^2_{H\text{-}H}$ = 15.5 Hz), 5.67 (s, 1H, O***H***), 6.08 (s, 2H, Ar-***H***), 6.23 (d, 2H, Ar-***H***, $J^4_{H\text{-}H}$ = 2.0 Hz), 6.26 (d, 2H, Ar-***H***, $J^4_{H\text{-}H}$ = 2.0 Hz), 6.64 (d, 2H, Ar-***H***, $J^4_{H\text{-}H}$ = 2.0 Hz), 6.69 (d, 2H, Ar-***H***, $J^4_{H\text{-}H}$ = 2.0 Hz), 6.74 (dd, 2H, Ar-***H***).

Reduction of compounds 3.4a, 3.15 or 3.5a, 3.16. In the flask under argon atmosphere solution of lithium aluminum hydride $LiAlH_4$ (0.40 g, 10.5 mmol) in absolute diethyl ether (50 mL) was prepared. The mixture was stirred at room temperature for 0.5 h, cooled to 0˚C and small portions of acid (2.3 mmol) was added. Resulting mixture was stirred another 1 hour at room temperature. The reaction was monitored by TLC. After completion of the reaction, 5 ml of ethyl acetate was added dropwise and the mixture was stirred for 15-20 min. Then, 10 ml of methanol, 25 ml of water and 25 ml of H_2SO_4 (10%) was added in corresponding order. Ether solution was separated, washed twice with 25 ml of distilled water, saturated aqueous sodium chloride, dried over Na_2SO_4 and evaporated to give product with nearly quantitative yield and 95% purity (according to ^{1}H NMR) which was used without further purification for further synthesis. For a complete purification products were recrystallized from acetonitrile.

25-Hydroxyethyloxy-26-propyloxy-tetra-p-tert.-butyl-calix[4]arene **3.6**.

Yield 98%, M.p. 85-89 ^{0}C (acetonitrile), $[\alpha]_D^{20}$ +24.04 (*c* 0.020 M, $CHCl_3$).

^{1}H NMR (δ (ppm), $CDCl_3$): 1.16 (t, 3H, OCH_2CH_2C***H₃***, $J^3_{H\text{-}H}$ = 7.4 Hz), 1.17 (s, 9H, t-Bu), 1.20 (s, 9H, t-Bu), 1.23 (s, 9H, t-Bu), 1.31 (s, 9H, t-Bu), 2.08-2.25 (m, 2H, OCH_2C***H₂***CH_3), 3.37 (d, 1H, Ar-C***H₂***-eq, $J^2_{H\text{-}H}$ = 12.8 Hz), 3.43 (d,

1H, Ar-C***H₂***-eq, $J^2_{H\text{-}H}$ = 11.7 Hz), 3.44 (d, 1H, Ar-C***H₂***-eq, $J^2_{H\text{-}H}$ = 14.0 Hz), 3.45 (d, 1H, Ar-C***H₂***-eq, $J^2_{H\text{-}H}$ = 13.8 Hz), 3.86-3.94 (m, 1H, OC***H₂***CH_2CH_3), 3.95-4.01 (m, 1H, OCH_2C***H₂***OH), 4.02-4.08 (m, 1H, OC***H₂***CH_2CH_3), 4.19 (d, 1H, Ar-C***H₂***-ax, $J^2_{H\text{-}H}$ = 13.8 Hz), 4.18-4.30 (m, 1H, OCH_2C***H₂***OH, 2H, OC***H₂***CH_2OH), 4.30 (d, 1H, Ar-C***H₂***-ax, $J^2_{H\text{-}H}$ = 13.7 Hz), 4.50 (d, 1H, Ar-C***H₂***-ax, $J^2_{H\text{-}H}$ = 12.4 Hz), 4.60 (d, 1H, Ar-C***H₂***-ax, $J^2_{H\text{-}H}$ = 12.8 Hz), 5.23-5.21 (s, br, 1H, OCH_2CH_2O***H***) 6.94 (d, 1H, Ar-***H***, $J^4_{H\text{-}H}$ = 2.4 Hz), 6.96 (d, 1H, Ar-***H***, $J^4_{H\text{-}H}$ = 2.4 Hz), 7.08 (d, 1H, Ar-***H***, $J^4_{H\text{-}H}$ = 2.4 Hz), 7.09-7.11 (m, 2H, Ar-***H***), 7.12 (d, 1H, Ar-***H***, $J^4_{H\text{-}H}$ = 2.4 Hz), 7.13-7.15 (m, 2H, Ar-***H***), 9.24 (s, 1H, O***H***), 9.66 (s, 1H, O***H***).

$^{13}C\{^1H\}$ NMR (δ (ppm), $CDCl_3$): 10.38 (-CH_2-***C***H_3), 23.15 (-***C***H_2-CH_3), 30.62 (***C***Me_3), 31.22 (-C(***C***$H_3)_3$), 31.36 (-C(***C***$H_3)_3$), 31.61 (-C(***C***$H_3)_3$), 31.46 (-C(***C***$H_3)_3$), 32.73 (***C***Me_3), 32.95 (***C***Me_3), 33.18 (***C***Me_3), 33.90 (Ar-***C***H_2-Ar), 34.97 (Ar-***C***H_2-Ar), 34.12 (Ar-***C***H_2-Ar), 34.13 (Ar-***C***H_2-Ar), 62.24 (HO-***C***H_2-CH2-OPH), 77.22 (PHO-***C***H_2-CH_2-OH), 78.67 (O-***C***H_2-CH_2), 124.97 (***C***H^{PH}), 125.46 (***C***H^{PH}), 125.46 (***C***H^{PH}), 125.60 (***C***H^{PH}), 125.80 (***C***H^{PH}), 126.08 (***C***H^{PH}), 126.46 (***C***H^{PH}), 126.59 (***C***H^{PH}), 126.94 (***C***^{Ar}-CH_2-C^{Ar}), 126.95 (***C***^{Ar}-CH_2-C^{Ar}), 127.97 (***C***^{Ar}-CH_2-C^{Ar}), 128.08 (***C***^{Ar}-CH_2-C^{Ar}), 130.11 (***C***^{Ar}-CH_2-C^{Ar}), 131.70 (***C***^{Ar}-CH_2-C^{Ar}), 133.87 (***C***^{Ar}-CH_2-C^{Ar}), 134.04 (***C***^{Ar}-CH_2-C^{Ar}), 142.70 (***C***^{PH}-*t*-Bu), 142.95 (***C***^{PH}-*t*-Bu), 146.61 (***C***^{PH}-*t*-Bu), 147.16 (***C***^{PH}-*t*-Bu), 148.28 (***C***^{PH}-OH), 148.94 (***C***^{PH}-OH), 150.15 (***C***^{PH}-O-CH_2-), 151.21 (***C***^{PH}-O-CH_2-).

Elementary Analysis : Founded, %: C 79.93; H 9.27. Calculated $C_{49}H_{68}O_5$, %: C 79.85; H 9.30.

25-Hydroxyethyloxy-26,27-dipropyloxy-tetra-p-tert.-butyl-calix[4]arene **3.17**.

Yield 88%, M.p. 93-95 ^{0}C (acetonitryl), $[\alpha]_D^{20}$ -3.11 (*c* 0.022 M, $CHCl_3$).

^1H NMR (δ (ppm), $CDCl_3$): 0.97 (s, 9H, t-Bu), 1.01 (t, 3H, OCH_2CH_2C***H₃***, $J^3_{H\text{-}H}$ = 7.8 Hz), 1.06 (t, 3H, OCH_2CH_2C***H₃***, $J^3_{H\text{-}H}$ = 7.8 Hz), 1.09 (s, 9H, t-Bu),

1.13 (s, 9H, t-Bu), 1.16 (s, 9H, t-Bu), 1.99-2.14 (m, 4H, $OCH_2C\boldsymbol{H_2}CH_3$), 3.18 (d, 1H, Ar-C$\boldsymbol{H_2}$-eq, $J^2_{H\text{-}H}$ = 13.1 Hz), 3.21 (d, 1H, Ar-C$\boldsymbol{H_2}$-eq, $J^2_{H\text{-}H}$ = 12.6 Hz), 3.23 (d, 1H, Ar-C$\boldsymbol{H_2}$-eq, $J^2_{H\text{-}H}$ = 13.7 Hz), 3.28 (d, 1H, Ar-C$\boldsymbol{H_2}$-eq, $J^2_{H\text{-}H}$ = 13.5 Hz), 3.78-3.92 (m, 3H, $OC\boldsymbol{H_2}CH_2CH_3$), 3.97-4.16 (m, 5H, $OCH_2C\boldsymbol{H_2}OH$, $OC\boldsymbol{H_2}CH_2CH_3$), 4.27 (d, 1H, Ar-C$\boldsymbol{H_2}$-ax, $J^2_{H\text{-}H}$ = 13.4 Hz), 4.39 (d, 1H, Ar-C$\boldsymbol{H_2}$-ax, $J^2_{H\text{-}H}$ = 12.4 Hz), 4.43 (d, 1H, Ar-C$\boldsymbol{H_2}$-ax, $J^2_{H\text{-}H}$ = 12.4 Hz), 4.46 (d, 1H, Ar-C$\boldsymbol{H_2}$-ax, $J^2_{H\text{-}H}$ = 12.6 Hz), 6.72 – 6.77 (m, 3H, Ar-***H***), 6.85-6.90 (m, 4H, Ar-***H***, O***H***), 6.92-6.95 (m, 2H, Ar-***H***).

$^{13}C\{^1H\}$ NMR (δ (ppm), $CDCl_3$): 10.10 (-CH_2-***C***H_3), 10.39 (-CH_2-***C***H_3), 22.89 (-***C***H_2-CH_3), 23.09 (-***C***H_2-CH_3), 30.92 (***C***Me_3), 31.08 (***C***Me_3), 31.31 (-C(***C***$H_3)_3$), 31.38 (-C(***C***$H_3)_3$), 31.40 (-C(***C***$H_3)_3$), 34.54 (-C(***C***$H_3)_3$), 31.54 (***C***Me_3), 32.39 (***C***Me_3), 33.82 (Ar-***C***H_2-Ar), 33.88 (Ar-***C***H_2-Ar), 33.95 (Ar-***C***H_2-Ar), 33.99 (Ar-***C***H_2-Ar), 62.25 (HO-***C***H_2-CH_2-OPH), 76.64 (HO-CH_2-***C***H_2-OPH), 77.32 (CH_3-CH_2-***C***H_2-OPH), 78.26 (CH_3-CH_2-***C***H_2-OPH), 124.33 (***C***H^{PH}), 124.95 (***C***H^{PH}), 124.95 (***C***H^{PH}), 125.11 (***C***H^{PH}), 125.26 (***C***H^{PH}), 125.45 (***C***H^{PH}), 125.60 (***C***H^{PH}), 125.84 (***C***H^{PH}), 129.87 (***C***^{Ar}-CH_2-C^{Ar}), 130.65 (***C***^{Ar}-CH_2-C^{Ar}), 133.32 (***C***^{Ar}-CH_2-C^{Ar}), 133.52 (***C***^{Ar}-CH_2-C^{Ar}), 133.75 (***C***^{Ar}-CH_2-C^{Ar}), 133.87 (***C***^{Ar}-CH_2-C^{Ar}), 133.98 (***C***^{Ar}-CH_2-C^{Ar}), 134.12 (***C***^{Ar}-CH_2-C^{Ar}), 142.46 (***C***^{PH}-*t*-Bu), 145.14 (***C***^{PH}-*t*-Bu), 145.63 (***C***^{PH}-*t*-Bu), 146.10 (***C***^{PH}-*t*-Bu), 148.73 (***C***^{PH}-OH), 151.69 (***C***^{PH}-O-CH_2-), 152.23 (***C***^{PH}-O-CH_2-), 152.32 (***C***^{PH}-O-CH_2-).

Elementary Analysis : Founded, %: C 80.03; H 9.17. Calculated $C_{52}H_{74}O_5$, %: C 80.16; H 9.57.

The solution of alcohol **3.6** or **3.17** (0.8 mmol) and triphenylphosphine (0.66 g, 2.5 mmol) was refluxed for 5 h in a mixture of carbon tetrachloride (4 ml) and THF (15 mL). Reaction was monitored using TLC. After completion of the reaction, mixture was diluted with THF, filtered through celite, obtained solution was evaporated, product was purified by flash-chromatography on

silica, using EtOAc/Hexanes = 1/3 mixture as eluent to obtain product as white solid.

25-Chloroethoxy-26-propyloxy-tetra-p-tert.-butyl-calix[4]arene **3.7**. Yield 84%, M.p. 89 ^{0}C (acetonitryl), $[\alpha]_D^{20}$ +39.22 (*c* 0.018 M, $CHCl_3$).

^{1}H NMR (δ (ppm), $CDCl_3$): 0.99 (s, 9H, t-Bu), 1.06 (t, 3H, $OCH_2CH_2C\boldsymbol{H_3}$, $J^3_{H\text{-}H}$ = 7.4 Hz), 1.17 (s, 9H, t-Bu), 1.21 (s, 18H, t-Bu), 1.98-2.22 (m, 2H, $OCH_2C\boldsymbol{H_2}CH_3$), 3.32 (d, 1H, Ar-C$\boldsymbol{H_2}$-eq, $J^2_{H\text{-}H}$ = 12.8 Hz), 3.35 (d, 1H, Ar-C$\boldsymbol{H_2}$-eq, $J^2_{H\text{-}H}$ = 14.0 Hz), 3.41 (d, 1H, Ar-C$\boldsymbol{H_2}$-eq, $J^2_{H\text{-}H}$ = 14.4 Hz), 3.46 (d, 1H, Ar-C$\boldsymbol{H_2}$-eq, $J^2_{H\text{-}H}$ = 14.2 Hz), 3.52-3.63 (m, 1H, $OCH_2C\boldsymbol{H_2}Cl$), 3.68-3.80 (m, 1H, $OC\boldsymbol{H_2}CH_2CH_3$), 3.80-3.90 (m, 1H, $OC\boldsymbol{H_2}CH_2CH_3$), 4.07-4.17 (m, 5H, 1H $OCH_2C\boldsymbol{H_2}Cl$, 2H $OC\boldsymbol{H_2}CH_2Cl$, 2H Ar-C$\boldsymbol{H_2}$-ax,), 4.40 (d, 1H, Ar-C$\boldsymbol{H_2}$-ax, $J^2_{H\text{-}H}$ = 13.2 Hz), 4.50 (d, 1H, Ar-C$\boldsymbol{H_2}$-ax, $J^2_{H\text{-}H}$ = 12.6 Hz), 6.86 (s, 2H, Ar-***H***), 6.94 (d, 1H, Ar-***H***, $J^4_{H\text{-}H}$ = 2.4 Hz), 6.99 (d, 2H, Ar-***H***, $J^4_{H\text{-}H}$ = 2.0 Hz), 7.03 (m, 2H, Ar-***H***), 7.09 (d, 1H, Ar-***H***, $J^4_{H\text{-}H}$ = 2.4 Hz), 8.31 (s, 1H, O***H***), 8.94 (s, 1H, O***H***).

^{13}C{^{1}H} NMR (δ (ppm), $CDCl_3$): 10.49 (-CH_2-***C***H_3), 23.32 (-***C***H_2-CH_3), 30.84 (***C***Me_3), 31.30 (-C(***C***$H_3)_3$), 31.44 (-C(***C***$H_3)_3$), 31.70 (-C(***C***$H_3)_3$), 31.62 (-C(***C***$H_3)_3$), 32.65 (***C***Me_3), 32.72 (***C***Me_3), 33.77 (***C***Me_3), 33.97 (Ar-***C***H_2-Ar), 34.04 (Ar-***C***H_2-Ar), 34.07 (Ar-***C***H_2-Ar), 34.27 (Ar-***C***H_2-Ar),41.87 (HO-***C***H_2-CH2-OPH), 74.70 (PHO-***C***H_2-CH_2-OH), 78.14 (O-***C***H_2-CH_2), 124.83 (***C***H^{PH}), 125.08 (***C***H^{PH}), 125.19 (***C***H^{PH}), 125.27 (***C***H^{PH}), 125.47 (***C***H^{PH}), 125.67 (***C***H^{PH}), 126.63 (***C***H^{PH}), 126.75 (***C***H^{PH}), 127.88 (***C***^{Ar}-CH_2-C^{Ar}), 127.33 (***C***^{Ar}-CH_2-C^{Ar}), 128.56 (***C***^{Ar}-CH_2-C^{Ar}), 129.57 (***C***^{Ar}-CH_2-C^{Ar}), 132.18 (***C***^{Ar}-CH_2-C^{Ar}), 133.01 (***C***^{Ar}-CH_2-C^{Ar}), 133.03 (***C***^{Ar}-CH_2-C^{Ar}), 134.61 (***C***^{Ar}-CH_2-C^{Ar}), 141.96 (***C***^{PH}-*t*-Bu), 142.91 (***C***^{PH}-*t*-Bu), 145.90 (***C***^{PH}-*t*-Bu), 147.09 (***C***^{PH}-*t*-Bu), 148.13 (***C***^{PH}-OH), 149.69 (***C***^{PH}-OH), 150.92 (***C***^{PH}-O-CH_2-), 151.27 (***C***^{PH}-O-CH_2-).

Elementary Analysis : Founded, %: C 78.03; H 8.87. Calculated $C_{49}H_{67}ClO_4$, %: C 77.90; H 8.94.

25- Chloroethoxy -26,27- dipropyloxy-tetra-p-tert.-butyl-calix[4]arene **3.18**.

Yield 77%, m.p. 162-164 ^{0}C (acetonitrile), $[\alpha]_D^{20}$ -2.17 (*c* 0.021 M, $CHCl_3$).

