This chapter describes the quest for acetylene-expanded asymmetric macrocycles, comprising a phosphorus atom at one apex and another heteroatom, selected from sulfur, silicon and boron, at the other. Synthetic attempts towards these P,S-, P,Si- and P,B-macrocycles involve a direct cyclization approach and several stepwise methodologies via various potential macrocyclic precursors. In the end, bisethynylbenzene, bearing two different protecting groups at both acetylene moieties turned out to be a valuable building block in the synthesis of the target macrocycles. Unfortunately, the final ring-closing reaction was not optimized and the electronically potentially interesting macrocycles were not isolated.
6 | Towards Acetylene-Expanded Phosphaborins and Related Macrocycles

6.1. Introduction

The quest for novel π-conjugated frameworks for application in electronic devices has recently uncovered phosphole rings as valuable building blocks in π-systems.\[1\] Their genuine electronic structure combines a low but not negligible degree of aromaticity, participation of the exocyclic σ*(P–R) orbital in the conjugation and presence of a reactive phosphorus atom. This combination enables efficient conjugation over the diene moiety and at the same time offers a handle to fine-tune the photophysical properties of the π-system by reaction at the λ^3σ^3-phosphorus centre.\[2\] In addition thereto, the phosphorus atom lacking any chemical modifications, thus bearing a lone pair, may act as an electron donor to the π-system, depending on the hybridization of the phosphorus atom and the overlap of its lone pair with the mainly carbon-based π-orbitals.\[3\]

Despite this plethora of possibilities, the incorporation of phosphorus in π-conjugated frameworks has only sparsely extended beyond phospholes. Among the non-phosphole phosphorus-based π-systems, the phosphaborins (1; Figure 6.1) exhibit intriguing properties.\[4\] The electron-accepting nature of the boron atom, bearing an empty pz-orbital, combined with the potential electron-donating properties of the phosphorus centre, bearing a lone pair, offers the foundation for intriguing photophysical properties.

A different strategy that has been used over the years to create novel compounds with intriguing properties is \textit{acetylenic scaffolding}, which targets the ‘extension’ of C–C single bonds by incorporation of one or two acetylene moieties creating C(–C≡C)\_\_–C fragments (n = 1 or 2).\[5\] So far, numerous phosphorus-containing compounds have been extended with acetylene units (termed ‘phosphapericyclines’), but their potential as electronically interesting compounds has hardly been recognized.\[6\] In this respect,

![Figure 6.1. Phosphorus-containing π-conjugated materials; phosphaborin 1 and phosphapericyclines 2 – 5.](image-url)
Chapter 6: P, S-, P, Si-h and P, B-macrocycles


Reagents for 7a: (a) n-BuLi; (b) (i-Pr)$_2$NP(O)Br. 7b: (a) LiN(SiMe$_3$)$_2$; (b) 0.5 eq. S(SO$_2$Ph)$_2$; (c) LiN(SiMe$_3$)$_2$; (d) 0.5 eq. S(SO$_2$Ph)$_2$. 7c: (a) LiN(SiMe$_3$)$_2$; (b) 0.5 eq. Si(i-Pr)$_2$Cl; (c) LiN(SiMe$_3$)$_2$; (d) 0.5 eq. Si(i-Pr)$_2$Cl.

The phospha[n]pericyclines prepared by Scott, Van Assema and Märkl are worth mentioning. Via stepwise addition of acetylenic Grignard reagents to dichlorophosphine corner units, Scott et al. were able to generate small quantities of triphospha[3]pericycline (2) and tetraphospha[4]pericycline (3a). The efforts of van Assema et al. afforded the similar tetraphospha[4]pericycline (3b), bearing amino-substituted phosphorus corner units. Interestingly, preliminary studies to extent such a system in the third dimension were performed via exchange of these amino substituents for –C≡CR moieties (R = H, SiMe$_3$). Similar phospha[n]pericyclines, wherein phosphorus corner units are alternated with other bridging atoms, such as carbon, sulfur and silicon, have also been prepared, but their photophysical properties are so far not investigated.

Märkl et al. focused on ‘exploded’ phosphapericyclines, employing diacetylene or butadiyne spacers (4), coupling bisacetylene phosphines in both a one-pot and a stepwise approach. Herein, the diyne moieties are prepared by homocoupling of pendant acetylene units by the oxidative Eglinton coupling procedure. A lowered phosphorus inversion barrier was observed for the triangular analogue (4a), which was attributed to an aromatic transition state. Analogous tetrameric (5a) and hexameric analogues (5b), bearing phosphorus oxide corner units, were prepared similarly by van Assema et al. by oxidative Hay coupling. One dimensional stacking was suggested for 30-membered macrocycle 5b in the solid state.

Acetylene extension has also been employed for the diphosphorus analogue of the above-mentioned phosphaborins 1. In this respect, (i-Pr)$_2$NP(O)Br$_2$ (6a) is reacted with dilithiated bisethynylbenzene, resulting in the formation of 7a (Scheme 6.1). Analogous disulfur (7b) and disilicon (7c) macrocycles have been prepared in similar fashion from S(SO$_2$Ph)$_2$ (6b) and Cl$_2$SiPh$_2$ (6c) precursors, respectively. X-ray crystal structure analysis of the trans-isomer of phosphorus-based 7a and sulfur-based 7b revealed that these macrocycles exhibited a puckered configuration due to the pyramidal nature of the phosphorus centers and the tetrahedral sulfur atoms.
Conversely, silicon-based 7c was shown to be almost planar. Also known are the stannyl analogues 7d (X = SnMe₂), 7e (X = SnPh₂), 7f (X = Sn(1-naphthyl)₂), 7g (X = Sn(CH₃)₃) and germanyl derivative 7h (X = GeMe₂).