^{1}H NMR (δ (ppm), $CDCl_3$): 0.82 (s, 9H, t-Bu), 0.91 (s, 9H, t-Bu), 1.01 (t, 3H, $OCH_2CH_2C\boldsymbol{H_3}$, $J^3_{H\text{-}H}$ = 7.4 Hz), 1.13 (t, 3H, $OCH_2CH_2C\boldsymbol{H_3}$, $J^3_{H\text{-}H}$ = 7.4 Hz), 1.35 (s, 9H, t-Bu), 1.36 (s, 9H, t-Bu), 1.86-2.06 (m, 2H, $OCH_2C\boldsymbol{H_2}CH_3$), 2.22-2.44 (m, 2H, $OCH_2C\boldsymbol{H_2}CH_3$), 3.21 (d, 2H, Ar-C$\boldsymbol{H_2}$-eq, $J^2_{H\text{-}H}$ = 12.9 Hz), 3.24 (d, 1H, Ar-C$\boldsymbol{H_2}$-eq, $J^2_{H\text{-}H}$ = 13.2 Hz), 3.31 (d, 1H, Ar-C$\boldsymbol{H_2}$-eq, $J^2_{H\text{-}H}$ = 13.6 Hz), 3.75-3.94 (m, 4H, $OC\boldsymbol{H_2}CH_2CH_3$), 4.00-4.08 (m, 1H, $OCH_2C\boldsymbol{H_2}Cl$), 4.15-4.21 (m, 1H, $OCH_2C\boldsymbol{H_2}Cl$), 4.27 (d, 1H, Ar-C$\boldsymbol{H_2}$-ax, $J^2_{H\text{-}H}$ = 13.4 Hz), 4.38 (d, 1H, Ar-C$\boldsymbol{H_2}$-ax, $J^2_{H\text{-}H}$ = 12.6 Hz), 4.43 (d, 1H, Ar-C$\boldsymbol{H_2}$-ax, $J^2_{H\text{-}H}$ = 12.8 Hz), 4.48 (d, 1H, Ar-C$\boldsymbol{H_2}$-ax, $J^2_{H\text{-}H}$ = 12.6 Hz), 5.53 (c, O***H***), 6.50 (c, 2H, Ar-***H***), 6.62 (d, 1H, Ar-***H***, $J^3_{H\text{-}H}$ = 2.8 Hz), 6.64 (d, 1H, Ar-***H***, $J^3_{H\text{-}H}$ = 2.8 Hz), 7.06 (d, 1H, Ar-***H***, $J^3_{H\text{-}H}$ = 2.8 Hz), 7.09 (d, 1H, Ar-***H***, $J^3_{H\text{-}H}$ = 2.8 Hz), 7.15 (dd, 2H, Ar-***H***, $J^3_{H\text{-}H}$ = 2.6 Hz).

^{13}C{^{1}H} NMR (δ (ppm), $CDCl_3$): 9.82 (-CH_2-***C***H_3), 10.81 (-CH_2-***C***H_3), 22.69 (-***C***H_2-CH_3), 23.42 (-***C***H_2-CH_3), 31.04 (***C***Me_3), 31.21 (***C***Me_3), 31.09 (-C(***C***$H_3)_3$), 31.12 (-C(***C***$H_3)_3$), 31.29 (***C***Me_3), 31.72 (-C(***C***$H_3)_3$), 31.74 (***C***Me_3), 31.80 (-C(***C***$H_3)_3$), 33.68 (Ar-***C***H_2-Ar), 33.79 (Ar-***C***H_2-Ar), 33.90 (Ar-***C***H_2-Ar), 34.16 (Ar-***C***H_2-Ar), 42.53 (HO-***C***H_2-CH_2-OPH), 75.07 (HO-CH_2-***C***H_2-OPH), 76.39 (CH_3-CH_2-***C***H_2-OPH), 78.17 (CH_3-CH_2-***C***H_2-OPH), 124.63 (***C***H^{PH}), 124.71 (***C***H^{PH}), 124.73 (***C***H^{PH}), 125.00 (***C***H^{PH}), 125.03 (***C***H^{PH}), 125.20 (***C***H^{PH}), 125.55 (***C***H^{PH}), 125.67 (***C***H^{PH}), 128.92 (***C***^{Ar}-CH_2-C^{Ar}), 130.03 (***C***^{Ar}-CH_2-C^{Ar}), 131.53 (***C***^{Ar}-CH_2-C^{Ar}), 132.00 (***C***^{Ar}-CH_2-C^{Ar}), 132.01 (***C***^{Ar}-CH_2-C^{Ar}), 132.57 (***C***^{Ar}-CH_2-C^{Ar}), 135.61 (***C***^{Ar}-CH_2-C^{Ar}), 135.92 (***C***^{Ar}-CH_2-C^{Ar}), 141.60 (***C***^{PH}-*t*-Bu), 145.18 (***C***^{PH}-*t*-Bu), 145.51 (***C***^{PH}-*t*-Bu), 145.55 (***C***^{PH}-*t*-Bu), 150.45 (***C***^{PH}-OH), 151.01 (***C***^{PH}-O-CH_2-), 151.41 (***C***^{PH}-O-CH_2-), 153.79 (***C***^{PH}-O-CH_2-).

Elementary Analysis : Founded, %: C 78.79; H 9.17; Cl 4.92. Calculated $C_{52}H_{73}ClO_4$, %: C 78.31; H 9.23; Cl 4.44.

The reaction of calix[4]arene 3.7 with three isopropyl phosphite. In the flask in an atmosphere of dry argon, dissolved 0.1 g (0.00013 mol) of chloride **3.7** in 2 mL of tryisopropylphosphite. The mixture was boiled overnight. Control of reaction was carried out by TLC. After the solvent completely removed from the reaction mixture, and the resulting solid residue was purified by column chromatography with chloroform as eluent. After evaporation of the solvent white solid was obtained.

25-phosphoethoxy-26-propyloxy-27,28-diphosphoxy-tetra-p-tert.-butyl-calix[4]arene **3.11**.

Yield 80%, M.p. 280^{0}C (acetonitryl), $[\alpha]_D^{20}$ +6.76 (*c* 0.022 M, $CHCl_3$).

^{1}H NMR (δ (ppm), $CDCl_3$): 0.58 (s, 9H, t-Bu), 1.00 (s, 9H, t-Bu), 1.11 (t, 3H, $OCH_2CH_2C\boldsymbol{H_3}$, $J^3_{H\text{-}H}$ = 7.4 Hz), 1.34 (s, 9H, t-Bu), 1.36 (s, 9H, t-Bu), 1.80-1.96 (m, 2H, $OCH_2C\boldsymbol{H_2}CH_3$), 2.50-2.71 (m, 1H, $OCH_2C\boldsymbol{H_2}PO$), 3.19 (d, 1H, Ar-$C\boldsymbol{H_2}$-eq, $J^2_{H\text{-}H}$ = 13.4 Hz), 3.24 (d, 1H, Ar-$C\boldsymbol{H_2}$-eq, $J^2_{H\text{-}H}$ = 13.4 Hz), 3.36 (d, 1H, Ar-$C\boldsymbol{H_2}$-eq, $J^2_{H\text{-}H}$ = 14.0 Hz), 3.48 (d, 1H, Ar-$C\boldsymbol{H_2}$-eq, $J^2_{H\text{-}H}$ = 15.0 Hz), 3.68-3.89 (m, 3H, 2H $OC\boldsymbol{H_2}CH_2CH_3$, 1H $OC\boldsymbol{H_2}CH_2PO$), 4.21 (m, 1H, $OCH_2C\boldsymbol{H_2}PO$, $J^3_{P\text{-}H}$ = 37.7 Hz), 4.30-4.40 (m, 1H, $OC\boldsymbol{H_2}CH_2PO$), 4.35 (d, 1H, Ar-$C\boldsymbol{H_2}$-ax, $J^2_{H\text{-}H}$ = 13.8 Hz), 4.39 (d, 1H, Ar-$C\boldsymbol{H_2}$-ax, $J^2_{H\text{-}H}$ = 13.8 Hz), 4.49 (d, 1H, Ar-$C\boldsymbol{H_2}$-ax, $J^2_{H\text{-}H}$ = 13.8 Hz), 4.70 (d, 1H, Ar-$C\boldsymbol{H_2}$-ax, $J^2_{H\text{-}H}$ = 14.9 Hz), 6.15 (d, 1H, Ar-***H***, $J^4_{H\text{-}H}$ = 2.2 Hz), 6.26 (d, 1H, Ar-***H***, $J^4_{H\text{-}H}$ = 2.0 Hz), 6.75 (d, 1H, Ar-***H***), 6.76 (s, 1H, Ar-***H***), 7.12 (d, 1H, Ar-***H***, $J^4_{H\text{-}H}$ = 2.0 Hz), 7.20 (m, 2H, Ar-***H***), 7.22 (s, 1H, Ar-***H***),

^{13}C{^{1}H} NMR (δ (ppm), $CDCl_3$): 11.13 (-CH_2-$\boldsymbol{C}H_3$), 23.60 (-$\boldsymbol{C}H_2$-CH_3), 29.70 ($\boldsymbol{C}Me_3$), 29.70 ($\boldsymbol{C}Me_3$), 30.89 (-C($\boldsymbol{C}H_3$)$_3$), 31.07 (-C($\boldsymbol{C}H_3$)$_3$), 31.55 (-C($\boldsymbol{C}H_3$)$_3$), 31.62 (-C($\boldsymbol{C}H_3$)$_3$), 31.40 ($\boldsymbol{C}Me_3$), 32.09 ($\boldsymbol{C}Me_3$), 33.42 (Ar-$\boldsymbol{C}H_2$-Ar),

33.82 (Ar-***C***H_2-Ar), 34.22 (Ar-***C***H_2-Ar), 34.33 (Ar-***C***H_2-Ar), 36.61 (HO-***C***H_2-CH2-OPH), 64.32 (PHO-***C***H_2-CH_2-OH), 77.05 (O-***C***H_2-CH_2), 124.03 (***C***H^{PH}), 124.20 (***C***H^{PH}), 125.05 (***C***H^{PH}), 125.11 (***C***H^{PH}), 125.51 (***C***H^{PH}), 125.58 (***C***H^{PH}), 125.96 (***C***H^{PH}), 126.63 (***C***H^{PH}), 128.33 (***C***^{Ar}-CH_2-C^{Ar}), 130.47 (***C***^{Ar}-CH_2-C^{Ar}), 130.88 (***C***^{Ar}-CH_2-C^{Ar}), 131.88 (***C***^{Ar}-CH_2-C^{Ar}), 132.31 (***C***^{Ar}-CH_2-C^{Ar}), 133.50 (***C***^{Ar}-CH_2-C^{Ar}), 135.31 (***C***^{Ar}-CH_2-C^{Ar}), 136.50 (***C***^{Ar}-CH_2-C^{Ar}), 144.94 (***C***^{PH}-*t*-Bu), 146.57 (***C***^{PH}-*t*-Bu), 146.81 (***C***^{PH}-*t*-Bu), 147.15 (***C***^{PH}-*t*-Bu), 146.28 (***C***^{PH}-OP), 147.15 (***C***^{PH}-Op), 152.32 (***C***^{PH}-O-CH_2-), 153.21 (***C***^{PH}-O-CH_2-).

^{31}P{^{1}H} NMR (δ (ppm), $CDCl_3$): 24.10.

HRMS (ESI) m/z: 763,4496 (100 %) [$(M+H)^+$].

Calixarene phosphonate **3.11** (40 mg, 0.0524 mmol) was dissolved in 3 ml of methanol at ambient temperature. 3 mL of 2M water sodium hydroxide solution was added and mixture heated to T = 90˚C and stirred at this temperature for 3 h. After cooling to ambient temperature, mixture was quenched with 2M hydrochloric acid, product was extracted with dichloromethane, washed with water, dried under sodium sulfate. Solvent was removed in vacuo to obtain product (39.2 mg, yield 96 %) as white solid.

25-phosphoethoxy-26-propyloxy-27-phosphoxy-28-hydroxy-tetra-p-tert.-butyl-calix[4]arene **3.12**. M.p. = 117˚C. [α]D^{20} -15.9 (c 0.0035 M, $CHCl_3$).

^{1}H NMR (δ (ppm), $CDCl_3$): 0.82 (s, 9H, t-Bu), 0.99 (s, 9H, t-Bu), 1.13 (t, J^3_{H-H} = 7.4 Hz, C***H***$_3$), 1.36 (s, 9H, t-Bu), 1.37 (s, 9H, t-Bu), 1.97 (m, 2H, C***H***$_2$-CH_3), 2.30 (m, 1H, OCH_2-C***H***$_2$-P), 2.65 (m, 1H, O-CH_2-C***H***$_2$-P), 3.25 (d, 2H, J^2_{H-H} = 13.2 Hz, Ar-C***H***$_2$-Ar), 3.29 (d, 1H, J^2_{H-H} = 14.5 Hz, Ar-C***H***$_2$-Ar), 3.49 (d, 1H, J^2_{H-H} = 14.0 Hz, Ar-C***H***$_2$-Ar), 3.85 (t, 2H, J^3_{H-H} = 6.9 Hz, O-C***H***$_2$-CH_2-CH_3), 4.04 (d, 1H, J^2_{H-H} = 13.6 Hz, Ar-C***H***$_2$-Ar), 4.04 (m, 1H, O-C***H***$_2$-CH_2-P), 4.24 (d, 1H, J^2_{H-H} = 12.8 Hz, Ar-C***H***$_2$-Ar), 4.43 (d, 1H, J^2_{H-H} = 13.8 Hz, Ar-C***H***$_2$-Ar), 4.59 (m, 2H, O-C***H***$_2$-CH_2-P), 4.75 (d, 1H, J^2_{H-H} = 14.2 Hz, Ar-C***H***$_2$-Ar), 6.27

(bs, 2H, O***H***), 6.43 (d, 1H, $J^4_{H\text{-}H}$ = 2.6 Hz, Ar-***H***), 6.53 (d, 1H, $J^4_{H\text{-}H}$ = 2.5 Hz, Ar-***H***), 6.72 (d, 1H, $J^4_{H\text{-}H}$ = 2.4 Hz, Ar-***H***), 6.79 (d, 1H, $J^4_{H\text{-}H}$ = 2.5 Hz, Ar-***H***), 7.07 (d, 1H, $J^4_{H\text{-}H}$ = 2.4 Hz, Ar-***H***), 7.10 (bs, 3H, Ar-***H***).

$^{13}C\{^1H\}$ NMR (δ (ppm), $CDCl_3$): 10.7 ($OCH_2CH_2\boldsymbol{C}H_3$), 23.6 ($OCH_2\boldsymbol{C}H_2CH_3$), 29.7 ($\boldsymbol{C}(CH_3)_3$), 30.9 ($\boldsymbol{C}(CH_3)_3$), 31.0 ($C(\boldsymbol{C}H_3)_3$), 31.1 ($C(\boldsymbol{C}H_3)_3$), 31.6 ($C(\boldsymbol{C}H_3)_3$), 31.7 (d, $J^1_{C\text{-}P}$ = 39.1 Hz, $OCH_2\boldsymbol{C}H_2P$), 31.8 ($C(\boldsymbol{C}H_3)_3$), 33.0 ($\boldsymbol{C}(CH_3)_3$), 33.5 ($Ar\boldsymbol{C}H_2Ar$), 33.6 ($\boldsymbol{C}(CH_3)_3$), 33.9 ($Ar\boldsymbol{C}H_2Ar$), 34.0 ($Ar\boldsymbol{C}H_2Ar$), 34.2 ($Ar\boldsymbol{C}H_2Ar$), 66.5 (d, $J^2_{C\text{-}P}$ = 10.0 Hz, $O\boldsymbol{C}H_2CH_2P$), 78.0 ($O\boldsymbol{C}H_2CH_2CH_3$), 124.8 ($\boldsymbol{C}H^{Ar}$), 125.3 ($\boldsymbol{C}H^{Ar}$), 125.55 ($\boldsymbol{C}H^{Ar}$), 125.60 ($\boldsymbol{C}H^{Ar}$), 125.62 ($\boldsymbol{C}H^{Ar}$), 125.70 ($\boldsymbol{C}H^{Ar}$), 125.74 ($\boldsymbol{C}H^{Ar}$), 126.5 ($\boldsymbol{C}H^{Ar}$), 126.9 ($\boldsymbol{C}^{Ar}$-$CH_2$-$C^{Ar}$), 129.1 ($\boldsymbol{C}^{Ar}$-$CH_2$-$C^{Ar}$), 129.6 ($\boldsymbol{C}^{Ar}$-$CH_2$-$C^{Ar}$), 130.8 (d, $J^4_{C\text{-}P}$ = 5.0 Hz, $\boldsymbol{C}^{PH}$-O-CH_2-CH_2-P), 131.4 ($\boldsymbol{C}^{Ar}$-CH_2-C^{Ar}), 132.9 ($\boldsymbol{C}^{Ar}$-CH_2-C^{Ar}), 134.8 ($\boldsymbol{C}^{Ar}$-CH_2-C^{Ar}), 136.6 ($\boldsymbol{C}^{Ar}$-CH_2-C^{Ar}), 141.7 ($\boldsymbol{C}^{PH}$-t-Bu), 144.6 ($\boldsymbol{C}^{PH}$-t-Bu), 146.03 (d, $J^2_{C\text{-}P}$ = 11.1 Hz, $\boldsymbol{C}^{PH}$-OP), 146.7 ($\boldsymbol{C}^{PH}$-t-Bu), 146.9 ($\boldsymbol{C}^{PH}$-t-Bu), 150.5 ($\boldsymbol{C}^{PH}$-O-CH_2-), 150.6 ($\boldsymbol{C}^{Ar}$-CH_2-C^{Ar}), 153.3 ($\boldsymbol{C}^{PH}$-OH).

$^{31}P\{^1H\}$ NMR (δ (ppm), $CDCl_3$): 23.04.

HRMS (ESI) m/z: 779,4433 (100 %) $[(M\text{-}H)^-]$.

Aza Mukaiyama reaction procedure.

In well dried vial under inert atmosphere mixture, a mixture of benzimine (0.100 mmol) and catalyst (0.010 mmol) was dissolved in 3 mL of dry toluene and stirred at ambient temperature for 5 min. After enolate (0.200 mmol) was added, mixture was further stirred at ambient temperature for 48 h. Resulting mixture was quenched with 2M water HCl, after diluted with $NaHCO_3$ saturated water solution, extracted with CH_2Cl_2. The organic phase was washed with water and then dried over Na_2SO_4. The solution was concentrated under reduced pressure to give a pale yellow oil which was further purified by flash chromatography using hexanes/ethylacetate (10/1, v/v) as eluting mixture gives product as yellow solid.

Aza Diels-Alder reaction procedure.

In a well dried vial under inert atmosphere, a mixture of benzimine (0.25 mmol) and catalyst (0.0125 mmol) dissolved in 3 mL of dry CH_3CN was stirred at room temperature for 30 min. After diene (0.50 mmol) adddition, the mixture was further stirred at room temperature for 24 h. The resulting mixture was quenched with 2M water HCl, diluted with $NaHCO_3$ saturated water solution an then extracted with CH_2Cl_2. The organic phase was washed with water, dried over Na_2SO_4. The solution was concentrated under reduced pressure to give pale yellow oil, which was further purified by flash chromatography using hexanes/ethylacetate (3/2, v/v) as eluting mixture to give the product as a yellow solid.

Asymmetric epoxide ring opening.

In a well dried vial under inert atmosphere, a mixture of benzoic acid (0.75 mmol) and catalyst (0.0125 mmol) was dissolved in 3 mL of dry toluene and then stirred at rt for 30 min. After epoxide (0.50 mmol) was added, the mixture was further stirred at room temperature for 24 h. The resulting mixture was quenched with 2M water HCl, diluted with $NaHCO_3$ saturated water solution and then extracted with CH_2Cl_2. The organic phase was washed with waterand then dried over Na_2SO_4. The solution was concentrated under reduced pressure to give pale yellow oil, which was further purified by flash chromatography using hexanes/ethylacetate (3/2, v/v) as eluting mixture to give the product as a yellow solid.

Phosphorylation general procedure.

Calix[4]arene (0.247 mmol) was dissolved in 20 mL of dry CH_3CN in presence of K_2CO_3 (0.617 mmol). Mixture was cooled with ice-bath and at this temperature diethyl chlorophosphate (0.370 mmol) was added dropwise.

Mixture was stirred and allowed to heat to ambient temperature for 2 h. The resulting mixture was diluted with water, extracted with CH_2Cl_2. The organic phase was washed with aqueous sodium bicarbonate solution and then dried under Na_2SO_4. After evaporation of the solvent in vacuo, crude materials was purified using chromatography on silica with EtOAc : hexanes (1/2, v/v) as eluent to give product as white solid.

5,11,17,23-Tetra-tert-butyl-26,28-dihydroxy-25-diethoxyphosphoryl-27-(R)-N-(phenylethyl)aminocarbonylmethoxycalix[4]arene **4.2**.

Yield 82 %.

M.p. = 112-114 ^{0}C. $[\alpha]_D^{20}$ +2.05 (c 1.235 g/100 mL, $CHCl_3$) 365 nm.

^{1}H NMR (δ (ppm), $CDCl_3$): 0.80 (s, 9H, t-Bu), 0.97 (s, 9H, t-Bu), 1.31 (t, 6H, J = 7.1 Hz, $POCH_2C\boldsymbol{H}_3$), 1.37 (s, 9H, t-Bu), 1.37 (s, 9H, t-Bu), 1.7 (d, 3H, $^3J_{HH}$ = 7.0 Hz, $CHC\boldsymbol{H}_3$), 3.29 (d, 1H, $^2J_{HH}$ = 13.3 Hz, $ArC\boldsymbol{H}_2Ar$), 3.44 (d, 2H, $^2J_{HH}$ = 13.3 Hz, $ArC\boldsymbol{H}_2Ar$), 3.45 (d, 1H, $^2J_{HH}$ = 14.1 Hz, $ArC\boldsymbol{H}_2Ar$), 4.05 (d, 1H, $^2J_{HH}$ = 13.3 Hz, $ArC\boldsymbol{H}_2Ar$), 4.14 (d, 1H, $^2J_{HH}$ = 14.1 Hz, $ArC\boldsymbol{H}_2Ar$), 4.24 (m, 4H, $POC\boldsymbol{H}_2CH_3$), 4.42 (d, 1H, $^2J_{HH}$ = 15.2 Hz, $OC\boldsymbol{H}_2CO$), 4.48 (d, 2H, $^2J_{HH}$ = 13.4 Hz, $ArC\boldsymbol{H}_2Ar$), 4.62 (d, 1H, $^2J_{HH}$ = 15.1 Hz, $OC\boldsymbol{H}_2CO$), 5.27 (q, 1 H, $^3J_{HH}$ = 7.0 Hz, $C\boldsymbol{H}CH_3$), 5.76, (s, 1H, OH), 6.11 (s, 1H, OH), 6.63 (s, 1H, ArH), 6.65 (s, 1H, ArH), 6.79 (s, 1H, ArH), 6.80 (s, 1H, ArH), 7.10 (d, 1H, $^4J_{HH}$ = 2.0 Hz, ArH), 7.13 (d, 1H, $^4J_{HH}$ = 2.0 Hz, ArH), 7.16 (d, 1H, $^4J_{HH}$ = 2.0 Hz, ArH), 7.18 (d, 1H, $^4J_{HH}$ = 2.0 Hz, ArH), 7.18 (m, 1H, PHH), 7.24 (m, 2H, PHH), 7.42 (d, 2H, J_{HP} = 7.5 Hz), 8.79 (d, 1H, $^3J_{HH}$ = 7.8 Hz, NH);

^{13}C{^{1}H} NMR (δ (ppm), $CDCl_3$): 16.11 ($POCH_2\boldsymbol{C}H_3$), 16.18 ($POCH_2\boldsymbol{C}H_3$), 22.41 ($PHCH\boldsymbol{C}H_3$), 30.7 ($C(\boldsymbol{C}H_3)_3$), 30.9 ($C(\boldsymbol{C}H_3)_3$), 31.7 ($C(\boldsymbol{C}H_3)_3$), 31.7 ($\boldsymbol{C}(CH_3)_3$), 31.8 ($\boldsymbol{C}(CH_3)_3$), 31.9 ($\boldsymbol{C}(CH_3)_3$), 31.9 ($\boldsymbol{C}(CH_3)_3$), 33.8 ($Ar\boldsymbol{C}H_2Ar$), 33.9 ($Ar\boldsymbol{C}H_2Ar$), 34.0 ($Ar\boldsymbol{C}H_2Ar$), 49.1 ($PH\boldsymbol{C}HCH_3$), 64.7 ($PO\boldsymbol{C}H_2CH_3$), 64.8 ($PO\boldsymbol{C}H_2CH_3$), 74.4 ($O\boldsymbol{C}H_2CO$), 125.2 (^{Ar}CH), 125.3 (^{Ar}CH), 125.4 (^{Ar}CH), 125.6 (^{Ar}CH), 125.6 (^{Ar}CH), 126.0 (^{Ar}CH), 126.1 (^{Ar}CH), 126.2

(^{Ar}CH), 126.3 (^{Ar}CH), 127.0 (^{Ar}C), 127.3 (^{Ar}C), 127.8 (^{Ar}C), 128.5 (^{Ar}C), 128.9 (^{Ar}C), 129.0 (^{Ar}C), 131.0 (^{Ar}C), 131.1 (^{Ar}C), 131.7 (^{Ar}C), 131.8 (^{Ar}C), 131.8 (^{Ar}C), 142.2 (d, J_{PC} = 7.2 Hz, ***C***OP), 142.7 (^{Ar}***C***-tBu), 143.0 (^{Ar}***C***-tBu), 143.5 (^{Ar}***C***-tBu), 147.8 (d, J_{PC} = 2.0 Hz, ^{Ar}***C***-tBu), 148.1 (^{Ar}***C***-CH_2-C^{Ar}), 148.8 (^{Ar}***C***-CH_2-C^{Ar}), 149.6 (^{Ar}***C***-CH_2-C^{Ar}), 149.9 (^{Ar}***C***-CH_2-C^{Ar}), 167.5 (OCH_2***C***O).

^{31}P{^{1}H} NMR (δ (ppm), $CDCl_3$): -4.39.

HRMS (ESI+): calcul. for $C_{58}H_{77}NO_8P$ [M + H] 946.5421; found 946.5397.

5,11,17,23-Tetra-tert-butyl-26,27-dihydroxy-25-diethoxyphosphoryl-28-(R)-N-(phenylethyl)aminocarbonylmethoxycalix[4]arene **4.3a**.

Yield 41 %.

M.p. = 98-101 ^{0}C. $[\alpha]_D^{20}$ -1.92 (c 1.120 g/100 mL, $CHCl_3$).

^{1}H NMR (δ (ppm), $CDCl_3$): 1.10 (s, 9H, t-Bu), 1.15 (s, 9H, t-Bu), 1.15 (t, 3H, $^{3}J_{HH}$ = 7.1 Hz, $POCH_2C\boldsymbol{H}_3$), 1.21 (s, 9H, t-Bu), 1.22 (s, 9H, t-Bu), 1.32 (t, 3H, $^{3}J_{HH}$ = 7.1 Hz, $POCH_2C\boldsymbol{H}_3$), 1.69 (d, 3H, $^{3}J_{HH}$ = 7.2 Hz, $CHC\boldsymbol{H}_3$), 3.35 (d, 1H, $^{2}J_{HH}$ = 13.9 Hz, $ArC\boldsymbol{H}_2Ar$), 3.38 (d, 1H, $^{2}J_{HH}$ = 13.9 Hz, $ArC\boldsymbol{H}_2Ar$), 3.39 (d, 1H, $^{2}J_{HH}$ = 13.9 Hz, $ArC\boldsymbol{H}_2Ar$), 3.40 (d, 1H, $^{2}J_{HH}$ = 13.5 Hz, $ArC\boldsymbol{H}_2Ar$), 3.93 (m, 2H, $POC\boldsymbol{H}_2CH_3$), 4.11 (d, 1H, $^{2}J_{HH}$ = 13.3 Hz, $OC\boldsymbol{H}_2CO$), 4.29 (m, 2H, $POC\boldsymbol{H}_2CH_3$), 4.31 (d, 1H, $^{2}J_{HH}$ = 13.8 Hz, $ArC\boldsymbol{H}_2Ar$), 4.45 (d, 1H, $^{2}J_{HH}$ = 13.5 Hz, $ArC\boldsymbol{H}_2Ar$), 4.60 (d, 1H, $^{2}J_{HH}$ = 13.3 Hz, $ArC\boldsymbol{H}_2Ar$), 4.62(d, 1H, $^{2}J_{HH}$ = 13.2 Hz, $ArC\boldsymbol{H}_2Ar$), 5.06 (d, 1H, $^{2}J_{HH}$ = 13.6 Hz, $OC\boldsymbol{H}_2CO$), 5.40 (q, 1H, $^{3}J_{HH}$ = 7.2 Hz, $C\boldsymbol{H}CH_3$), 6.92 (d, 1H, $^{4}J_{HH}$ = 2.5 Hz, ArH), 6.99 (m, 6H, ArH), 7.28 (m, 1H, ArH), 7.39 (m, 2H, ArH), 7.58 (m, 2H, ArH), 7.94 (s, 1H, OH), 8.55 (s, 1H, OH), 8.84 (d, 1H, $^{3}J_{HH}$ = 8.3 Hz, NH).

^{13}C{^{1}H} NMR (δ (ppm), $CDCl_3$): 16.0 (d, $J^3_{P\text{-}C}$ = 6.5 Hz, $POCH_2\boldsymbol{C}H_3$), 16.1 (d, J^3_{PC} = 6.4 Hz $POCH_2\boldsymbol{C}H_3$), 22.1 ($CH\boldsymbol{C}H_3$), 31.1 ($C(\boldsymbol{C}H_3)_3$), 31.2 ($C(\boldsymbol{C}H_3)_3$), 31.4 ($C(\boldsymbol{C}H_3)_3$), 31.5 ($C(\boldsymbol{C}H_3)_3$), 31.9 ($Ar\boldsymbol{C}H_2Ar$), 32.0 ($Ar\boldsymbol{C}H_2Ar$), 32.1 ($Ar\boldsymbol{C}H_2Ar$), 32.6 ($Ar\boldsymbol{C}H_2Ar$), 33.8 ($\boldsymbol{C}(CH_3)_3$), 33.9 ($\boldsymbol{C}(CH_3)_3$), 34.0

(***C***$(CH_3)_3$), 34.1 (***C***$(CH_3)_3$), 48.9 (***C***HCH_3), 64.8 (d, J^2_{PC} = 6.4 Hz, PO***C***H_2CH_3), 65.3 (d, J^2_{PC} = 6.4 Hz, PO***C***H_2CH_3), 74.8 (O***C***H_2CO), 125.2 (^{Ar}CH), 125.3 (^{Ar}CH), 125.4 (^{Ar}CH), 125.5 (^{Ar}CH), 125.9 (d, J = 2.0 Hz, ^{Ar}CH), 126.1 (^{Ar}CH), 126.2 (d, J = 2.0 Hz, ^{Ar}CH), 126.4 (^{Ar}CH), 126.8 (^{Ar}CH), 127.1 (^{PH}CH), 127.5 (^{Ar}***C***-CH_2-C^{Ar}), 127.7 (^{Ar}***C***-CH_2-C^{Ar}), 127.7 (^{Ar}***C***-CH_2-C^{Ar}), 128.2 (^{Ar}***C***-CH_2-C^{Ar}), 128.5 (^{PH}CH), 132.7 (d, J = 3.2 Hz, ^{Ar}***C***-CH_2-C^{Ar}), 133.0 (^{Ar}***C***-CH_2-C^{Ar}), 133.2 (d, J = 3.2 Hz, ^{Ar}***C***-CH_2-C^{Ar}), 133.7 (^{Ar}***C***-CH_2-C^{Ar}), 142.5 (^{Ar}***C***-tBu), 142.8 (^{Ar}C-tBu), 143.6 (^{PH}***C***-CH), 147.4 (^{Ar}***C***-tBu), 147.8 (d, J = 2.4 Hz, ^{Ar}***C***-tBu), 148.1 (^{Ar}***C***-OH), 149.1 (^{Ar}***C***-OH), 151.9 (Ar), 168.4 (***C***ONH).

$^{31}P\{^1H\}$ NMR (δ (ppm), $CDCl_3$): -5.73.

HRMS (ESI+): calcul. for $C_{58}H_{77}NO_8P$ [M + H] 946.5421; found 946.5376.

5,11,17,23-Tetra-tert-butyl-27,28-dihydroxy-25-diethoxyphosphoryl-26-(R)-N-(phenylethyl)aminocarbonylmethoxycalix[4]arene **4.3b**.

Yield 41 %.

M.p. = 97-98 ^{0}C. $[\alpha]_D^{20}$ -1.55 (c 1.230 g/100 mL, $CHCl_3$).

^{1}H NMR (δ (ppm), $CDCl_3$): 1.05 (s, 9H, t-Bu), 1.18 (s, 9H, t-Bu), 1.20 (s, 9H, t-Bu), 1.24 (s, 9H, t-Bu), 1.32 (t, 6H, $^3J_{HH}$ = 7.1 Hz, $POCH_2C\boldsymbol{H}_3$), 1.73 (d, 3H, $^3J_{HH}$ = 7.0 Hz, $CHC\boldsymbol{H}_3$), 3.35 (d, 1H, $^2J_{HH}$ = 13.4 Hz, $ArC\boldsymbol{H}_2Ar$), 3.35 (d, 1H, $^2J_{HH}$ = 13.5 Hz, $ArC\boldsymbol{H}_2Ar$), 3.37 (d, 1H, $^2J_{HH}$ = 14.1 Hz, $ArC\boldsymbol{H}_2Ar$), 3.42 (d, 1H, $^2J_{HH}$ = 13.4 Hz, $ArC\boldsymbol{H}_2Ar$), 4.17 (d, 1H, $^2J_{HH}$ = 13.3 Hz, $ArC\boldsymbol{H}_2Ar$), 4.24 (m, 4H, $POC\boldsymbol{H}_2CH_3$) 4.35 (d, 1H, $^2J_{HH}$ = 13.4 Hz, $ArC\boldsymbol{H}_2Ar$), 4.57 (d, 2H, $^2J_{HH}$ = 13.4 Hz, $ArC\boldsymbol{H}_2Ar$), 4.62 (d, 1H, $^2J_{HH}$ = 13.7 Hz, $OC\boldsymbol{H}_2CO$), 5.02 (d, 1H, $^2J_{HH}$ = 13.7 Hz, $OC\boldsymbol{H}_2CO$), 5.32 (q, 1H, $^3J_{HH}$ = 7.0 Hz, $C\boldsymbol{H}CH_3$), 6.88 (d, 1H, $^4J_{HH}$ = 2.0 Hz, ArH), 6.92 (d, 1H, $^4J_{HH}$ = 2.0 Hz, ArH), 6.95 (d, 1H, $^4J_{HH}$ = 2.0 Hz, ArH), 6.98 (m, 2H, ArH), 7.01 (d, 1H, $^4J_{HH}$ = 2.0 Hz, ArH), 7.05 (m, 2H, ArH), 7.22 (t, 1H, ArH), 7.32 (m, 2H, ArH), 7.55 (m, 2H, PHH), 8.05 (s, 1H, OH), 8.55 (s, 1H, OH), 8.62 (d, 1H, $^3J_{HH}$ = 7.4 Hz, NH);

$^{13}C\{^1H\}$ NMR (δ (ppm), $CDCl_3$): 16.13 (d, $^3J_{PC}$ = 4.4 Hz, $POCH_2\boldsymbol{C}H_3$), 16.19 (d, $^3J_{P\text{-}C}$ = 4.7 Hz $POCH_2\boldsymbol{C}H_3$), 22.80 ($CH\boldsymbol{C}H_3$), 29.71 ($\boldsymbol{C}(CH_3)_3$), 31.06 ($C(\boldsymbol{C}H_3)_3$), 31.27 ($C(\boldsymbol{C}H_3)_3$), 31.44 ($C(\boldsymbol{C}H_3)_3$), 31.56 ($C(\boldsymbol{C}H_3)_3$), 31.84 ($Ar\boldsymbol{C}H_2Ar$), 32.04 ($Ar\boldsymbol{C}H_2Ar$), 32.15 ($Ar\boldsymbol{C}H_2Ar$), 32.56 ($Ar\boldsymbol{C}H_2Ar$), 33.87 ($\boldsymbol{C}(CH_3)_3$), 34.08 (2C, $\boldsymbol{C}(CH_3)_3$), 34.12 ($\boldsymbol{C}(CH_3)_3$), 49.25 ($\boldsymbol{C}HCH_3$), 64.90 (d, 2C, $^2J_{PC}$ = 6.4 Hz, $PO\boldsymbol{C}H_2CH_3$), 65.15 (d, 2C, $^3J_{PC}$ = 6.4 Hz, $PO\boldsymbol{C}H_2CH_3$), 74.68 ($O\boldsymbol{C}H_2CO$), 125.22 (^{Ar}CH), 125.31 (^{Ar}CH), 125.38 (^{Ar}CH), 125.48 (^{Ar}CH), 125.81 (d, J = 2.0 Hz, ^{Ar}CH), 126.30 (^{Ar}CH), 126.34 (^{Ar}CH), 126.53 (^{Ar}CH), 126.97 (^{PH}CH), 127.41 ($^{Ar}\boldsymbol{C}$-CH_2-C^{Ar}), 127.44 ($^{Ar}\boldsymbol{C}$-CH_2-C^{Ar}), 127.52 ($^{Ar}\boldsymbol{C}$-CH_2-C^{Ar}), 128.32 ($^{Ar}\boldsymbol{C}$-CH_2-C^{Ar}), 128.49 (^{PH}CH), 132.66 (d, J = 3.2 Hz, $^{Ar}\boldsymbol{C}$-CH_2-C^{Ar}), 132.79 (d, J = 3.2 Hz, $^{Ar}\boldsymbol{C}$-CH_2-C^{Ar}), 133.09 ($^{Ar}\boldsymbol{C}$-CH_2-C^{Ar}), 133.82 ($^{Ar}\boldsymbol{C}$-CH_2-C^{Ar}), 142.35 ($^{Ar}\boldsymbol{C}$-tBu), 142.90 ($^{Ar}\boldsymbol{C}$-tBu), 143.04 (d, J = 8.9 Hz, $^{Ar}\boldsymbol{C}$-O-PO), 143.66 ($^{PH}\boldsymbol{C}$-CH), 147.59 ($^{Ar}\boldsymbol{C}$-tBu), 147.65 (d, J = 2.4 Hz, $^{Ar}\boldsymbol{C}$-tBu), 147.78 ($^{Ar}\boldsymbol{C}$-OH), 149.36 (Ar), 147.78 ($^{Ar}\boldsymbol{C}$-O), 149.36 (Ar C-OH), 151.9 (Ar), 168.3 ($\boldsymbol{C}ONH$).