No investigation of the photophysical properties has been performed for phosphorus-based macrocycle 7a, but the UV-vis absorption spectra of 7b and 7c showed that some conjugation was present between the acetylene units and the sulfur or selenium heteroatoms. Sulfur analogue 7b exhibited a slightly higher degree of conjugation, as evidenced by its lower energy absorption maximum and lower oxidation potential in a cyclic voltammetry experiment, which was also confirmed by semi-empirical calculations.

In this chapter, the attempts towards the synthesis of analogues of macrocycles 7 are described, that bear a phosphorus atom on one side and a sulfur (8), silicon (9) or boron (10) atom on the other (Figure 6.2). Especially the P,B-macrocycles are envisioned to have intriguing photophysical properties, in view of the combination of donor and acceptor properties, as outlined above for phosphaborins 1. In fact, macrocycles 10 can be considered the acetylene extended analogues of the phosphaborins. The sulfur and silicon analogues are also targeted, for their electron donating and electroneutral capacities, respectively.

As a second degree of freedom, the steric bulk of the exocyclic aromatic substituent on the phosphorus atom may vary from small (phenyl or Ph (a)), to medium (mesityl or Mes (b)) and large (2,4,6-tri-tert-butylphenyl or Mes* (c)). The size of the substituent was found to have some influence on the phosphorus lone pair participation in the π-conjugation in a series of P,S-bridged trans-stilbenes, but the corresponding translation into varying photophysical properties was small. However, it was envisioned that within the macrocyclic framework of 8 – 10, the effect of phosphorus lone pair participation on the electronic structure and the photophysical properties might be more pronounced, especially since no conjugation is possible without the participation of the lone pair.

6.2. Results and discussion

6.2.1. Direct cyclization
The first attempt towards an asymmetrical P,S-macrocycle was attempted via a direct cyclization of bisethynylbenzene (11), in analogy to the synthesis of 7b. The strategy was that reacting 11 with one equivalent of LiN(SiMe₃)₂ would give the corresponding monoanion, and subsequent quenching with 0.5 equivalent of S(SO₂Ph)₂ would result in bisethynylsulfide 12a (Scheme 6.2). Subsequent dilithiation, followed by quenching
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<table>
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**Figure 6.2.** Target P,S-, P,Si- and P,B-macrocycles 8–10.

**Scheme 6.2.** Direct cyclization towards macrocycle 8a.

Reagents: (a) 1: LiN(SiMe₃)₂, hexane, THF; 2: 0.5 eq. S(SO₂Ph)₂, hexane, THF; (b) 1: 2 eq. LiN(SiMe₃)₂, hexane, THF; 2: PhPCl₂, hexane, THF.

In view of these results, a stepwise approach towards the P,X-macrocycles 8–10 (X = S, Si, Br) was targeted, employing mono-protected bisethynylbenzene derivatives. As such, both heteroatoms can be introduced in a selective manner, which would enable the efficient introduction of a great variety of atoms at the corner positions of these π-systems, and as such provide easy access to a plethora of macrocycles, which are expected to exhibit intriguing optical properties.

**6.2.2. Stepwise approach via 1-silylethynyl-2-ethynylbenzene 17**

The Sonogashira coupling is an efficient method in the formation of C–C bonds between an aromatic ring and an acetylene unit, using mono-substituted acetylenes and halobenzenes. As iodobenzenes are reactive at room temperature in a Sonogashira reaction, and bromobenzenes only at elevated temperatures, 1-bromo-2-iodobenzene (13) is an ideal starting material for asymmetrically substituted 1,2-diethynylbenzenes, such as 17 (Scheme 6.3).
Thus, reacting 13 with ethynyltrimethylsilane in the presence of a palladium catalyst, a copper co-catalyst and an amine base gave ethynylbenzene 14 in excellent yield (Scheme 6.3(a)). In the next step, a second acetylene unit is introduced, bearing a different protecting group. Reaction of 14 with 2-methylbut-3-yn-2-ol gave no reaction in refluxing THF (66 °C) and only traces of 16 were observed in refluxing 1,4-dioxane (101 °C). After a six day period of refluxing in pure NEt₃ (90 °C), 16 could be isolated in 48% yield (Scheme 6.3(b)), which is indicative of a low reactivity of bromine 14 in a Sonogashira coupling. This result prompted the investigation of a less time-consuming and higher yielding route towards 16, using the more reactive iodo analogue 15.

In a first attempt towards iodobenzene 15, a Sonogashira coupling between 1,2-diiodobenzene and ethynyltrimethylsilane was performed, a known procedure in literature (Scheme 6.3(c)). Unfortunately, a statistical mixture of starting material, desired mono-substituted 15 and the corresponding di-substituted analogue was obtained, in a molar ratio of 1/2/1. After careful purification by column chromatography, 15 could be isolated in 28% yield. In order to circumvent these selectivity problems, 15 was prepared by a halogen exchange from 14. Thus, treatment of bromobenzene 14 with n-BuLi and subsequent reaction with diiodoethane gave iodobenzene 15 in 90% yield (Scheme 6.3(d)). A Sonogashira coupling between 15 and 2-methylbut-3-yn-2-ol could then be performed without difficulty affording bisethynylbenzene 16 in 91% yield (Scheme 6.3(e)), bearing two different protecting groups on either acetylene unit.

Single deprotection of 16 proved to be problematic, as the trimethylsilyl group is sensitive to similar conditions as the acetone protecting group. The latter can be removed by treatment with NaOH or NaH, but the trimethylsilyl group is also

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**Scheme 6.3.** Synthetic approach towards mono-protected bisethynylbenzene 17.

Reagents: (a) HCCSiMe₃, Pd(OAc)₂, PPh₃, CuI, NEt₃; (b) HCCCC(Me)₂OH, Pd(OAc)₂, PPh₃, Cu, NEt₃; (c) HCCSiMe₃, PdCl₂(PPh₃)₂, Cu, NEt₃, toluene; (d) 1: n-BuLi, hexane, Et₂O; 2: CH₂CH₂I, hexane, Et₂O; (e) HCCCMe₂OH, Pd(OAc)₂, PPh₃, Cu, NEt₃; (f) 0.16 eq. NaOH, toluene; (g) 1: n-BuLi, hexane, THF; 2: CI(SiMe₃)₂ hexane, THF; (h) HCCMgBr, Pd(PPh₃)₄, THF.
sensitive to basic conditions and thus several reaction conditions were screened to find the optimal reaction conditions for the mono-deprotection (Table 6.1). When NaOH is used as base, the reaction time and stoichiometry of the base is of crucial importance to the outcome of the reaction. Refluxing for two hours with 0.16 equivalents of NaOH gave the best results (Scheme 6.3(f)), but increasing the stoichiometry of NaOH by just 0.03 equivalents results in significantly increased amounts of double deprotection. On the other hand, decreasing the stoichiometry to 0.10 equivalent did not result in complete reaction. Using NaH instead, also significant double deprotection was observed. Thus, careful controlling the stoichiometry and reaction times is absolutely essential for good results, and reproduction of the optimal conditions proved to be difficult.

In an attempt to prepare 17 via a different route, a selective mono-protection of bisethynylbenzene (11) with one equivalent chlorotrimethylsilane was attempted (Scheme 6.3(g)). However, mono-silylated 17 was only formed together with large quantities of its di-silylated analogue, which were difficult to separate by common purification techniques. As an alternative approach, 15 was reacted with the Grignard reagent HCC\text{=}\text{CMgBr} in the presence of a palladium catalyst, which also did not result in the isolation of 17.

Despite the problematic formation of mono-protected bisethynylbenzene 17, this compound could be obtained in pure form (entry 2, Table 6.1) and was used for further studies towards phosphine-containing macrocycles 8 – 10 (Scheme 6.4). Lithiation of 17 using Li\text{N(SiMe}_3\text{)}_2 and treatment with the appropriate cyclization reagent XR\text{2} to give the double protected macrocycle precursors 18 was attempted next. Using S(SO\text{2Ph})_2 as cyclization reagent{[13]} this resulted in the formation of silane analogue 18a in 51% yield (Scheme 6.4(a)), and the subsequent deprotection{[21]} gave 12a efficiently in 89% yield (Scheme 6.4(d)). As indicated before, this compound proved to

| Table 6.1. Reaction conditions for the deprotection of 16. |
|----------------|----------------|----------------|
| entry | base | conditions | product ratio[^a] |
|       |      |            | 16 | 17 | 11 |
| 1     | 0.10 eq. NaOH | toluene, 2h reflux | 1 | 6 | - |
| 2     | 0.16 eq. NaOH | toluene, 2h reflux | - | 70% | trace |
| 3     | 0.19 eq. NaOH | toluene, 2h reflux | - | 58% | 18% |
| 4     | 0.60 eq. NaOH | toluene, 3h reflux | 1 | 13 | 4 |
| 5     | 0.20 eq. NaH | toluene, 2h reflux | - | 40% | 16% |

[^a] molar ratios of the products in the crude mixture or isolated yields (given in %).
be relatively unstable, and thus the ensuing ring-closing reaction had to be performed immediately after chromatographic isolation of 12a. Thus, addition of two equivalents of LiN(SiMe$_3$)$_2$ to 12a resulted in the formation of its double deprotonated analogue, which then was quenched with PhPCl$_2$ (Scheme 6.4(e)). Dilute conditions were used to promote ring-closure over co-polymerization. $^{31}$P NMR analysis of the reaction mixture showed a single singlet at $\delta = -60.5$ ppm, which is attributed to a bisethynyl-phosphine.$^{[19,22]}$ After work-up of the mixture, a blue solid was obtained which was insoluble in all common solvents, which implied the formation of an oligomer or polymer and hampered further analysis. The analogous reaction pathway with Cl$_2$Si(i-Pr)$_2$ $^{[23]}$ gave 18b in 66% yield (Scheme 6.4(b)) and after deprotection$^{[24]}$ the silicon-based macrocycle precursor 12b in 83% yield (Scheme 6.4(d)). An attempt to ring-close this precursor with LiN(SiMe$_3$)$_2$ and MesPCl$_2$ resulted in the appearance of a $^{31}$P NMR signal at $\delta = -81.2$ ppm in the reaction mixture (Scheme 6.4(e)). Again, the resulting brown solid could not be analyzed further due to solubility problems. In view thereof, this reaction sequence was not repeated with the boron-analogue.

In view of the obtained results, incorporation of the phosphine moiety in the last step seems to result in co-polymerization with the macrocyclic precursor instead of the desired ring-closure. Therefore, the next strategy was to incorporate the phosphorus heteroatom first. Thus, treatment of 17 with LiN(SiMe$_3$)$_2$ was followed by addition of PhPCl$_2$ (Scheme 6.4(f)). Subsequently, S$_8$ was added in order to protect the trigonal phosphorus center from oxidation. A signal in the $^{31}$P NMR spectrum of the reaction

Scheme 6.4. Ring-closure procedure towards macrocycles 8 – 10.

Reagents: (a) 1: LiN(SiMe$_3$)$_2$, hexane, THF; 2: 0.5 eq. S(SO$_2$Ph)$_2$; (b) 1: LiN(SiMe$_3$)$_2$, hexane, THF; 2: 0.5 eq. Si(i-Pr)$_2$Cl$_2$; (c) 1: LiN(SiMe$_3$)$_2$, hexane, THF; 2: 0.5 eq. MesB(OMe)$_2$; (d) NaOH, H$_2$O, MeOH, Et$_2$O; (e) 1: 2 eq. LiN(SiMe$_3$)$_2$, hexane, THF; 2: ArPCl$_2$, hexane, THF; (f) 1: LiN(SiMe$_3$)$_2$, hexane, THF; 2: 0.5 eq. PhPCl$_2$, hexane, THF; 3: S$_8$, hexane, THF.
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A mixture was observed in the expected region for bisethynylphosphine sulfides ($\delta^{(31\text{P})} = 122.2$ ppm), but chromatographic purification of the crude product did not result in the isolation of 19a. Further optimization of these synthesis routes was hampered by the difficult formation of 17, which could not be obtained in large quantities and high purity, as described above. Therefore, a new route was developed in which the difficult mono-deprotection of 1-(4-(2-methyl-2-hydroxy)-3-butynyl)-2-trimethylsilylethynyl-benzene (16) was circumvented.