$^{31}P\{^1H\}$ NMR (δ (ppm), $CDCl_3$): -5.47.

HRMS (ESI+): calcul. for $C_{58}H_{77}NO_8P$ [M + H] 946.5421; found 946.5383.

5,11,17,23-Tetra-tert-butyl-27-hydroxy-28-propoxy-25-diethoxyphosphoryl-26-(R)-N-(phenylethyl)aminocarbonylmethoxycalix[4]arene **4.6a**.

Yield 36 %.

M.p. = 118-120 ^{0}C. $[\alpha]_D^{20}$ -3.87 (c 1.07 g/100 mL, $CHCl_3$) 365 nm.

^1H NMR (δ (ppm), $CDCl_3$): 0.77 (s, 9H, t-Bu), 0.89 (s, 9H, t-Bu), 0.97 (t, 3H, $^3J_{HH}$ = 7.4 Hz, $OCH_2CH_2C\boldsymbol{H}_3$), 1.31 (m, 6H, $POCH_2C\boldsymbol{H}_3$) 1.37 (s, 9H, t-Bu), 1.38 (s, 9H, t-Bu), 1.65 (d, 3H, $^3J_{HH}$ = 7 Hz, $CHC\boldsymbol{H}_3$), 2.19 (m, 2H, $OCH_2C\boldsymbol{H}_2CH_3$), 3.10 (d, 1H, $^2J_{HH}$ = 13.3 Hz, $ArC\boldsymbol{H}_2Ar$), 3.25 (d, 1H, $^2J_{HH}$ = 12.7 Hz, $ArC\boldsymbol{H}_2Ar$), 3.31 (d, 1H, $^2J_{HH}$ = 13.4 Hz, $ArC\boldsymbol{H}_2Ar$), 3.41 (d, 1H, $^2J_{HH}$ = 13.8

Hz, ArC***H***$_2$Ar), 3.97 (d, 1H, $^2J_{HH}$ = 13.5 Hz, ArC***H***$_2$Ar), 4.00 (m, 1H, OC***H***$_2$CH$_2$CH$_3$), 4.05 (d, 1H, $^2J_{HH}$ = 15.2 Hz, OC***H***$_2$CO), 4.13 (m, 1H, OC***H***$_2$CH$_2$CH$_3$), 4.22 (m, 4 H, POC***H***$_2$CH$_3$), 4.37 (d, 1H, $^2J_{HH}$ = 12.7 Hz, ArC***H***$_2$Ar), 4.48 (d, 1H, $^2J_{HH}$ = 13.7 Hz, ArC***H***$_2$Ar), 4.55 (d, 1H, $^2J_{HH}$ = 13.5 Hz, ArC***H***$_2$Ar), 5.02 (d, 1H, $^2J_{HH}$ = 15.2 Hz, OC***H***$_2$CO), 5.30 (квінт., 1H, C***H***CH$_3$), 6.48 (d, 1H, $^4J_{HH}$ = 2.4 Hz, ArH), 6.53 (d, 1H, $^4J_{HH}$ = 2.4 Hz, ArH), 6.58 (d, 1H, $^4J_{HH}$ = 2.4 Hz, ArH), 6.64 (d, 1H, $^4J_{HH}$ = 2.4 Hz, ArH), 7.02 (m, 4H, PHH, OH), 7.17 (d, 2H, $^4J_{HH}$ = 2.4 Hz, ArH), 7.21 (d, 1H, $^4J_{HH}$ = 2.4 Hz, ArH), 7.27 (d, 1H, $^4J_{HH}$ = 2.4 Hz, ArH), 7.29 (m, 1H, PHH), 8.66 (d, 1 H, $^3J_{HH}$ = 8.4 Hz, NH).

^{13}C{^{1}H} NMR (δ (ppm), $CDCl_3$): 9.9 (OCH$_2$CH$_2$***C***H$_3$), 16.2 (dd, $^3J_{PC}$ = 7.2 Hz POCH$_2$***C***H$_3$), 22.4 (CH***C***H$_3$), 22.8 (OCH$_2$***C***H$_2$CH$_3$), 30.8 (C(***C***H$_3$)$_3$), 30.9 (C(***C***H$_3$)$_3$), 31.1 (Ar***C***H$_2$Ar), 31.6 (C(***C***H$_3$)$_3$), 31.7 (C(***C***H$_3$)$_3$), 31.7 (Ar***C***H$_2$Ar), 32.5 (Ar***C***H$_2$Ar), 32.7 (Ar***C***H$_2$Ar), 33.7 (***C***(CH$_3$)$_3$), 33.8 (***C***(CH$_3$)$_3$), 34.0 (***C***(CH$_3$)$_3$), 34.2 (***C***(CH$_3$)$_3$), 48. 6 (***C***HCH$_3$), 64.4 (dd, $^2J_{PC}$ = 5.6 Hz, PO***C***H$_2$CH$_3$), 65.2 (d, 2C, $^2J_{PC}$ = 6.4 Hz, PO***C***H$_2$CH$_3$), 74.7 (O***C***H$_2$CO), 125.2 (^{Ar}CH), 125.3 (^{Ar}CH), 125.4 (^{Ar}CH), 125.5 (^{Ar}CH), 125.8 (d, J = 2.0 Hz, ^{Ar}CH), 126.3 (^{Ar}CH), 126.3 (^{Ar}CH), 126.5 (^{Ar}CH), 127.0 (^{PH}CH), 127.4 (^{Ar}***C***-CH$_2$-C^{Ar}), 127.4 (^{Ar}***C***-CH$_2$-C^{Ar}), 127.5 (^{Ar}***C***-CH$_2$-C^{Ar}), 128.3 (^{Ar}***C***-CH$_2$-C^{Ar}), 128.5 (^{PH}CH), 132.7 (d, J = 3.2 Hz, ^{Ar}***C***-CH$_2$-C^{Ar}), 132.8 (d, J = 3.2 Hz, ^{Ar}***C***-CH$_2$-C^{Ar}), 133.1 (^{Ar}***C***-CH$_2$-C^{Ar}), 133.8 (^{Ar}***C***-CH$_2$-C^{Ar}), 142.4 (^{Ar}***C***-tBu), 142.9 (^{Ar}***C***-tBu), 143.1 (d, J = 8.9 Hz, ^{Ar}***C***-O-PO), 143.7 (^{PH}***C***-CH), 147.6 (^{Ar}***C***-tBu), 147.7 (d, J = 2.4 Hz, ^{Ar}***C***-tBu), 147.8 (^{Ar}C-OH), 149.4 (^{Ar}C-O), 150.7 (^{Ar}***C***-CH$_2$-C^{Ar}), 153.4 (^{Ar}***C***-CH$_2$-C^{Ar}), 168.4 (***C***ONH).

^{31}P{^{1}H} NMR (δ (ppm), $CDCl_3$): -4.12.

HRMS (ESI): calcul. for $C_{61}H_{81}NO_8P$ [M - H] 986.5731; found 986.5697.

5,11,17,23-Tetra-tert-butyl-25-hydroxy-28-propoxy-27-diethoxyphosphoryl-26-(R)-N-(phenylethyl)aminocarbonylmethoxycalix[4]arene **4.6b**.

Yield 36 %.

M.p. = 112-114 ^{0}C. $[\alpha]_D^{20}$ -5.09 (c 0.990 g/100 mL, $CHCl_3$) 365 nm.

^{1}H NMR (δ (ppm), $CDCl_3$): 0.75 (s, 9H, t-Bu), 0.92 (t, 3H, $^{3}J_{HH}$ = 7.4 Hz, $OCH_2CH_2C\boldsymbol{H}_3$), 0.97 (s, 9H, t-Bu), 1.18 (m, 6H, $POCH_2C\boldsymbol{H}_3$) 1.35 (s, 9H, t-Bu), 1.36 (s, 9H, t-Bu), 1.79 (m, 2H, $OCH_2C\boldsymbol{H}_2CH_3$), 1.83 (d, 3H, $^{2}J_{HH}$ = 7.0 Hz, $CHC\boldsymbol{H}_3$), 3.27 (d, 1H, $^{2}J_{HH}$ = 12.9 Hz, $ArC\boldsymbol{H}_2Ar$), 3.28 (d, 1H, $^{2}J_{HH}$ = 13.3 Hz, $ArC\boldsymbol{H}_2Ar$), 3.35 (d, 1H, $^{2}J_{HH}$ = 13.2 Hz, $ArC\boldsymbol{H}_2Ar$), 3.37 (d, 1H, $^{2}J_{HH}$ = 13.8 Hz, $ArC\boldsymbol{H}_2Ar$), 3.75 (m, 2H, $OC\boldsymbol{H}_2CH_2CH_3$), 4.00 (m, 4H, $POC\boldsymbol{H}_2CH_3$), 4.13 (d, 1H, $^{2}J_{HH}$ = 14.4 Hz, $OC\boldsymbol{H}_2CO$), 4.29 (d, 1H, $^{2}J_{HH}$ = 14.1 Hz, $ArC\boldsymbol{H}_2Ar$), 4.32 (d, 1H, $^{2}J_{HH}$ = 12.7 Hz, $ArC\boldsymbol{H}_2Ar$), 4.40 (d, 1H, $^{2}J_{HH}$ = 13.1 Hz, $ArC\boldsymbol{H}_2Ar$), 4.43 (d, 1H, $^{2}J_{HH}$ = 13.3 Hz, $Ar\boldsymbol{C}H_2Ar$), 4.45 (d, 1H, $^{2}J_{HH}$ = 14.2 Hz, $OC\boldsymbol{H}_2CO$), 5.13 (q, 1H, $C\boldsymbol{H}CH_3$), 6,03 (s, 1H, OH), 6.41 (d, 1H, $^{4}J_{HH}$ = 2.4 Hz, ArH), 6.48 (d, 1H, $^{4}J_{HH}$ = 2.4 Hz, ArH), 6.66 (d, 1H, $^{4}J_{HH}$ = 2.4 Hz, ArH), 6.78 (d, 1H, $^{4}J_{HH}$ = 2.4 Hz, ArH), 7.06 (d, 1H, $^{4}J_{HH}$ = 2.4 Hz, ArH), 7.13 (d, 1H, $^{4}J_{HH}$ = 2.6 Hz, ArH), 7.17 (d, 1H, $^{4}J_{HH}$ = 2.5 Hz, ArH), 7.20 (d, 1H, $^{4}J_{HH}$ = 2.0 Hz, ArH), 7.31 (m, 2H, PHH), 7.64 (m, 2H, PHH), 8.07 (d, 1 H, $^{3}J_{HH}$ = 8.4 Hz, NH).

^{13}C{^{1}H} NMR (δ (ppm), $CDCl_3$): 10.1 ($OCH_2CH_2\boldsymbol{C}H_3$), 16.0 (d, $^{3}J_{PC}$ = 7.2 Hz $POCH_2\boldsymbol{C}H_3$), 21.6 ($CH\boldsymbol{C}H_3$), 22.4 ($OCH_2\boldsymbol{C}H_2CH_3$), 29.7 ($Ar\boldsymbol{C}H_2Ar$), 30.5 ($Ar\boldsymbol{C}H_2Ar$), 30.9 ($C(\boldsymbol{C}H_3)_3$),31.1 ($C(\boldsymbol{C}H_3)_3$), 31.6 ($C(\boldsymbol{C}H_3)_3$), 31.6 ($Ar\boldsymbol{C}H_2Ar$), 31.7 ($C(\boldsymbol{C}H_3)_3$), 32.3 ($Ar\boldsymbol{C}H_2Ar$), 33.6 ($\boldsymbol{C}(CH_3)_3$), 33.9 ($\boldsymbol{C}(CH_3)_3$), 33.9 ($\boldsymbol{C}(CH_3)_3$), 34.1 ($\boldsymbol{C}(CH_3)_3$), 50.9 ($\boldsymbol{C}HCH_3$), 64.2 (dd, $^{2}J_{PC}$ = 5.6 Hz), 74.4 ($O\boldsymbol{C}H_2CH_2$), 78.6 ($O\boldsymbol{C}H_2CO$), 124.8 (^{Ar}CH), 124.8 (^{Ar}CH), 124.9 (^{Ar}CH), 124.9 (^{Ar}CH), 125.1 (^{Ar}CH), 125.2 (^{Ar}CH), 125.4 (^{Ar}CH), 125.8 (^{Ar}CH), 126.1 (^{Ar}CH), 126.6 (^{Ar}CH), 127.3 (^{Ar}CH), 127.4 (^{Ar}C), 128.2 (^{PH}CH), 129.5 ($^{Ar}\boldsymbol{C}$-CH_2-C^{Ar}), 132.2 ($^{Ar}\boldsymbol{C}$-CH_2-C^{Ar}), 131.5 (d, J = 3.2 Hz, $^{Ar}\boldsymbol{C}$-CH_2-C^{Ar}), 132.2 (d, J = 3.2 Hz, $^{Ar}\boldsymbol{C}$-CH_2-C^{Ar}), 132.6 ($^{Ar}\boldsymbol{C}$-CH_2-C^{Ar}), 134.9 ($^{Ar}\boldsymbol{C}$-CH_2-C^{Ar}), 135.4 ($^{Ar}\boldsymbol{C}$-CH_2-C^{Ar}),

141.8 (^{Ar}***C***-tBu), 143.0 (d, J = 8.9 Hz, ^{Ar}***C***-O-PO), 144.0 (^{Ar}***C***-tBu), 146.4 (d, J = 2.4 Hz, ^{Ar}***C***-tBu), 146.4 (^{PH}***C***-CH), 147.9 (^{Ar}***C***-tBu), 150.0 (^{Ar}***C***-OH), 150.2 (^{Ar}***C***-O), 151.9 (^{Ar}***C***-CH_2-C^{Ar}), 168.2 (***C***ONH).

^{31}P{^{1}H} NMR (δ (ppm), $CDCl_3$): -3.69.

HRMS (ESI-): calcul. for $C_{61}H_{81}NO_8P$ [M - H] 986.5731; found 986.5698.

Calix[4]arene (**4.2**, **4.3a-b**, **4.6a-b**), (0.247 mmol) was dissolved in 20 mL of dry CH_2Cl_2. Bromotrimethylsilane (4.940 mmol) was added dropwise. The reaction mixture was stirred at room temperature for 24 h and was then evaporated under reduced pressure. An excess of absolute methanol was added to the residue. The methanolic solution was boiled for 2 h and then evaporated. The solid residue was dried in vacuum for 2 h to give product as white solid.

5,11,17,23-Tetra-tert-butyl-26,28-dihydroxy-25-dihydroxyphosphoryl-27-(R)-N-(phenylethyl)aminocarbonylmethoxycalix[4]arene **4.4**.

Yield 89 %.

M.p. = 162-163 ^{0}C. $[\alpha]_D^{20}$ +1.86 (c 1.31 g/100 mL, $CHCl_3$).

^{1}H NMR (δ (ppm), DMCO): 0.91 (s, 9H, t-Bu), 1.02 (s, 9H, t-Bu), 1.33 (s, 9H, t-Bu), 1.34 (s, 9H, t-Bu), 1.74 (d, 3H, $^{3}J_{HH}$ = 7.0 Hz, CHC***H***$_3$), 3.35 (m, 2H, ArC***H***$_2$Ar), 3.49 (d, 1H, $^{2}J_{HH}$ = 13.3 Hz, ArC***H***$_2$Ar), 3.48 (d, 2H, $^{2}J_{HH}$ = 13.3 Hz, ArC***H***$_2$Ar), 4.08 (d, 1H, $^{2}J_{HH}$ = 13.2 Hz, ArC***H***$_2$Ar), 4.16 (d, 1H, $^{2}J_{HH}$ = 13.6 Hz, ArC***H***$_2$Ar), 4.37 (d, 1H, $^{2}J_{HH}$ = 15.0 Hz, OC***H***$_2$CO), 4.54 (d, 1H, $^{2}J_{HH}$ = 13.9 Hz, ArC***H***$_2$Ar), 4.61 (d, 1H, $^{2}J_{HH}$ = 13.7 Hz, ArC***H***$_2$Ar), 4.70 (d, 1H, $^{2}J_{HH}$ = 15.0 Hz, OC***H***$_2$CO), 5.19 (q, 1 H, $^{3}J_{HH}$ = 7.0 Hz, C***H***CH_3), 6.82 (d, 1H, $^{4}J_{HH}$ = 2.7 Hz, ArH), 6.85 (d, 1H, $^{4}J_{HH}$ = 2.5 Hz, ArH), 6.95 (m, 1H, PHH), 7.24 (m, 7H, PHH), 7.45 (m, 7H, PHH);

^{13}C{^{1}H} NMR (δ (ppm), DMCO): 21.3 (PHCH***C***H_3), 30.1 (C(***C***$H_3)_3$), 30.7 (C(***C***$H_3)_3$), 30.7 (C(***C***$H_3)_3$), 31.2 (***C***$(CH_3)_3$), 31.6 (***C***$(CH_3)_3$), 31.6 (***C***$(CH_3)_3$), 33.35 (Ar***C***H_2Ar), 33.38 (Ar***C***H_2Ar), 33.41 (Ar***C***H_2Ar), 33.54 (Ar***C***H_2Ar), 49.4

(PH***C***HCH$_3$), 73.8 (O***C***H$_2$CO), 124.7 (^{Ar}CH), 125.1 (^{Ar}CH), 125.2 (^{Ar}CH), 125.24 (^{Ar}CH), 125.4 (^{Ar}CH), 125.7 (^{Ar}CH), 126.0 (^{Ar}CH), 126.1 (^{Ar}CH), 126.7 (^{Ar}CH), 127.1 (^{Ar}C), 127.9 (^{Ar}C), 128.1 (^{Ar}C), 128.7 (^{Ar}C), 128.9 (^{Ar}C), 132.0 (^{Ar}C), 132.2 (^{Ar}C), 132.3 (^{Ar}C), 132.9 (d, J_{PC} = 7.2 Hz, ***C***OP), 142.1 (^{Ar}***C***-tBu), 142.6 (^{Ar}***C***-tBu), 143.5 (^{Ar}***C***-tBu), 143.36 (^{Ar}***C***-tBu), 147.9 (^{Ar}***C***-CH$_2$-C^{Ar}), 149.5 (^{Ar}***C***-CH$_2$-C^{Ar}), 149.5 (^{Ar}***C***-CH$_2$-C^{Ar}), 149.8 (^{Ar}***C***-CH$_2$-C^{Ar}), 168.5 (OCH$_2$***C***O).