6.2.3. Stepwise approach via bisethynyl-aryl-phosphine 21

The new synthetic approach targets the building block ArP(S)(C≡CH)$_2$ (21a (Ar = Ph); 21b (Ar = Mes); 21c (Ar = Mes*)) , which was prepared by two different methods. In the first approach, the Grignard reagent of ethynyltrimethylsilane was added slowly to ArPCl$_2$, to give the intermediate ArP(C≡CSiMe$_3$)$_2$ (Scheme 6.5(a)). Elemental sulfur was added to the reaction mixture to protect the phosphorus atom from oxidation and to prevent metal complexation in subsequent steps. Then, the silyl protecting groups of 20a – 20c were removed by catalytic Bu$_4$NF and water. As such, PhP(S)(C≡CH)$_2$ (21a) and MesP(S)(C≡CH)$_2$ (21b) were prepared in 35% and 50% yield respectively from ArPCl$_2$ (Scheme 6.5(b)). Mes*-substituted 21c has not been prepared. Secondly, a direct addition of the acetylene Grignard reagent (HC≡CMgBr) to ArPCl$_2$ was also attempted, which resulted in the formation of phenyl-substituted 21a in slightly higher yield after addition of S$_8$ (46%), but this reaction sequence was unsuccessful for mesityl-substituted 21b (Scheme 6.5(c)). Care should be taken, as excess Grignard

![Scheme 6.5](image.png)

**Scheme 6.5.** Synthetic approach towards macrocyclic precursor 19 via diethynylphosphines.

*Reagents: (a) 1: Me$_3$SiCCMgBr, THF; 2: S$_8$, THF; (b) Bu$_4$NF, H$_2$O, THF; (c) 1: HCCMgBr, THF; 2: S$_8$, THF; (d) 1: n-BuLi, hexane, THF; 2: 14, hexane, THF; (e) 15, Pd(OAc)$_2$, PPh$_3$, Cul, NEt$_3$, (THF).
deprotonate the pending acetylene moieties via MgBr-proton exchange upon concentration of the reaction mixture, which initiates polymerization of 21. Hence, addition of a small amount of water to the product solution to destroy the remaining Grignard reagents is of the utmost importance.

Next, two routes were envisioned to connect the distal carbon atom of bisethynylphosphine 21 and the ortho-carbon atom of a protected ethynylbenzene for the construction of protected macrocycle precursors 19 (Scheme 6.5(d)). For this, bromoethynylbenzene 14 was chosen as the first reaction partner. Double deprotonation of 21a by n-BuLi was followed by the addition of 14, but this did not result in the desired nucleophilic aromatic substitution, as the trimethylsilylethylnyl group does not activate the aromatic ring enough to undergo addition of the terminal acetylenic carbanions. Alternatively, iodobenzene 15 was used in a Sonogashira coupling with the terminal acetylenes of 21a (Scheme 6.5(e)). However, the formation of 19a was never observed, not even by increasing the temperature to 80 °C or using pure NEt₃ as solvent. After chromatographic purification, no fractions were collected that gave a signal during ³¹P NMR analysis, and only starting material 15 was recovered. It seems likely that the phosphine acetylenes are very reactive towards the copper co-catalyst and end up as polymeric material in the black precipitate, which is found at the bottom of the flask after each reaction. Application of hydrogen atmosphere to prevent acetylene homologation gave no improvement of this undesired reaction. Apparently, a Sonogashira coupling is not feasible with phosphine sulfide-substituted acetylenes. As 19a could not be obtained via this approach, these reactions were not repeated with the Mes- and Mes*-substituted analogues.

6.2.4. Stepwise approach via bis(2-iodophenyl)ethynyl-aryl-phosphine 24

As phosphine acetylenes had proven to be too reactive for application in a Sonogashira coupling, an alternative synthetic route, employing phosphine sulfides bearing aromatic iodides was developed for the synthesis of 19 (Scheme 6.6(a)). These bis-iodides 24 were prepared by various routes, as described below.

In a first attempt, 1-ethynyl-2-trimethylsilylbenzene (22) was prepared from ethynylbenzene by double deprotonation with n-BuLi, trapping with an excess of ClSiMe₃ and deprotection of the acetylenic silyl group (Scheme 6.6(a)). Introduction of the phosphine unit was then attempted via coupling of the Grignard reagent of 22 with ArPCl₂ (Scheme 6.6(b)), analogous to the formation of 20 and 21. The intermediate PhP(C≡CAr) could be observed in the reaction mixture (δ(³¹P) = –60.7 ppm), together with two side-products. After prolonged stirring, the composition of the mixture did not change, and sulfur was added to obtain air-stable 23a. Unfortunately,
in a first attempt 23a could not be isolated from the crude mixture. As the copper catalyzed P–C coupling reaction\textsuperscript{[26]} performed much better, no optimization of the Grignard reaction has been performed. In this second approach, 22 was treated with Cul and NEt\textsubscript{3} in the presence of PhPCl\textsubscript{2}, which resulted in the formation of 23a in 52\% yield after purification by column chromatography (Scheme 6.6(c)).

In parallel to this route, bis-iodide analogue 24 was also successfully prepared via a similar route from 1-iodo-2-(trimethylsilyl)ethylbenzene (15), and thus the SiMe\textsubscript{3} to I exchange, by treatment of 23a with ICl, has not been investigated (Scheme 6.6(d)).\textsuperscript{[27]} Thus, deprotection of 15 in the presence of NaOH afforded 1-ethynyl-2-iodobenzene (25) in 89\% yield (Scheme 6.6(e)).\textsuperscript{[28]} Despite the envisioned problems, a Grignard mediated coupling with PhPCl\textsubscript{2} was tried anyway. Addition of sulfur and chromatographic purification resulted in a small amount of 24a (4\% yield; Scheme 6.6(f)). Again, the copper catalyzed P–C coupling performed much better, giving 24a in 66\% yield upon treatment with Cul, NEt\textsubscript{3} and PhPCl\textsubscript{2} (Scheme 6.6(g)).