^{31}P{^{1}H} NMR (δ (ppm), DMCO): -4.49.

HRMS (ESI-): calcul. for $C_{54}H_{67}NO_8P$ [M - H] 888.4665; found 888.4615.

5,11,17,23-Tetra-tert-butyl-26,27-dihydroxy-25- dihydroxyphosphoryl-28-(R)-N-(phenylethyl)aminocarbonylmethoxycalix[4]arene **4.5a**.

Yield 93 %.

M.p. = 113-115 ^{0}C. $[\alpha]_D^{20}$ -2.64 (c 1.09 g/100 mL, $CHCl_3$).

^{1}H NMR (δ (ppm), DMCO): 1.03 (s, 9H, t-Bu), 1.12 (s, 9H, t-Bu), 1.19 (s, 9H, t-Bu), 1.20 (s, 9H, t-Bu), 1.47 (d, 3H, $^3J_{HH}$ = 7.0 Hz, CHC***H***$_3$), 3.22 (d, 1H, $^2J_{HH}$ = 12.9 Hz, ArC***H***$_2$Ar), 3.26 (d, 1H, $^2J_{HH}$ = 13.4 Hz, ArC***H***$_2$Ar), 3.35 (d, 1H, $^2J_{HH}$ = 13.3 Hz, ArC***H***$_2$Ar), 3.44 (d, 1H, $^2J_{HH}$ = 12.9 Hz, ArC***H***$_2$Ar), 4.17 (d, 1H, $^2J_{HH}$ = 14.0 Hz, OC***H***$_2$CO), 4.02 (d, 1H, $^2J_{HH}$ = 13.2 Hz, ArC***H***$_2$Ar), 4.31 (d, 1H, $^2J_{HH}$ = 12.9 Hz, ArC***H***$_2$Ar), 4.60 (d, 1H, $^2J_{HH}$ = 12.9 Hz, ArC***H***$_2$Ar), 4.66 (d, 1H, $^2J_{HH}$ = 12.9 Hz, ArC***H***$_2$Ar), 5.11 (m, 1H, C***H***CH$_3$), 5.37 (d, 1H, $^2J_{HH}$ = 14.0 Hz, OC***H***$_2$CO), 6.92 (d, 1H, $^4J_{HH}$ = 2.5 Hz, ArH), 6.96 (d, 1H, $^4J_{HH}$ = 2.4 Hz, ArH), 6.98 (d, 1H, $^4J_{HH}$ = 2.4 Hz, ArH), 7.03 (d, 1H, $^4J_{HH}$ = 2.4 Hz, ArH), 7.05 (d, 1H, $^4J_{HH}$ = 2.5 Hz, ArH), 7.13 (d, 1H, $^4J_{HH}$ = 2.4 Hz, ArH), 7.15 (d, 1H, $^4J_{HH}$ = 2.5 Hz, ArH), 6.99 (m, 1H, ArH), 7.35 (m, 5H, ArH), 9.0 (d, 1H, $^3J_{HH}$ = 7.9 Hz, NH).

^{13}C{^{1}H} NMR (δ (ppm), DMCO): 22.8 (CH***C***H$_3$), 31.3 (C(***C***H$_3$)$_3$), 31.5 (C(***C***H$_3$)$_3$), 31.6 (C(***C***H$_3$)$_3$), 31.9 (C(***C***H$_3$)$_3$), 31.9 (Ar***C***H$_2$Ar), 32.0 (***C***(CH$_3$)$_3$), 32.0 (***C***(CH$_3$)$_3$), 32.3 (***C***(CH$_3$)$_3$), 32.3 (***C***(CH$_3$)$_3$), 34.0 (Ar***C***H$_2$Ar), 34.1

(Ar***C***H_2Ar), 34.2 (Ar***C***H_2Ar), 34.4 (Ar***C***H_2Ar), 48.7 (***C***HCH_3), 74.4 (O***C***H_2CO), 125.2 (^{Ar}CH), 125.3 (^{Ar}CH), 125.4 (^{Ar}CH), 125.5 (^{Ar}CH), 125.9 (d, J = 2.0 Hz, ^{Ar}CH), 126.0 (^{Ar}CH), 126.1 (d, J = 2.0 Hz, ^{Ar}CH), 126.4 (^{Ar}CH), 127.1 (^{Ar}***C***-CH_2-C^{Ar}), 127.2 (^{Ar}***C***-CH_2-C^{Ar}), 128.8 (^{PH}CH), 133.5 (^{Ar}***C***-CH_2-C^{Ar}), 133.6 (d, J = 3.2 Hz, ^{Ar}***C***-CH_2-C^{Ar}), 135.2 (^{Ar}***C***-CH_2-C^{Ar}), 141.7 (^{Ar}***C***-tBu), 142.5 (^{Ar}C-tBu), 144.4 (^{PH}***C***-CH), 147.4 (^{Ar}***C***-tBu), 147.7 (d, J = 2.4 Hz, ^{Ar}***C***-tBu), 148.1 (^{Ar}***C***-OH), 150.3 (^{Ar}***C***-OH), 153.2 (Ar), 169.8 (***C***ONH).

^{31}P{^{1}H} NMR (δ (ppm), DMCO): -5.41.

HRMS (ESI-): calcul. for $C_{54}H_{67}NO_8P$ [M - H] 888.4665; found 888.4602.

5,11,17,23-Tetra-tert-butyl-27,28-dihydroxy-25- dihydroxyphosphoryl-26-(R)-N-(phenylethyl)aminocarbonylmethoxycalix[4]arene **4.5b**.

Yield 92 %.

M.p. = 106-105 ^{0}C. $[\alpha]_D^{20}$ -1.78 (c 1.205 g/100 mL, $CHCl_3$).

^{1}H NMR (δ (ppm), DMCO): 1.13 (s, 9H, t-Bu), 1.19 (s, 9H, t-Bu), 1.20 (s, 9H, t-Bu), 1.23 (s, 9H, t-Bu), 1.74 (d, 3H, $^{3}J_{HH}$ = 7.0 Hz, CHC***H***$_3$), 3.46 (m, 4H, ArC***H***$_2$Ar), 4.13 (d, 1H, $^{2}J_{HH}$ = 14.4 Hz, ArC***H***$_2$Ar), 4.26 (d, 1H, $^{2}J_{HH}$ = 13.5 Hz, ArC***H***$_2$Ar), 4.45 (d, 2H, $^{2}J_{HH}$ = 12.8 Hz, ArC***H***$_2$Ar), 4.61 (d, 2H, $^{2}J_{HH}$ = 12.8 Hz, ArC***H***$_2$Ar), 4.80 (d, 1H, $^{2}J_{HH}$ = 13.7 Hz, OC***H***$_2$CO), 5.04 (d, 1H, $^{2}J_{HH}$ = 13.7 Hz, OC***H***$_2$CO), 5.26 (q, 1H, $^{3}J_{HH}$ = 7.0 Hz, C***H***CH_3), 7.05 (d, 1H, $^{4}J_{HH}$ = 2.5 Hz, ArH), 7.10 (d, 2H, $^{4}J_{HH}$ = 2.4 Hz, ArH), 7.14 (d, 1H, $^{4}J_{HH}$ = 2.4 Hz, ArH), 7.16 (m, 3H, ArH) 7.22 (d, 1H, $^{4}J_{HH}$ = 2.4 Hz, ArH), 7.24 (m, 1H, ArH), 7.32 (m, 2H, ArH), 7.48 (m, 2H, PhH);

^{13}C{^{1}H} NMR (δ (ppm), DMCO): 21.3 (CH***C***H_3), 29.8 (***C***$(CH_3)_3$), 31.1 (C(***C***$H_3)_3$), 31.2 (C(***C***$H_3)_3$), 31.5 (C(***C***$H_3)_3$), 31.6 (C(***C***$H_3)_3$), 31.8 (Ar***C***H_2Ar), 32.1 (Ar***C***H_2Ar), 32.2 (Ar***C***H_2Ar), 32.6 (Ar***C***H_2Ar), 33.9 (***C***$(CH_3)_3$), 34.2 (2C, ***C***$(CH_3)_3$), 34.3 (***C***$(CH_3)_3$), 49.1 (***C***HCH_3), 73.4 (O***C***H_2CO), 125.22 (^{Ar}CH), 125.31 (^{Ar}CH), 125.38 (^{Ar}CH), 125.48 (^{Ar}CH), 125.81 (d, J = 2.0 Hz, ^{Ar}CH),

126.30 (^{Ar}CH), 126.34 (^{Ar}CH), 126.53 (^{Ar}CH), 126.97 (^{PH}CH), 127.41 (^{Ar}***C***-CH_2-C^{Ar}), 127.44 (^{Ar}***C***-CH_2-C^{Ar}), 127.52 (^{Ar}***C***-CH_2-C^{Ar}), 128.32 (^{Ar}***C***-CH_2-C^{Ar}), 128.49 (^{PH}CH), 132.66 (d, J = 3.2 Hz, ^{Ar}***C***-CH_2-C^{Ar}), 132.79 (d, J = 3.2 Hz, ^{Ar}***C***-CH_2-C^{Ar}), 133.09 (^{Ar}***C***-CH_2-C^{Ar}), 133.82 (^{Ar}***C***-CH_2-C^{Ar}), 142.35 (^{Ar}***C***-tBu), 142.90 (^{Ar}***C***-tBu), 143.04 (d, J = 8.9 Hz, ^{Ar}***C***-O-PO), 143.66 (^{PH}***C***-CH), 147.59 (^{Ar}***C***-tBu), 147.65 (d, J = 2.4 Hz, ^{Ar}***C***-tBu), 147.78 (^{Ar}***C***-OH), 149.36 (Ar), 147.78 (^{Ar}***C***-O), 149.36 (Ar C-OH), 151.4 (Ar), 170.3 (***C***ONH).

^{31}P{^{1}H} NMR (δ (ppm), DMCO): -5.37.

HRMS (ESI-): calcul. for $C_{54}H_{67}NO_8P$ [M - H] 888.4665; found 888.4612.

5,11,17,23-Tetra-tert-butyl-27-hydroxy-28-propoxy-25-di hydroxyphosphoryl-26-(R)-N-(phenylethyl)aminocarbonylmethoxycalix[4]arene **4.7a**.

Yield 92 %.

M.p. = 188-189 ^{0}C. $[\alpha]_D^{20}$ -2.49 (c 1.00 g/100 mL, $CHCl_3$).

^{1}H NMR (δ (ppm), CD_3OD): 0.64 (t, 3H, $^{3}J_{HH}$ = 7.5 Hz, $OCH_2CH_2C\boldsymbol{H}_3$), 0.86 (s, 9H, t-Bu), 0.97 (s, 9H, t-Bu), 1.33 (s, 9H, t-Bu), 1.35 (s, 9H, t-Bu), 1.50 (d, 3H, $^{3}J_{HH}$ = 7 Hz, CHC***H***$_3$), 2.02 (m, 2H, $OCH_2C\boldsymbol{H}_2CH_3$), 3.27 (d, 1H, $^{2}J_{HH}$ = 12.6 Hz, ArC***H***$_2$Ar), 3.32 (d, 2H, $^{2}J_{HH}$ = 12.7 Hz, ArC***H***$_2$Ar), 3.40 (d, 1H, $^{2}J_{HH}$ = 13.9 Hz, ArC***H***$_2$Ar), 3.48 (m, 1H, $OC\boldsymbol{H}_2CH_2CH_3$), 4.05 (m, 1H, $OC\boldsymbol{H}_2CH_2CH_3$), 4.11 (d, 1H, $^{2}J_{HH}$ = 14.9 Hz, OC***H***$_2$CO), 4.29 (d, 1H, $^{2}J_{HH}$ = 13.3 Hz, ArC***H***$_2$Ar), 4.39 (d, 1H, $^{2}J_{HH}$ = 12.7 Hz, ArC***H***$_2$Ar), 4.60 (d, 1H, $^{2}J_{HH}$ = 13.3 Hz, ArC***H***$_2$Ar), 4.62 (d, 1H, $^{2}J_{HH}$ = 13.9 Hz, ArC***H***$_2$Ar), 4.70 (d, 1H, $^{2}J_{HH}$ = 14.9 Hz, OC***H***$_2$CO), 5.19 (q, 1H, C***H***CH_3), 6.63 (d, 1H, $^{4}J_{HH}$ = 2.4 Hz, ArH), 6.67 (d, 1H, $^{4}J_{HH}$ = 2.4 Hz, ArH), 6.76 (d, 1H, $^{4}J_{HH}$ = 2.4 Hz, ArH), 6.78 (d, 1H, $^{4}J_{HH}$ = 2.4 Hz, ArH), 7.19 (m, 6H, PhH, OH), 7.31 (m, 1H, PhH),7.48 (m, 4H, PhH, ArH, NH).

^{13}C{^{1}H} NMR (δ (ppm), CD_3OD): 8.8 ($OCH_2CH_2\boldsymbol{C}H_3$), 21.3 ($CH\boldsymbol{C}H_3$), 22.6 ($OCH_2\boldsymbol{C}H_2CH_3$), 30.19 ($C(\boldsymbol{C}H_3)_3$), 30.21 ($C(\boldsymbol{C}H_3)_3$), 30.69 ($C(\boldsymbol{C}H_3)_3$), 30.73 ($C(\boldsymbol{C}H_3)_3$), 31.3 (Ar***C***$H_2$Ar), 31.8 (Ar***C***$H_2$Ar), 31.9 (Ar***C***$H_2$Ar), 33.3 (***C***$(CH_3)_3$),

33.4 (***C***$(CH_3)_3$), 33.5 (***C***$(CH_3)_3$), 33.6 (***C***$(CH_3)_3$), 49.1 (***C***HCH_3), 73.7 (O***C***$H_2CH_2CH_3$), 76.4 (O***C***H_2CO), 124.9 (^{Ar}CH), 125.0 (^{Ar}CH), 125.1 (^{Ar}CH), 125.2 (^{Ar}CH), 125.3 (^{Ar}CH), 126.1 (^{Ar}CH), 127.0 (^{PH}CH), 128.5 (^{PH}CH), 130.9 (^{Ar}***C***$-CH_2-C^{Ar}$), 131.4 (^{Ar}***C***$-CH_2-C^{Ar}$), 131.6 (^{Ar}***C***$-CH_2-C^{Ar}$), 131.7 (d, J = 3.2 Hz, ^{Ar}***C***$-CH_2-C^{Ar}$), 132.9 (d, J = 3.2 Hz, ^{Ar}***C***$-CH_2-C^{Ar}$), 133.0 (^{Ar}***C***$-CH_2-C^{Ar}$), 135.3 (^{Ar}***C***$-CH_2-C^{Ar}$), 135.7 (^{Ar}***C***$-CH_2-C^{Ar}$), 143.0 (^{Ar}***C***-tBu), 143.4 (d, J = 8.9 Hz, ^{Ar}***C***-O-PO), 143.6 (^{PH}***C***-CH), 145.9 (^{Ar}***C***-tBu), 146.2 (^{Ar}***C***-tBu), 146.3 (^{Ar}***C***-tBu), 149.3 (^{Ar}C-OH), 151.1 (^{Ar}C-O), 153.3 (^{Ar}C-O), 169.3 (***C***ONH).

^{31}P{^{1}H} NMR (δ (ppm), CD_3OD): -4.03.

HRMS (ESI): calcul. for $C_{57}H_{73}NO_8P$ [M - H] 930.5126; found 930.5070.

5,11,17,23-Tetra-tert-butyl-25-hydroxy-28-propoxy-27-di hydroxyphosphoryl-26-(R)-N-(phenylethyl)aminocarbonylmethoxycalix[4]arene **4.7b**.

Yield 93 %.

M.p. = 124-125 ^{0}C. $[\alpha]_D^{20}$ -8.11 (c 1.18 g/100 mL) 365 nm.

^{1}H NMR (δ (ppm), CD_3OD): 0.64 (t, 3H, $^3J_{HH}$ = 7.4 Hz, OCH_2CH_2C***H***$_3$), 0.86 (s, 9H, t-Bu), 0.97 (s, 9H, t-Bu), 1.32 (s, 9H, t-Bu), 1.35 (s, 9H, t-Bu), 1.50 (d, 3H, $^3J_{HH}$ = 7.0 Hz, CHC***H***$_3$), 3.27 (d, 1H, $^2J_{HH}$ = 12.6 Hz, ArC***H***$_2$Ar), 3.28 (d, 2H, $^2J_{HH}$ = 13.3 Hz, ArC***H***$_2$Ar), 3.40 (d, 1H, $^2J_{HH}$ = 13.9 Hz, ArC***H***$_2$Ar), 3.95 (m, 2H, OC***H***$_2CH_2CH_3$), 4.11 (d, 1H, $^2J_{HH}$ = 14.9 Hz, OC***H***$_2$CO), 4.29 (d, 1H, $^2J_{HH}$ = 13.2 Hz, ArC***H***$_2$Ar), 4.39 (d, 1H, $^2J_{HH}$ = 12.6 Hz, ArC***H***$_2$Ar), 4.60 (d, 1H, $^2J_{HH}$ = 12.6 Hz, ArC***H***$_2$Ar), 4.62 (d, 1H, $^2J_{HH}$ = 13.8 Hz, Ar***C***H_2Ar), 4.70 (d, 1H, $^2J_{HH}$ = 14.9 Hz, OC***H***$_2$CO), 5.19 (q, 1H, C***H***CH_3), 6.63 (d, 1H, $^4J_{HH}$ = 2.4 Hz, ArH), 6.67 (d, 1H, $^4J_{HH}$ = 2.5 Hz, ArH), 6.76 (d, 1H, $^4J_{HH}$ = 2.4 Hz, ArH), 7.78 (d, 1H, $^4J_{HH}$ = 2.4 Hz, ArH), 7.18 (m, 5H, PhH), 7.31 (m, 1H, PhH), 7.48 (m, 4H, PhH).