Next, the Sonogashira coupling towards 19a was investigated by reacting bis(2-iodophenyl)ethynyl-phenyl-phosphine sulfide (24a) with ethynyltrimethylsilane

\begin{figure}
\centering
\includegraphics[width=\textwidth]{Scheme_6.6.png}
\caption{Synthetic approach towards macrocyclic precursor 19 via P–C coupling reaction.}
\begin{itemize}
\item Reagents: (a) 1: n-BuLi, hexane, THF; 2: t-BuOK, hexane, THF; 3: ClSiMe\textsubscript{3}, hexane, THF; 4: KOH, MeOH, hexane, THF; (b) 1: EtMgBr, THF; 2: ArPCl\textsubscript{2}, THF; 3: S\textsubscript{8}, THF; (c) 1: ArPCl\textsubscript{2}, Cul, NEt\textsubscript{3}, toluene; 2: S\textsubscript{8}, toluene; (d) ICl, CH\textsubscript{2}Cl\textsubscript{2}; (e) NaOH, H\textsubscript{2}O, MeOH, Et\textsubscript{2}O; (f) 1: EtMgBr, THF; 2: ArPCl\textsubscript{2}, THF; 3: S\textsubscript{8}, THF; (g) ArPCl\textsubscript{2}, Cul, NEt\textsubscript{3}, toluene; 2: S\textsubscript{8}, toluene; (h) HCCSiMe\textsubscript{3}, Pd(OAc)\textsubscript{2}, PPh\textsubscript{3}, Cul, NEt\textsubscript{3}, THF.
\end{itemize}
\end{figure}
Scheme 6.6(h)). Despite the absence of reactive ethynylphosphine moieties, the reaction did not proceed successfully. The reaction could be hampered by the presence of a multitude of possible ligands, which are present in the reaction mixture and could possibly interfere with the catalytic cycles. Therefore, again a different synthetic approach towards macrocycles $8 - 10$ was developed, avoiding a Sonogashira coupling in the presence of ethynylphosphines completely.

6.2.5. Stepwise approach via 1-silylethynyl-2-ethynyl-benzene 29
As a Sonogashira coupling did not proceed effectively in the presence of phosphine sulfides, the initial idea to functionalize bisethynylbenzene with two different acetylenic protecting groups was revitalized. As the combination of the acetone and the trimethylsilyl group did not give satisfactory results (see section 6.2.2), the use of differently sized silyl groups was investigated (Scheme 6.7). Thus, SiMe$_3$-protected ethynylbenzene 15 was coupled with ethynyltriphenylsilane and ethynyltriisopropylsilane to give SiPh$_3$-derivative 26 in 50% yield (Scheme 6.7(a)) and Si(i-Pr)$_2$-derivative 28 in 91% yield (Scheme 6.7(c)) respectively. The first attempt to deprotect the trimethylsilyl group in 26 with K$_2$CO$_3$\textsuperscript{[29]} to afford 27 failed (Scheme 6.7(b)), as the steric bulk of the SiPh$_3$ moiety might disable the base to approach the SiMe$_3$ group efficiently. As the analogous reaction with the triisopropylsilyl derivative functioned smoothly to give 29 in quantitative yield (Scheme 6.7(d))\textsuperscript{[30]}, the deprotection of 26 was not investigated further.

With mono-protected bisethynylbenzene 29 in hand, the copper-catalyzed P–C coupling with ArPCl$_2$ was performed (Scheme 6.7(e)). The progress of the reaction was followed by $^{31}$P NMR spectroscopy, which showed that the phosphine was converted completely to the product. Surprisingly, besides the isolation of 30a, a large amount of starting material 29 (47%) was recovered after chromatographic separation of the crude mixture. Therefore, 30a is effectively prepared in 89% yield. Analogously, the reaction with MesPCl$_2$ gave 30b together with 63% recovered 29, thus resulting in an 79% effective yield of 30b. Due to the presence of the bulky triisopropylsilyl moieties, the trigonal phosphorus center was not susceptible to oxidation in air, or to reaction with sulfur.

In view of these promising results, the same reaction was also performed with Mes*PCl$_2$, but this did not result in formation of 30c, even at elevated temperatures. The amalgamation of two triisopropylsilyl moieties and a supermesityl group in such a confined space might be too sterically demanding.

Deprotection of silyl-protected bisethynylphosphines 30a and 30b could not be achieved by treatment with NaOH, but the analogous reaction with Bu$_4$NF and H$_2$O was successful and gave macrocyclic precursors 31a and 31b in 87% and 82% yield,
Scheme 6.7. Synthetic approach towards protected macrocyclic precursor 30 via asymmetrically protected bisethynylbenzene 28.

Reagents: (a) HCCSiPh$_3$, Pd(OAc)$_2$, PPh$_3$, CuI, NEt$_3$, THF; (b) K$_2$CO$_3$, THF, MeOH; (c) HCCSi(i-Pr)$_3$, PdCl$_2$, PPh$_3$, CuI, NEt$_3$, THF; (d) K$_2$CO$_3$, THF, MeOH; (e) ArPCl$_2$, CuI, NEt$_3$, toluene.


Reagents: (a) Bu$_4$NF, H$_2$O, THF; (b) 1: LiN(SiMe$_3$)$_2$, hexane, THF; 2: B(OCH$_3$)$_3$, hexane, THF; 3: MesLi, hexane, THF; (c) 1: LiN(SiMe$_3$)$_2$, hexane, THF; 2: Si(i-Pr)$_2$Cl$_2$, hexane, THF.

respectively (Scheme 6.8(a)). With these phenyl- and mesityl-substituted precursors in hand, preliminary ring-closing reactions were performed with the initial focus on the boron-containing macrocycles, as these are expected to have the most interesting photophysical properties.