^{13}C{^{1}H} NMR (δ (ppm), CD_3OD): 8.76 (OCH_2CH_2***C***H_3), 21.3 (CH***C***H_3), 22.6 (OCH_2***C***H_2CH_3), 30.2 (C(***C***$H_3)_3$), 30.21 (C(***C***$H_3)_3$), 30.7 (C(***C***$H_3)_3$), 30.72

(C(***C***H_3)$_3$), 31.3 (***C***$(CH_3)_3$), 31.9 (***C***$(CH_3)_3$), 32.0 (***C***$(CH_3)_3$), 33.3 (Ar***C***H_2Ar), 33.4 (Ar***C***H_2Ar), 33.5 (Ar***C***H_2Ar), 33.6 (Ar***C***H_2Ar), 49.11 (***C***HCH_3), 73.7 (O***C***H_2CH_2), 76.4 (O***C***H_2CO), 124.8 (^{Ar}CH), 124.8 (^{Ar}CH), 124.9 (^{Ar}CH), 124.9 (^{Ar}CH), 125.1 (^{Ar}CH), 125.2 (^{Ar}CH), 125.4 (^{Ar}CH), 125.8 (^{Ar}CH), 126.1 (^{Ar}CH), 126.6 (^{Ar}CH), 127.3 (^{Ar}CH), 127.4 (^{Ar}C), 128.5 (^{PH}CH), 129.5 (^{Ar}***C***-CH_2-C^{Ar}), 132.2 (^{Ar}***C***-CH_2-C^{Ar}), 131.5 (d, J = 3.2 Hz, ^{Ar}***C***-CH_2-C^{Ar}), 132.2 (d, J = 3.2 Hz, ^{Ar}***C***-CH_2-C^{Ar}), 132.6 (^{Ar}***C***-CH_2-C^{Ar}), 134.9 (^{Ar}***C***-CH_2-C^{Ar}), 135.4 (^{Ar}***C***-CH_2-C^{Ar}), 141.8 (^{Ar}***C***-tBu), 143.0 (d, J = 8.9 Hz, ^{Ar}***C***-O-PO), 144.0 (^{Ar}***C***-tBu), 146.4 (d, J = 2.4 Hz, ^{Ar}***C***-tBu), 146.4 (^{PH}***C***-CH), 147.9 (^{Ar}***C***-tBu), 150.0 (^{Ar}***C***-OH), 151.2 (^{Ar}***C***-O), 153.3 (^{Ar}***C***-CH_2-C^{Ar}), 169.2 (***C***ONH).

^{31}P{^{1}H} NMR (δ (ppm), CD_3OD): -4.03.

HRMS (ESI-): calcul. for $C_{57}H_{73}NO_8P$ [M - H] 930.5126; found 930.5070.

CONCLUSIONS

1. The effective methods of synthesis of new phosphorus-containing calix[4]arenes, phosphonic and phosphoric acid and phosphine, including phosphino-ferrocenes were explored and efficiency of obtained catalyst were investigated in asymmetric catalysis in five different model reactions. Calix[4]arene phosphoric acids were for the first-time used in asymmetric organocatalysis.

2. It was shown that synthetic sequence using Mitsunobu reaction is a preparative method for the synthesis of new mono and diphosphine ferrocenyl supramolecular ligands based on calix[4]arene. Using the proposed method three new ligands were synthesized and their structures were proved by spectroscopic methods.

3. The catalytic properties of novel mono- and diphosphine supramolecular ligands were checked in model reactions: Suzuki-Miyaura and Tsuji-Trost (high yields of products achieved (up to 99%) in the both model reactions and high enantioselectivity (ee up to 86%) in the Tsudji-Trost reaction).

4. Using regioselective stepwise alkylation and phosphorylation methods for modification of phenolic hydroxyls of calix[4]arene, a series of six new inherently chiral calix[4]arene phosphoric acid in enantiomerically pure form were synthesized and their properties tested three model reactions (aza-Diels-Alder reaction: yield up to 95%, ee up to 21%; aza-Mukaiyama: yield up to 89%; asymmetric epoxides ring opening: yield up to 92%, ee up to 25%).

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CONTENU PRINCIPAL

Dans **l'introduction** le cadre général et les objectifs de l'étude sont présentés.

Le **premier chapitre** est une étude bibliographique présentant la synthèse et l'utilisation en catalyse des différents calix[4]arènes phosphorés. Tout d'abord sont présentés les principales méthodes de synthèse des diverses classes des calix[4]arènes phosphorés avec une analyse des principales stratégies de synthèse. Dans la dernière section du chapitre sont présentées les travaux utilisant des composés calix[4]arènes phosphorés en catalyse en insistant sur la dépendance structure-activité de certains de ces composés dans des réactions de catalyse métallique. En conclusion sont identifiés des domaines peu ou pas développés de la catalyse avec des calix[4]arènes phosphorés comme la catalyse asymétrique ou l'organocatalyse.

La **deuxième chapitre** est consacrée à la synthèse des ligands supramoléculaires basés sur un squelette calix[4]arène contenant des fragments ferrocènyl-phosphines chiraux (Fig. 1). Le chapitre commence par un rappel bibliographique sur l'importance des phosphines chirales ferrocéniques en catalyse asymétrique au laboratoire et dans l'industrie (hydrogénation des composés carbonylés, des alcènes, réactions de couplage croisé, etc.).

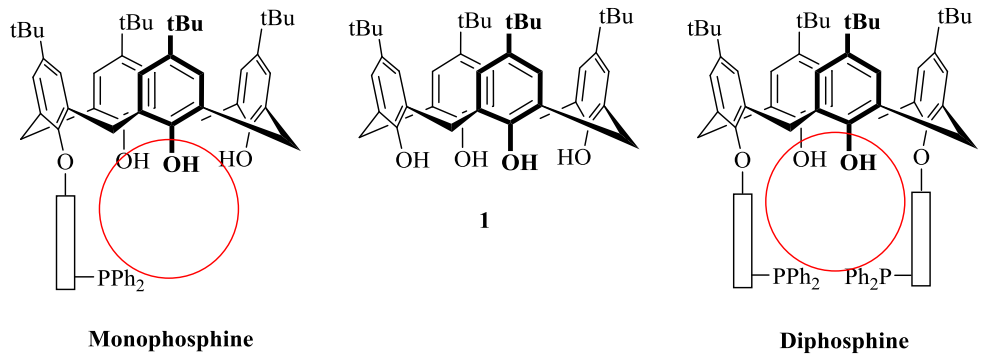


Figure. 1. Ligands mono- et diphosphine supramoléculaires à la base de calix[4]arènes.

La deuxième partie du chapitre est consacrée à la conception de fragments de phosphines ferrocéniques chirales liés de façon covalente à des macrocycleS calix[4]arène.

Pour accomplir cette tâche, il a été synthétisé une série de composés **3**-**5** à partir de l'alcool énantiomériquement pur **2** par action d'acide fort, l'acide tétrafluroborique(Schéma 1).

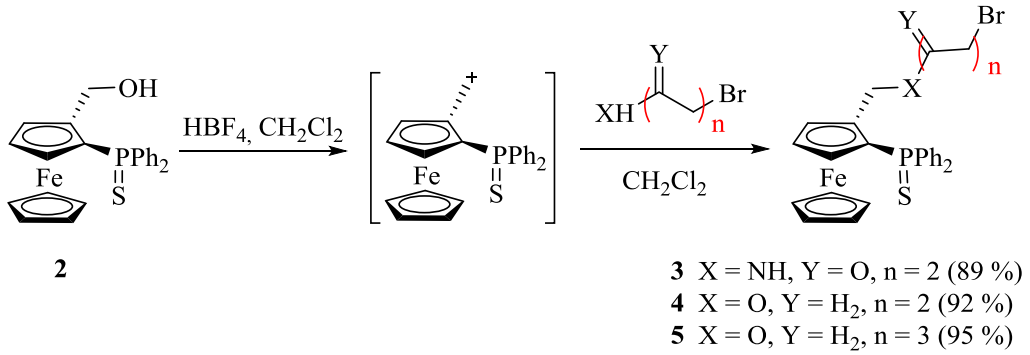
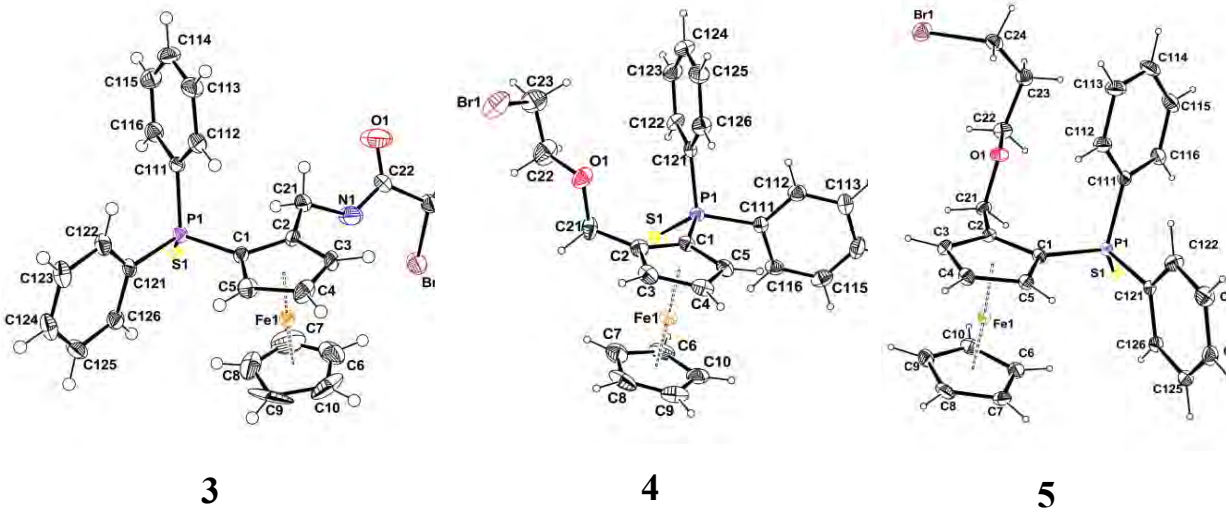


Schéma 1. Synthèse des composés **3**-**5**.



3 **4** **5**

Figure. 2. La structure moléculaire des composés **3**-**5**.

Les différents thiophosphines ferrocéniques chirales **3-5** (Fig. 2) ont été testés dans le greffage sur la couronne inférieure d'un squelette macrocyclique de calix[4]arène, en utilisant divers systèmes alkylants connus des hydroxyles phénoliques: NaOH dans un mélange DMSO-eau, CH_3ONa dans du DMF absolu, NaH dans du DMF absolu, $Ba(OH)_2$ dans du DMF absolu et K_2CO_3 dans de l'acétonitrile. Cependant dans toutes les conditions utilisées, la réaction n'a été observée. Une raison possible est la faible réactivité electrophile des réactifs et le fort encombrement stérique des substrats calixaréniques. Dans nombre de réaction de greffage, la dégradation des composés ferrocéniques a été observée.

Cependant en utilisant la réaction de Mitsunobu, il a été possible de greffer efficacement les fragment thiophosphines ferrocéniques à la plateforme calix[4]arène. Ainsi, la variation de la température permet d'obtenir sélectivement le produit mono- ou di-substitué avec un excellent rendement et une excellent sélectivité (Schéma 2).

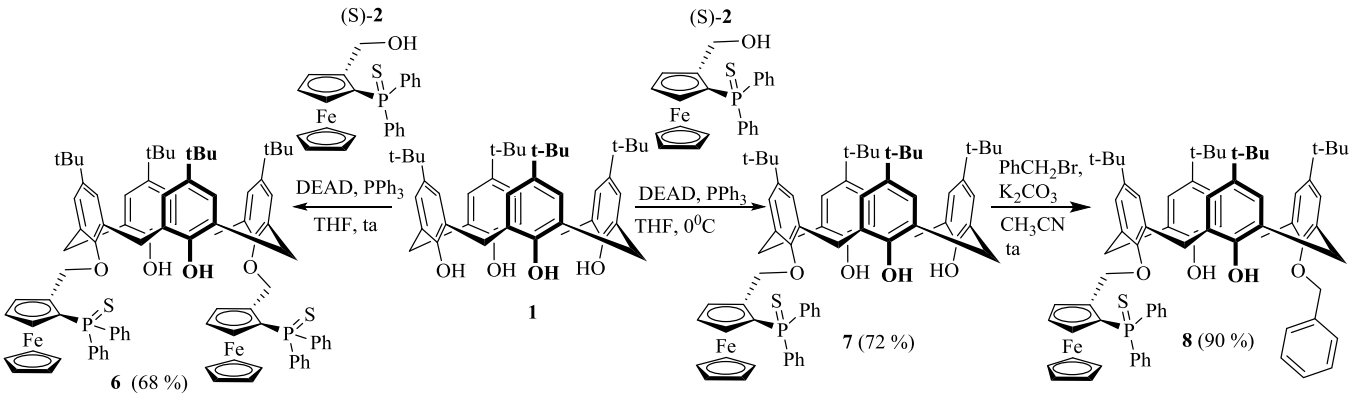
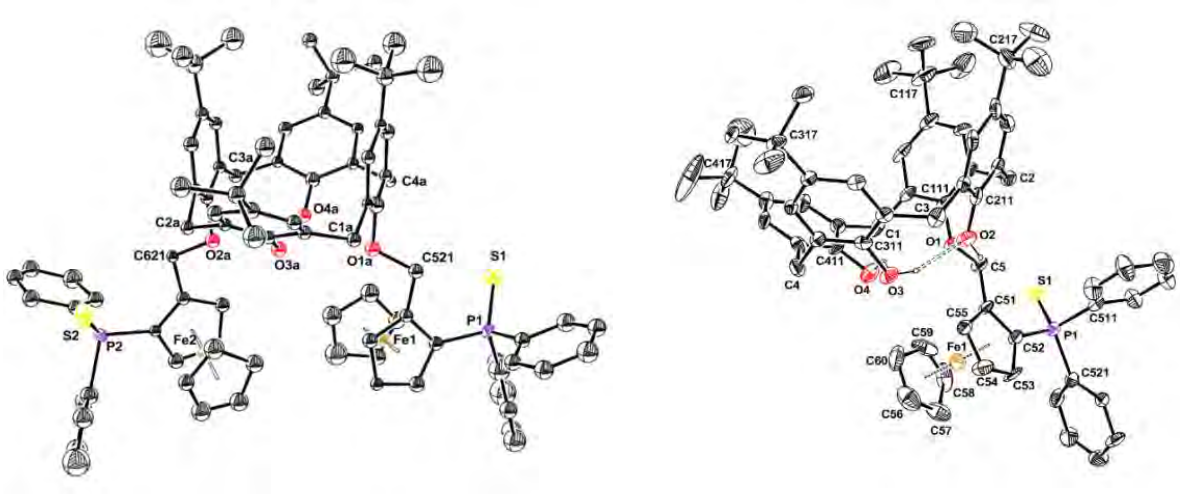


Schéma 2. Synthèse des composés **6-8**.

Les phosphines sont obtenues dans la conformation de *cône*, et la réaction de greffage ne conduit pas à une racémisation même partielle des entités ferrocéniques comme confimé par analyse RMN et étude structurale par diffraction des rayons X sur monocristaux (Fig. 3).



6 **7**

Figure 3. Structure moléculaire des composés **6** et **7**.

Pour déprotéger les fonctions phosphine des thiophosphines ferrocéniques plusieurs approches expérimentales ont été utilisées : utilisation de nickel de Raney ou de phosphine - hexamethylene phosphoramine $P(N(CH_3)_2)_3$. Toutes les tentatives de déprotection des composés **6-8** par le nickel de Raney ont échoué et ont conduit à la décomposition en calix[4]arène **1** et (2-diphénylthiophosphinoferrocènyl)-méthanol **2**. L'utilisation de $P(N(CH_3)_2)_3$ dans du toluène au reflux pendant 10 heures, permet d'obtenir les phosphines libres correspondantes avec des de bons rendements (87-92 %) (Schema 3).

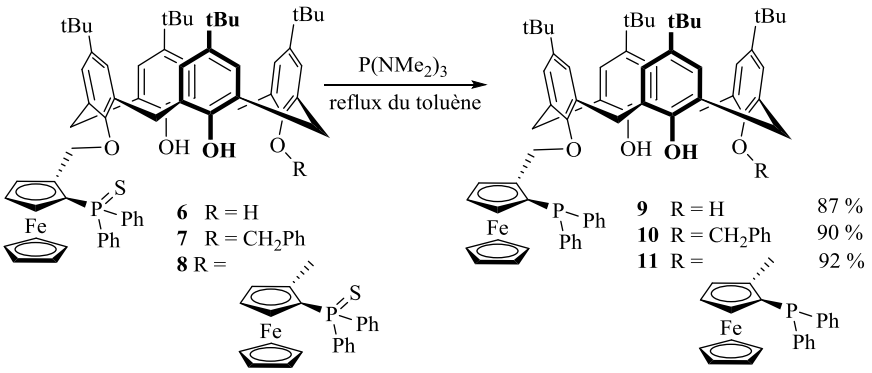


Schéma 3. Synthèse des composés **9-11**.

Les propriétés catalytiques des ligands monophosphine chiraux synthétisés **9** et **10** ont été testés dans une réaction de couplage de Suzuki-Miyaura. La conversion est complète et un bon rendement est observé au bout de 24 heures, mais l'excès énantiomérique du 2-méthyl-1,1'-binaphtalène était très faible (moins de 5%). Contrairement aux attentes, les groupes hydroxyle libres sur le bord inférieur des ligands macrocycliques n'ont pas un effet positif sur la catalyse en créant des liaisons hydrogène avec le substrat acide boronique.

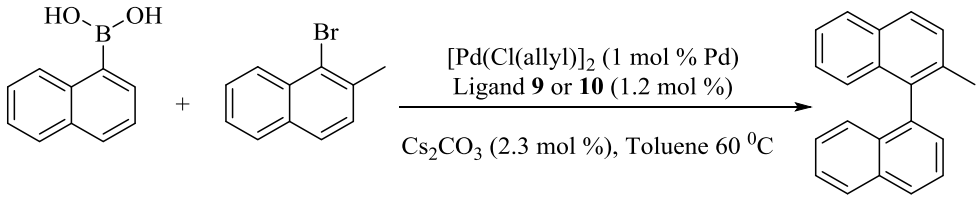


Schéma 4. Réaction de couplage croisé de Suzuki-Miyaura en utilisant des ligands **9-10**.

Le ligand diphosphine **11** a été testé dans le réaction de substitution allylique asymétrique du 1,3-diphénylprop-2-enyl acetate avec l'anion diméthylmalonate (Schéma 5). Une conversion totale et de bons rendements

sontobtenus quel que soit le sel d'acétate qui a été utilisé conjointement avec la probase N,O-bis-(triméthylsilyl) acétamide (BSA).

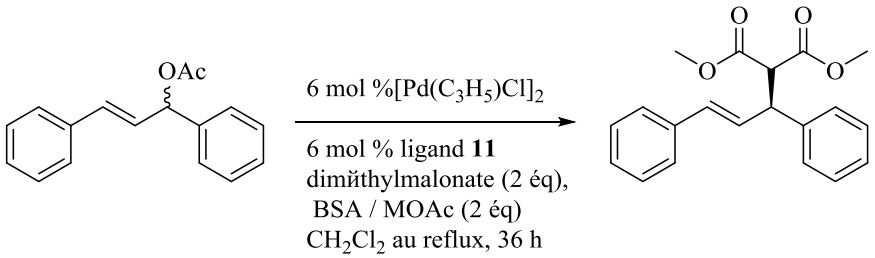


Schéma 5. Réaction Tsuji–Trost utilisant le ligand **11**.

Cependant, l'excès énantiomérique du produit est fortement dépendant du cation de métal alcalin. Cela peut être expliqué par la chélation du cation dans le domaine des groupes hydroxyle phénoliques. La meilleure énantioselectivité a été obtenue avec l'utilisation de l'acétate de potassium (Tableau 1).

Tableau 1

Résultats des réactions de substitution allylique asymétrique catalytique

№	**Base**	**Rendement, %**	***ee*, %**
1.	CH_3COOLi/BSA	86	14
2.	CH_3COONa/BSA	76	25
3.	CH_3COOK/BSA	75	86
4.	CH_3COOK/BSA (+ 1.2 eq 18-crown-6)	86	32
5.	CH_3COOCs/BSA	88	71

L'excès énantiomérique de 86% est, à notre connaissance, le meilleur obtenu par substitution allylique asymétrique en utilisant des ligands calix[4]arènique.

La troisième chapitre est consacrée à la synthèse des acides phosphoniques intrinsèquement chiraux par remplacement par étapes des hydroxyles sur la couronne inférieure du macrocycle et ses premières applications en organocatalyse.

La synthèse commence à partir du calix[4]arènes amide **12** intrinsèquement chiral énantiomériquement pur possédant un positionnement précis des substituants sur la couronne macrocyclique inférieure et obtenu en deux étapes à partir du calix[4]arène **1**.

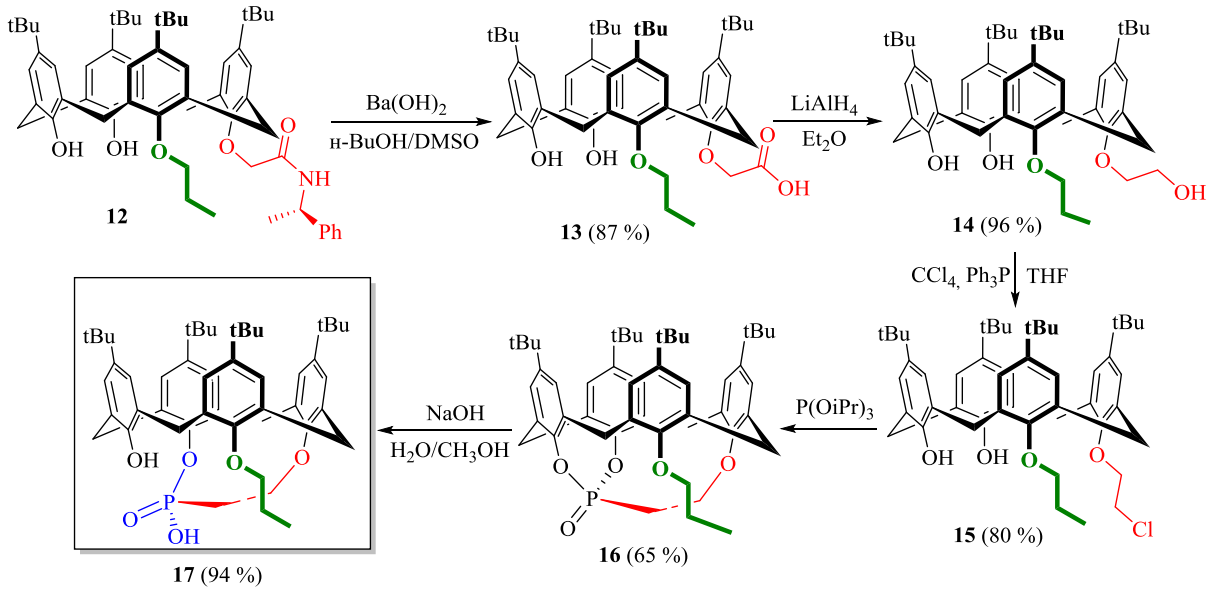


Schéma 6. Synthèse de l'acide phosphonique **17** intrinsèquement chiral calix[4]arénique sous forme énantiomériquement pure.

La copule chirale du composé chiral amide **12** énantiomériquement pur a été éliminée par hydrolyse pour obtenir l'acide carboxylique calix[4]arène intrinsèquement chiral **13**, Après réduction de l'acide **13** par action de l'hydrure de lithium aluminium, on obtient l'alcool **14** correspondant, qui est ensuite halogéné pour donner le chlorure **15**.

La phosphorylation du chlorure **15** par le triisopropylphosphite commence la cascade de réactions : réarrangement d'Arbuzov et réesterification de l'acide

phosphonique exclusivement en phosphonate cyclique **16** (Fig. 4.). L'hydrolyse régiosélective du phosphonate **16** dans des conditions douces avec un rendement quantitatif a permis d'obtenir le mono-ester d'acide phosphonique **17**, où seulemnt une liaison C-O-P liaison a été hydrolysée (Schéma 6, Fig. 4.). Pendant la synthèse, la conformation *cône* du squelette calix[4]arène est préservé (Fig. 4).

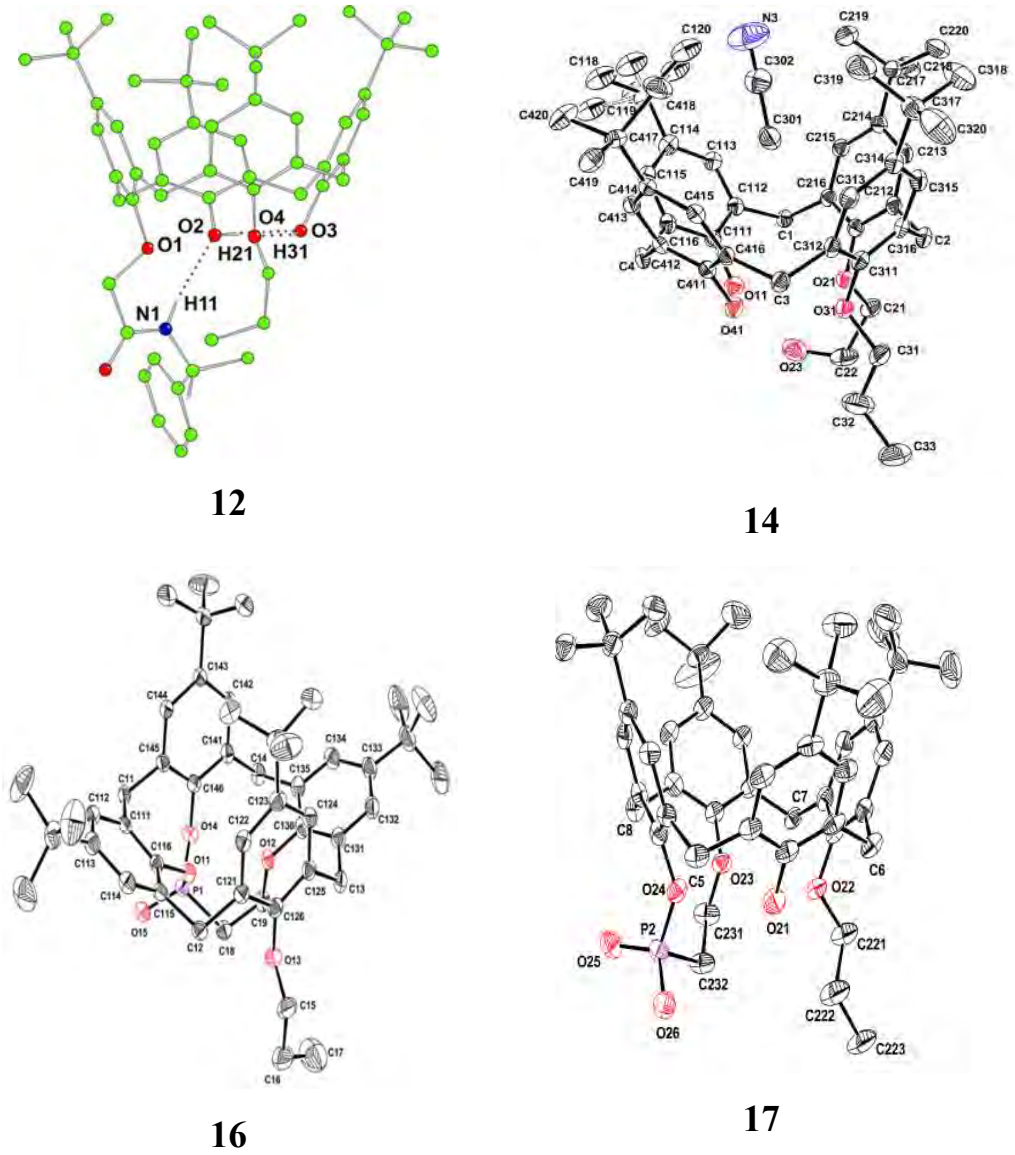


Figure. 4. Structure moléculaire des composés **12**, **14** et **16-17**.

Les propriétés organocatalytiques de l'acide **16** ont été testées dans les réactions d' aza-Diels–Alder (Schéma 7), aza-Mukaiyama (Schéma 8) et

d'ouverture asymétrique des époxydes symétriques (Schéma 9) (sur Schéma: AH - terme générique des acides phosphoriques chiraux).

L'utilisation de l'acide **17** dans la réaction d'aza-Diels–Alder conduit au produit désiré avec de bon rendements (56-95%) pour presque tous les substrats. Seuls les substrats avec des groupes isopropyle en *ortho* de l'aniline ne régissent pas, probablement pour des raisons stériques. Les énantioselectivités sont dans tous le cas relativement faible (*ee* 5-21%). Le meilleur résultat – *ee* 21% est obtenu pour la N-phényl benzylidène imine moins stériquement encombré. Les résultats obtenus peuvent être expliqués par l'encombrement stérique du centre catalytique, qui entrave la coordination efficace du substrat au catalyseur.

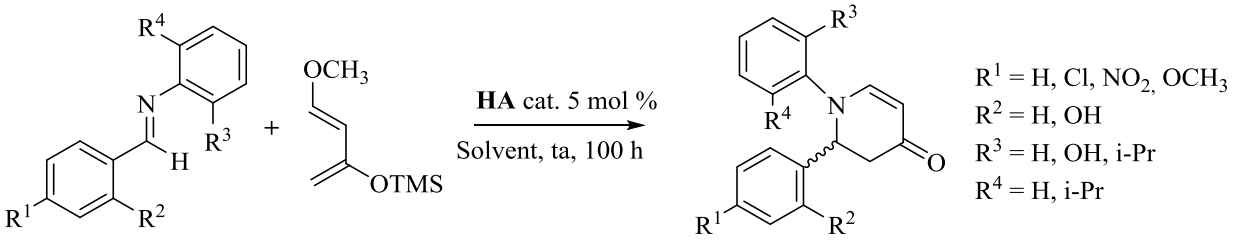


Schéma 7. Réaction aza-Diels–Alder catalysee par acide chiral.

Un résultat inattendu a été d'obtenir lors une réaction d'aza-Mukaiyama des produits de crotonisation au lieu des produits de condensation aldolique normale dans le cas de presque toutes les imines testées (Schéma 8). Nous avons mené des travaux pour obtenir d'autres informations sur le mécanisme de cette réaction, en analysant les mélanges réactionnels obtenus à conversion incomplète de l'imine.

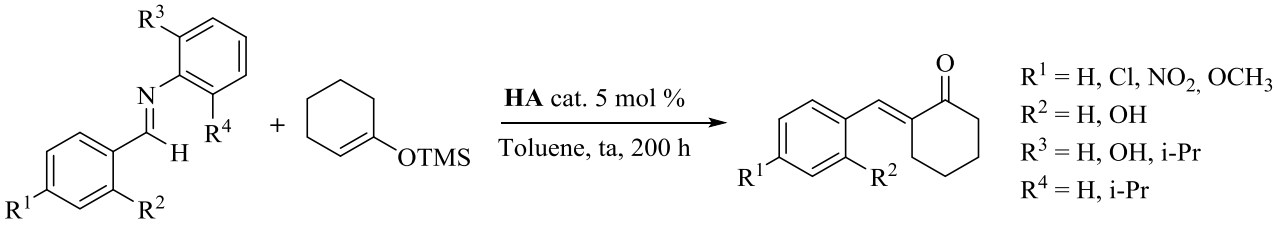


Schéma 8. Aza-Mukaiyama catalysée par des acides chiraux.

Au bout de 100 heures de réaction, la conversion était de 62 % avec dans le mélange la 2-((phenylamino)méthyl)cyclohexanone et (*E*)-2-phenylméthylidencyclohexanone dans un rapport 72:28. Pour la 2-((phenylamino)méthyl) cyclohexanone, le rapport entre les deux diastéréoisomères *syn* et *anti* est 87:13. Les données suggèrent que la première étape de la catalyse est la formation attendue de la 2-((phenylamino)méthyl) cyclohexanone qui est ensuite converti dans le milieu acide en (*E*)-2-phenylmethylidencyclohexanone par élimination diastereosélective de l'aniline (dans les spectres RMN ^{1}H, la présence du distéréoisomère Z n'est pas observé) qui n'a pas été précédemment rapporté.

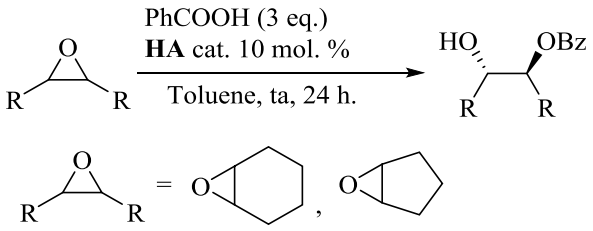


Schéma 9. Ouverture asymétrique des époxydes symétriques catalysée par un acide chiral.

L'ouverture asymétrique d'époxydes symétriques par l'acide benzoïque (Schéma 9) a été mené en présence de l'acide **17** comme organocatalyseur. La réaction a liau avec un rendement élevé (rendement 71-75 %), mais avec une faible énantiosélectivité (*ee* du produit=11-18%).

L’activité catalytique et la sélectivité faibles suggère que le site actif de l’acide **17** est bloqué partiellement par une liaison hydrogène intramoléculaire (Fig. 7).

La quatrième chapitre est consacrée à la synthèse d’acides phosphoriques calix[4]arèniques de nombre et de position différents des substituants sur la couronne inférieure du macrocycle macrocyclique dans la but de faire varier leurs propriétés amphiphiles (Fig. 5). La première partie du quatrième chapitre est consacré à la conception d'acides phosphoriques calix[4]aréniques de type ABHH intrinsèquement chiraux par substitution sur les couronnes inférieures. La stratégie de synthèse commence par l'alkylation du calix[4]arène **1** par le N-(1'-phenylethyl)bromoacétamide énantimériquement pur ((R) ou (S)). Une phosphorylation ultérieure régiosélective du calix[4]arène monosubstitué **18** par le diéthylchlorophosphate dans l'acétonitrile anhydre et en présence d'une base K_2CO_3 fournit le phosphate disubstitué distalement **19** (Schéma 10).

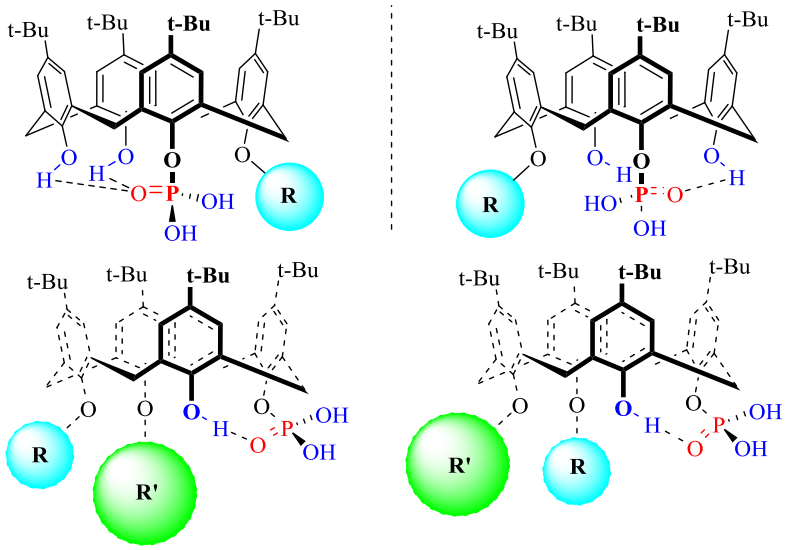


Fig.. 5. Acides phosphoriques cible avec la possibilité de faire varier les propriétés amphiphiles du calix[4]arène.