Thus, 31a was treated with 2.2 equivalents of LiN(Si(CH$_3$)$_3$)$_2$. Subsequently, one equivalent of B(OCH$_3$)$_3$ was added to form intermediary B,P-macrocycle 10a' (Ar = Ph; X = BOCH$_3$). Separately prepared MesLi, obtained by the treatment of MesBr with $n$-BuLi, was then added to replace the remaining methoxy substituent on boron by a mesityl group to form macrocycle 10a (Scheme 6.8(b)). In order to circumvent oligomerization by coupling of one boron species with two different molecules of 31a, the reaction was carried out under dilute conditions (c(31a) = 12 mM), which
hampered *in situ* analysis of the reaction mixture by NMR spectroscopy. After concentration, the $^{31}\text{P}$ NMR signal at $\delta(^{31}\text{P}) = -60.8$ ppm is consistent with a bisethynylphenyl-phosphine, and also the $^1\text{H}$ NMR signals pointed at the successful formation of macrocycle 10a. However, no $^{11}\text{B}$ NMR signals could be observed. The apparent instability of the product hampered further isolation and characterization, and thus the reaction was repeated with the more sterically shielded 31b, bearing a mesityl substituent on phosphorus (Scheme 6.8(b)). This reaction was performed analogously, except for a slightly increased concentration ($c(31a) = 30$ mM) to enable *in situ* spectroscopic analysis. Thus, 31b was doubly deprotonated with LiN(Si(CH$_3$)$_3$)$_2$ and treated with B(OCH$_3$)$_3$. NMR analysis of the intermediate macrocycle 10b’ (Ar = Mes; $X = \text{BOCH}_3$) showed signals at $\delta(^{31}\text{P}) = -82.9$ ppm and $\delta(^{11}\text{B}) = 3.4$ ppm, and after the addition of MesLi, signals were observed at $\delta(^{31}\text{P}) = -83.0$ ppm and $\delta(^{11}\text{B}) = -2.0$ ppm. The reaction mixture was quenched with a few drops of degassed water, dried over MgSO$_4$ and extracted with pentane. Unfortunately, the yellow solid that was isolated after column chromatography was found to be regenerated 31b.

In a next attempt, the ring closing reaction was performed with Si(1-Pr)$_2$Cl$_2$. Double deprotonation of 31a by LiN(Si(CH$_3$)$_3$)$_2$ was followed by addition of Si(1-Pr)$_2$Cl$_2$, which was expected to result in Si,P-macrocycle 9a (Scheme 6.8(c)). Unfortunately, the same ambiguous results as for the boron equivalent were obtained. After aqueous work-up with degassed water, the $^{31}\text{P}$ NMR spectrum of the brown crude product revealed two signals ($\delta(^{31}\text{P}) = -58.2$ ppm and $-60.8$ ppm). The high-field signal most probably corresponds to unreacted 31a, while the lower field one possibly corresponds to a macrocyclic species. In addition, a $^{29}\text{Si}$ NMR signal was observed at $\delta(^{29}\text{Si}) = -11.5$ ppm, which could correspond to the (1-Pr)$_2$Si(C≡CR)$_2$ center, together with an abundant SiMe$_3$ signal at $\delta(^{29}\text{Si}) = -1.78$ ppm. Careful column chromatography over aluminum oxide gave a yellow solid, which exhibited only the $^{31}\text{P}$ NMR signal at $\delta(^{31}\text{P}) = -60.8$ ppm, but showed in the $^1\text{H}$ NMR spectrum a signal at $\delta(^1\text{H}) = 3.14$ ppm, corresponding to the acetylenic hydrogen atoms of 31a. So, either the reaction was unsuccessful or desilylation took place during column chromatography.

Due to the limited amount of time and the small quantity of mono-protected bisethynylbenzene 29 available, the ring-closing reaction could not be further optimized. No attempts have been done to ring-close precursors 31 with S(SO$_2$Ph)$_2$, in order to prepare sulfur-containing macrocycles 8.

### 6.3. Conclusion

In this chapter, the synthetic efforts towards asymmetric $P,S$-, $P,Si$- and $P,B$-macrocycles have been described. As the direct cyclization by the treatment of
bisethynylbenzene with one equivalent of LiN(SiMe$_3$)$_2$ gave not the desired selectivity, several alternative routes for a stepwise approach have been investigated. A Sonogashira coupling reaction was found to be incompatible with a phosphine sulfide moiety, present either at the acetylene or at the halobenzene building block. Therefore, in the assembly of the different fragments, the two Sonogashira coupling reactions to introduce both acetylenic moieties have to be performed prior to the incorporation of the phosphorus center. Asymmetrically protected bisethynylbenzene 28 and its mono-deprotected analogue 29 were found to be the core building blocks for the assemblage of these asymmetric macrocycles. Subsequent incorporation of the phosphine unit was readily achieved via a copper catalyzed P–C coupling reaction. Incorporation of the second heteroatom, either sulfur, silicon or boron, was envisioned as last step, but so far the ring-closure protocols to obtain the targeted macrocycles in pure form have not been optimized.

6.4. Experimental section
This section describes all of the successful reactions, as well as the relevant failed ones. All reactions are carried out under nitrogen atmosphere using standard Schlenk techniques and dry solvents, unless stated otherwise. THF and Et$_2$O were distilled from Na/benzophenone, NEt$_3$ and MeOH from CaH$_2$, CH$_2$Cl$_2$ from CaCl$_2$ and toluene and pentane from Na. Bisethynylbenzene,$^{[31]}$ mesityldichlorophosphine,$^{[32]}$ ethynyltriisopropylsilane$^{[33]}$ and 1-ethynyl-2-iodobenzene (25, Scheme 6.6(e))$^{[28]}$ have been prepared via literature procedures.