Un réarrangement phosphotropique du composé **19** en milieu basique permet d'obtenir les produits disubstués proximalement **20a** (Fig. 6) et **20b** (Schéma 10).

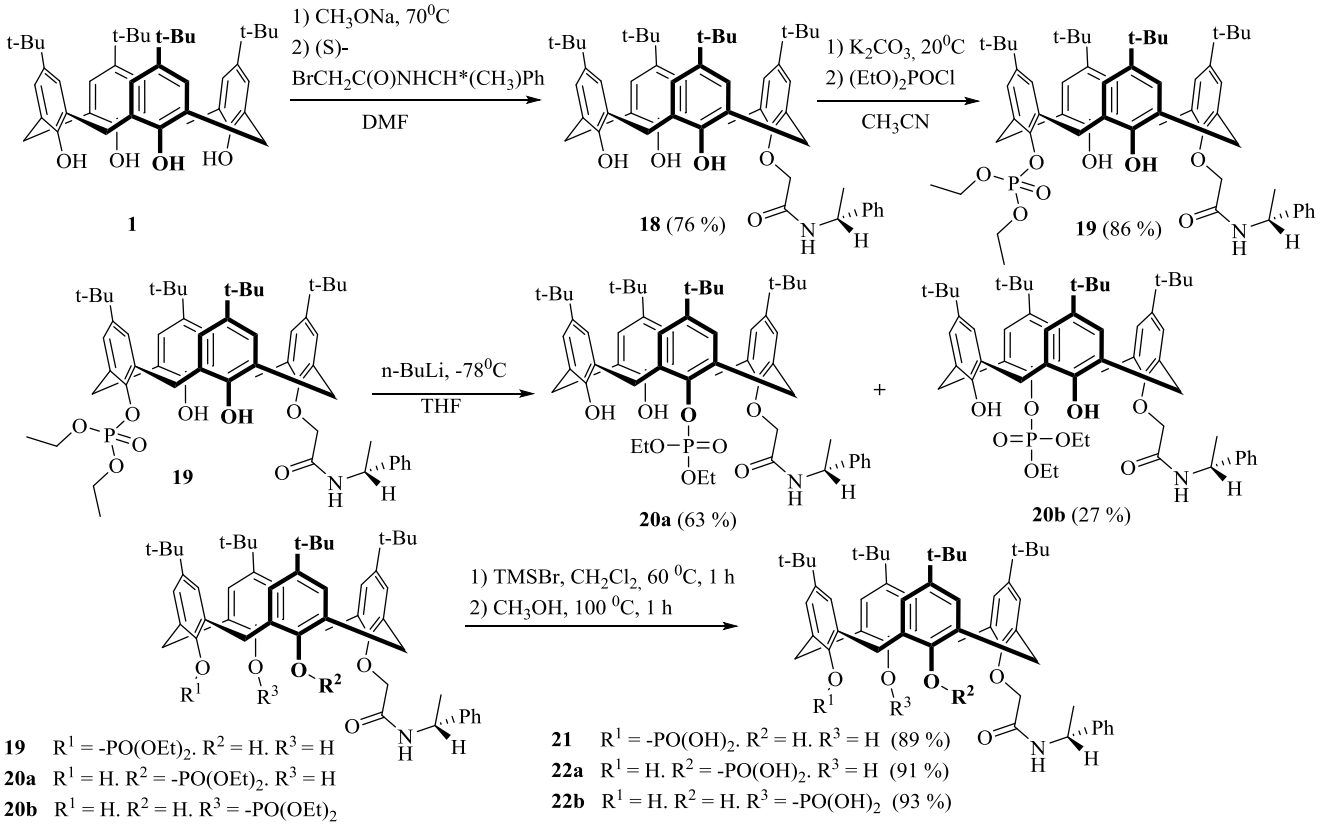


Schéma 10. Synthèse d'acides phosphoriques calix[4]aréniques de type de substitution sur la couronne macrocyclique inférieure ABHH.

Le réarrangement phosphotropique se fait avec une certaine diastéréosélectivite due au groupe inducteur chiral supplémentaire (*de* 43%) (Schéma 10). Le mécanisme proposé pour réarrangement implique une attaque nucléophile de l'anion phénolate généré sur l'atome de phosphore suivi par une migration du groupe phosphoré via un intermédiaire pentacoordiné transitoire **IIa-b** (Schéma 11), qui est détecté par RMN ^{31}P. Pour cela, la réaction est effectuée dans du THF-d_4 sous argon dans untube RMN et le signal RMN des intermédiaires transitoires **IIa-b** sont observés dans la plage de -4,7 à -5,1 ppm.

IIIa-b est thermodynamiquement favorisé en raison de la stabilisation supplémentaire de la charge négative par liaisons hydrogène par le groupe hydroxyle en position proximale. Dans les phénolates **Ia-b**, la possibilité d'une telle stabilisation est absente.

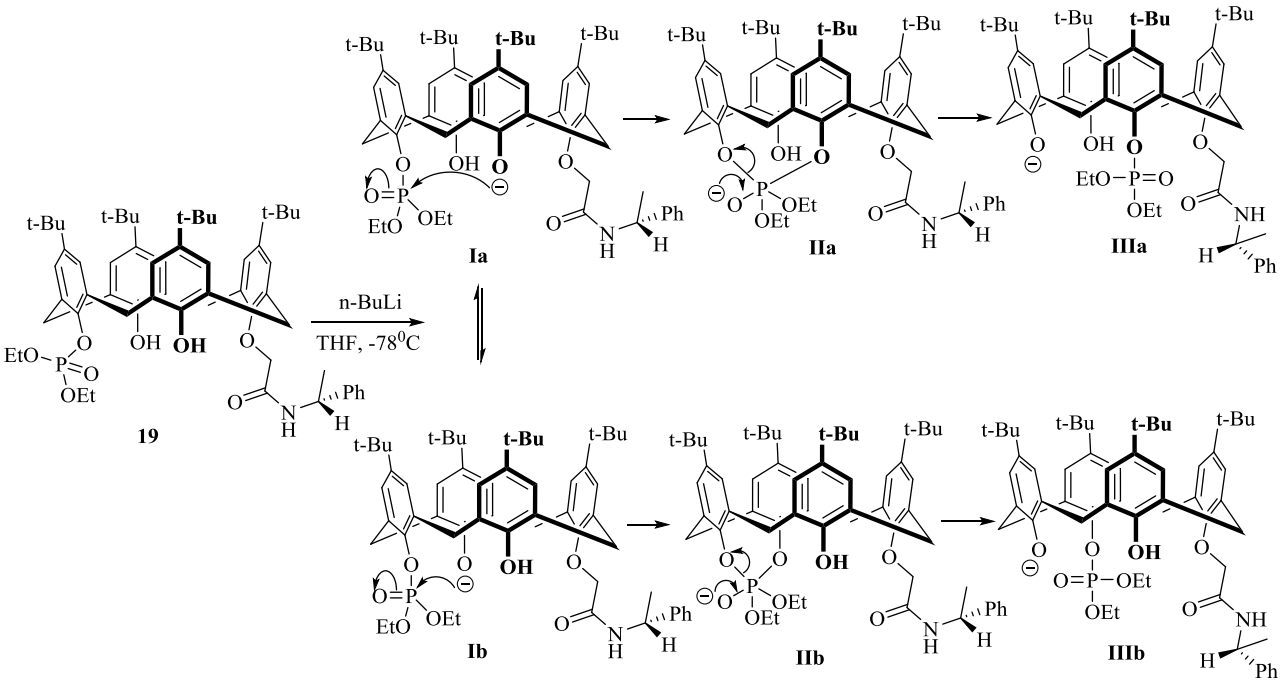
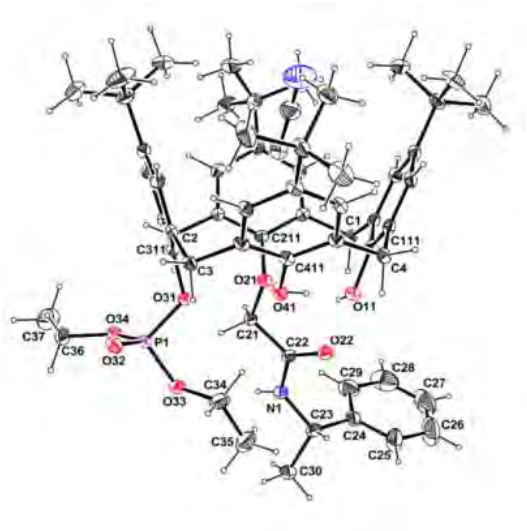


Schéma 11. Mécanisme proposé de réarrangement phosphotropique.

L'hydrolyse sélective des phosphates **20-21** se fait au reflux du dichlorométhane en présence TMSBr sous argon pendant une heure(Schéma 10). Après élimination des composants volatils, le résidu solide est agité dans du methanol bouillant. L'évaporation du solvant sous vide permet obtenir des acides **21** et **22a-b** avecune pureté de 95%.



Des. 6. La structure moléculaire de composé **22a**.

Les propriétés organocatalytique des acides **21** et **22a-b** ont été testées dans les réactions d'aza-Diels–Alder (Schéma 7) (rendement: 63-90%; *ee*: 16% pour **22a**, 11% pour **22b**) et d'ouverture asymétrique d'époxydes symétriques (Schéma 9) (rendement: 89-92%; *ee*: 5% pour **22a**, 5% pour **22b**). Dans les réactions d'aza-Diels–Alder, la sélectivité la plus élevée est observée pour les substrats les moins encombrés stériquement qui ne possèdent pas de groupes de coordination supplémentaires. L'utilisation d'un substrat avec d'autres groupes de coordination hydroxy entraîne une diminution de sélectivité (*ee* =5%). L'tilisation d'un acide non intrinséquement chirad **21** dans les deux mêmes réactions permet d'ontenir les produits désirés mais avec une très faible énantioselectivité (*ee* <5%). La faible sélectivité de ces acides est probablement lié à la présence de deux groupes hydroxyles supplémentaires. Il est en effet probable que, dans la solution les acides **21** et **22a-b** sont dans la même conformation fermés dans laquelle le groupe hydroxyle de l'acide phosphorique est bloqué par liaison hydrogène intramoléculaire (Fig.. 7).

La deuxième partie du quatrième chapitre est consacré à la synthèse d'acides phosphoriques calix[4]aréniques intrinsèquement chiraux avec type de substitution ABCH sur les couronnes inférieures. L'utilisation du précurseur

chiral **12** sous forme énantiomériquement pure traité par le diethylchlorophosphate dans des conditions douces (K_2CO_3 comme base dans l'acétonitrile à 0 °C) permet d'obtenir uniquement la monophosphorylation. Le mélange de composés est alors séparé par chromatographie sur colonne de silice fornissant des isomères purs. L'hydrolyse sélective des esters alkyliques de l'acide phosphorique, les phosphate **23a** ou **23b** est réalisée pendant 3 heures dans une solution de dichlorométhane au treflux et en présence Tde MSBr sous argon (Schéma 12). Après élimination des composants volatils, le résidu solide est agité dans du methanol au nreflux pendant 5 heures. L'élimination du solvant sous vide permet obtenir les acides **24a-b** avec 95% de pureté.

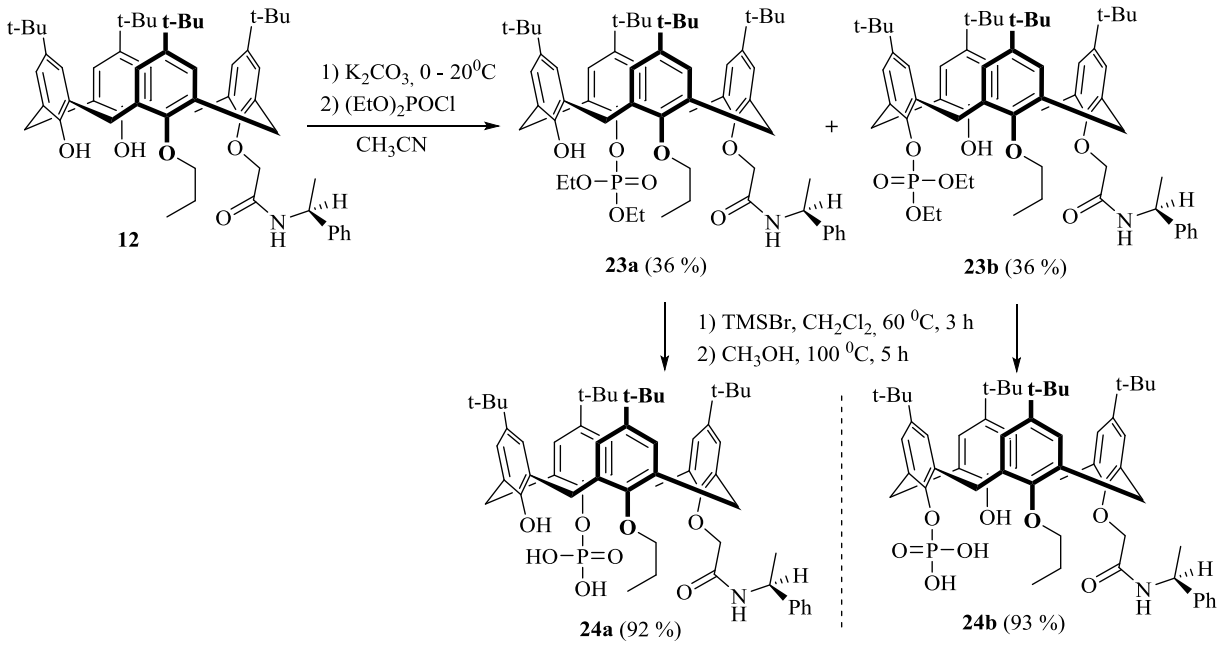
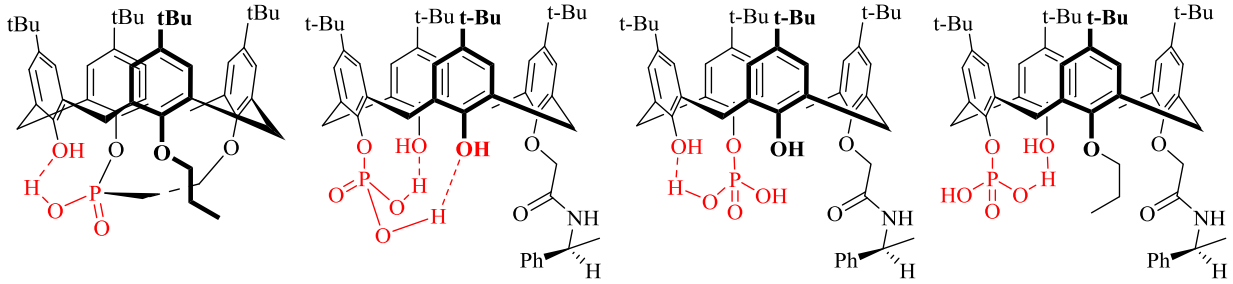


Schéma 12. Synthèse d'acides phosphoriques calix[4]aréniques intrinsèquement chiraux avec un type de substitution ABCH sur les couronnes inférieures**.**

Les propriétés organocatalytiques des acides **24a-b** ont été testées dans les réactions d'aza-Diels–Alder (Schéma 7) (rendement: 57-91%; *ee*: 27% avec **24a**, 11% avec **24b**) et d'ouverture asymétrique des époxydes symétriques (Schéma 9) (rendement: 59-65%; *ee*: 25% pour **24a**, 5% pour **24b**). Dans les

réactions d'aza-Diels–Alder, la sélectivité la plus élevée est observée en utilisant **24a** pour les substrats à moindre encombrement stérique qui ne comprennent pas des groupes de coordination supplémentaires. L'utilisation d'un substrat avec des groupes de coordination supplémentaires hydroxyles à proximité du centre d'interaction entraîne une baisse d'énantiosélectivité (*ee* 5%) dans le cas de **24a** et une augmentation d'énantiosélectivité (*ee* 11%) dans le cas de **24b**. Ce fait suggère que la position relative des groupes fonctionnels spécifiques de **24b** affecte la coordination du substrat au catalyseur et conduit à une meilleure sélectivité dans la formation des produits de réaction.

La comparaison des performances catalytiques des acides **24a-b** (type de substitution ABCH) des acides **22a-b** (type de substitution ABHH) et des acides **21** (type de substitution AHBH) montre un plus grand effet inhibiteur des deux groupes hydroxyle supplémentaires sur la sélectivité pour différentes réactions catalytiques par rapport à un groupe hydroxyle.



17 **21** **22b** **24b**

Figure. 7. Hypothétiques structures«fermées» pour acides **17-24**.

La cinquième chapitre de la thèse est une partie expérimentale, qui décrit les méthodes de synthèse des composés décrits dans le travail, et une description de leurs caractéristiques spectrales et physiques.

CONCLUSIONS

Les méthodes efficaces de synthèse de nouveaux calix[4]arenes phosphorés, acides phosphoniques et phosphoriques, etphosphines, y compris ferrocénique, ont été développé.

Ces divers composés ont été testés dans diverses réactions modèles différentes. Les acides phosphoriques à base de calix[4]arène ont été utilisé pour la première fois à notre connaissance en organocatalyse asymétrique.

1. Il est montré que la séquence de synthèse utilisant la réaction de Mitsunobu est un procédé de préparation pour la synthèse de nouveaux ligands mono et diphosphines supramoléculaires à base de calix[4]arène. En utilisation de la méthode proposée trois nouveaux ligands ont été synthétisés et leur structure déterminée.

2. Les propriétés catalytiques des nouveaux ligands mono- et diphosphine ont été étudiés dans les réactions modèle: Suzuki-Miyaura et Tsuji-Trost. Les rendements obtenus sont élevés (99%) dans les deux réactions modèles et les énantiosélectivités importantes (ee jusqu'à 86%) dans la réaction Tsuji-Trost.

3. En utilisant les méthodes régiosélectives d'alkylation et de phosphorylation de hydroxyles phénoliques, nous avons synthétisé une série de six nouveaux acides phosphoriques calix[4]aréniques intrinsèquement chiraux sous forme d'énantiomère pur et nous les avons testés comme organocatalyseurs dans trois réactions modèles différentes avec divers substrats (réaction aza-Diels –Alder : rendement jusqu'à 95%, *ee* jusqu'à 21%; aza-Mukayiama : rendement jusqu'à 89%; ouverture asymétrique d'époxydes symétriques : rendement jusqu'à 92%, *ee* jusqu'à 25%).