NMR measurements were performed on a Brüker Advance 250 or a Bruker Advance 400. NMR chemical shifts were externally referenced to SiMe$_4$ ($^1$H, $^{13}$C and $^{29}$Si), 85% H$_3$PO$_4$ ($^{31}$P) or BF$_3$·OEt$_3$ ($^{11}$B). Multiplicities are given as: s (singlet), d (doublet), dd (double doublet), ddd (double double doublet), t (triplet), dt (double triplet) and m (multiplet). IR spectra were recorded on a Mattson-6030 Galaxy FTIR (KBr) or a Shimadzu FTIR-8400S (neat). Signal appearances are given as: s (strong), m (medium), w (weak). High-resolution mass spectra were measured at 70 eV using a Finnigan Mat 900 mass spectrometer operating at an ionization potential of 70 eV (EI) or a JEOL JMS SX/SX 102A four-sector mass spectrometer, equipped with a Xenon primary atom beam, utilizing a 3-nitrobenzyl (3-NOBA) matrix (FAB). Melting points are measured on a Stuart Scientific SMP3 melting point apparatus in unsealed capillaries and are uncorrected.
Attempted direct cyclization from bisethynylbenzene

To a solution of bisethynylbenzene in THF (1.0 M, 500 μL, 500 μmol) at 0 °C was added dropwise a solution of LiN(SiMe₃)₂ in hexane (1.0 M, 500 μL, 500 μmol, 1 eq.). The reaction mixture was stirred for 30 min at 0 °C, after which a solution of S(SO₂Ph)₂ (79.0 mg, 250 μmol, 0.5 eq.) in THF (0.5 mL) was added dropwise. After 1 h of stirring at 0 °C, the reaction mixture was allowed to warm to room temperature and two drops of water were added. The solution was concentrated in vacuo and the residue was diluted with Et₂O (10 mL) and H₂O (10 mL). The organic layer was separated and the aqueous layer was extracted with Et₂O (2 × 5 mL). The combined organic layers were dried over MgSO₄, filtered and the solvents evaporated.

1H NMR analysis of the crude dark brown solid proved the presence of intermediary 12a, together with many side-products.

1-Bromo-2-(trimethylsilyl)benzene (14)

A suspension of 1-bromo-2-iodobenzene (5.20 mL, 40.0 mmol), HC≡CSiMe₃ (8.30 mL, 60.0 mmol, 1.5 eq.), Pd(OAc)₂ (180 mg, 800 μmol, 2 mol%), PPh₃ (420 mg, 1.60 mmol, 4 mol%) and CuI (304 mg, 1.60 mmol, 4 mol%) in NEt₃ (200 mL) was stirred at room temperature for 42 h, affording a dark green suspension. The mixture was concentrated in vacuo and the residue was diluted with EtOAc (150 mL) and H₂O (150 mL). The organic layer was separated and the aqueous layer was extracted with EtOAc (3 × 50 mL). The combined organic layers were washed with brine (50 mL) and evaporated. The residue was redissolved in hexane (250 mL) and filtered through a silica gel pad. The filtrate was concentrated in vacuo and the residue was subjected to column chromatography on silica gel with hexane as eluent (RF = 0.40) to give 14 (10.1 g, 40.0 mmol, 100% yield) as a yellow oil.

1H NMR (CDCl₃; 250.1 MHz): δ (ppm) = 7.57 (dd, 3JHH = 7.9 Hz, 4JHH = 1.4 Hz, 1H, H₆); 7.49 (dd, 3JHH = 7.6 Hz, 4JHH = 1.8 Hz, 1H, H₃); 7.24 (dt, 3JHH = 7.6 Hz, 4JHH = 1.4 Hz, 1H, H⁴); 7.15 (dt, 3JHH = 7.8 Hz, 4JHH = 1.8 Hz, 1H, H⁵); 0.28 (s, 9H, Si(CH₃)₃).

1-Iodo-2-(trimethylsilyl)benzene (15)

Method A (Scheme 6.3 (c)): A suspension of 1,2-diiodobenzene (1.30 mL, 10.0 mmol), HC≡CSiMe₃ (1.70 mL, 12.0 mmol, 1.2 eq.), Cl₂Pd(PPh₃)₂ (140 mg, 20.0 μmol, 2 mol%) and CuI (380 mg, 200 μmol, 20 mol%) in NEt₃ (2 mL) and toluene (6 mL) was stirred at room temperature for 15 h, affording a dark green suspension. The mixture was concentrated in vacuo and the residue was diluted with CH₂Cl₂ (15 mL) and H₂O (10 mL). The organic layer was separated and the aqueous layer was extracted with CH₂Cl₂ (2 × 10 mL). The combined organic layers were washed with H₂O (2 × 10 mL),
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dried over MgSO<sub>4</sub>, filtered and evaporated. The residue was subjected to column chromatography on silica gel with hexane as eluent to give three products; double protected 1,2-bis(trimethylsilylethynyl)benzene (32, \( R_F = 0.15 \), 120 mg, 360 \( \mu \text{mol} \), 4% yield) as a colorless oil, unreacted 1,2-diiodobenzene (\( R_F = 0.50 \), 510 mg, 1.55 mmol, 16% yield) as a colorless oil and desired 15 (\( R_F = 0.40 \), 850 mg, 2.83 mmol, 28% yield) as a yellow oil.

**Method B (Scheme 6.3 (d))**: A solution of n-BuLi in hexane (1.6 M, 5.30 mL, 8.50 mmol, 1.1 eq.) was added dropwise to a solution of 14 (1.96 g, 774 mmol) in Et<sub>2</sub>O (18 mL) at –78 °C. The dark yellow solution was stirred for 30 min at –78 °C and then allowed to warm to 0 °C over a period of 2.5 h. The reaction mixture was cooled again to –78 °C and a solution of 1,2-diiodoethane (2.62 g, 9.29 mmol, 1.2 eq.) in Et<sub>2</sub>O (15 mL) was added dropwise, affording a white suspension. The reaction mixture was stirred for 1 h at –78 °C and warmed to 0 °C. H<sub>2</sub>O (5 mL) was added to the reaction mixture, and the organic layer was separated, washed with H<sub>2</sub>O (3 × 20 mL) and dried over MgSO<sub>4</sub>. The solution was filtered and concentrated in vacuo and the residue was subjected to column chromatography on silica gel with hexane as eluent (\( R_F = 0.40 \)) to give 15 (2.10 g, 7.00 mmol, 90% yield) as a yellow oil.

\[^1\text{H}\text{ NMR}\] (15; CDCl<sub>3</sub>; 250.1 MHz): \( \delta \) (ppm) = 7.87 (dd, \( ^3J_{HH} = 8.0 \text{ Hz}, ^4J_{HH} = 1.4 \text{ Hz}, 1\text{H}, H^6 \)); 7.47 (dd, \( ^3J_{HH} = 7.7 \text{ Hz}, ^4J_{HH} = 1.5 \text{ Hz}, 1\text{H}, H^3 \)); 7.28 (dt, \( ^3J_{HH} = 7.6 \text{ Hz}, ^4J_{HH} = 1.5 \text{ Hz}, 1\text{H}, H^5 \)); 6.98 (dt, \( ^3J_{HH} = 7.6 \text{ Hz}, ^4J_{HH} = 1.4 \text{ Hz}, 1\text{H}, H^4 \)); 0.29 (s, 9H, Si(C<sub>3</sub>H<sub>3</sub>)).

\[^1\text{H}\text{ NMR}\] (32; CDCl<sub>3</sub>; 250.1 MHz): \( \delta \) (ppm) = 7.46 (m, 2H, H<sub>3,6</sub>); 7.23 (m, 2H, H<sub>4,5</sub>); 0.27 (s, 18H, Si(C<sub>3</sub>H<sub>3</sub>)).

1-(4-(2-Methyl-2-hydroxy)-3-butynyl)-2-(trimethylsilylethynyl)benzene (16)

**Method A (Scheme 6.3 (b))**: A suspension of 14 (2.01 g, 7.93 mmol), 2-methyl-but-3-yn-2-ol (850 \( \mu \text{L} \), 8.70 mmol, 1.1 eq.), Pd(OAc)<sub>2</sub> (18.0 mg, 79.0 \( \mu \text{mol} \), 1 mol%), PPh<sub>3</sub> (42.0 mg, 160 \( \mu \text{mol} \), 2 mol%) and CuI (8.00 mg, 40.0 \( \mu \text{mol} \), 0.5 mol%) in NEt<sub>3</sub> (40 mL) was stirred at room temperature for 6 d, affording a dark green suspension. The mixture was concentrated in vacuo and the residue was diluted with EtOAc (100 mL) and H<sub>2</sub>O (100 mL). The organic layer was separated and the aqueous layer was extracted with EtOAc (2 × 50 mL). The combined organic layers were washed with brine (100 mL) and evaporated. The residue was subjected to column chromatography on silica gel with hexane/EtOAc (4/1 \( \text{v/v} \)) as eluent (\( R_F = 0.33 \)) to give 16 (980 mg, 3.82 mmol, 48% yield) as a yellow oil.

**Method B (Scheme 6.3 (e))**: A suspension of 15 (2.04 g, 6.80 mmol), 2-methyl-but-3-yn-2-ol (2.00 mL, 20.0 mmol, 3 eq.), Pd(PPh<sub>3</sub>)<sub>2</sub>Cl<sub>2</sub> (98.0 mg, 140 \( \mu \text{mol} \), 2 mol%), and CuI (13.0 mg, 70.0 \( \mu \text{mol} \), 1 mol%) in NEt<sub>3</sub> (34 mL) was heated to reflux for 69 h. The resulting dark green suspension was concentrated in vacuo and the residue was diluted with EtOAc (100 mL) and H<sub>2</sub>O (100 mL). The organic layer was separated and
the aqueous layer was extracted with EtOAc (2 × 40 mL). The combined organic layers were washed with brine (30 mL) and the solvents evaporated. The residue was redissolved in hexane/EtOAc (4/1 (v/v), 200 mL) and filtered through a silica gel pad. The filtrate was concentrated in vacuo and the residue was subjected to column chromatography on silica gel with hexane/EtOAc (4/1 (v/v)) and 1% NEt₃ as eluent (Rᶠ = 0.33) to give 16 (1.59 g, 6.20 mmol, 91% yield) as a yellow oil.

\[ 1H \text{ NMR (CDCl}_3; 250.1 \text{ MHz): } \delta (\text{ppm}) = 7.39 – 7.48 (m, 2H, H3,6); 7.20 – 7.28 (m, 2H, H4,5); 1.65 (s, 6H, C(CH}_3)_2OH); 0.27 (s, 9H, Si(CH}_3)_3). \]

\[ 13C \text{ NMR (CDCl}_3; 62.90 \text{ MHz): } \delta (\text{ppm}) = 132.8 (s, C6); 132.2 (s, C3); 128.5 (s, C5); 128.3 (s, C4); 126.0 (s, C1); 125.7 (s, C2); 103.7 (s, ArC≡CSi); 98.6 (s, ArC≡CSi); 98.2 (s, ArC≡CC); 81.3 (s, ArC≡CC); 66.1 (s, C(CH}_3)_2OH); 31.9 (s, C(CH}_3)_2OH); 0.4 (s, Si(CH}_3)_3). \]

1-Ethynyl-2-(trimethylsilylthethyl)benzene (17)

Method A (Scheme 6.3 (f)): The mixture of 16 (1.59 g, 6.20 mmol) and finely powdered NaOH (40.0 mg, 1.00 mmol, 0.16 eq.) in toluene (62 mL) was heated to reflux for 2 h. The resulting dark red suspension was filtered and the filtrate concentrated in vacuo. The residue was subjected to column chromatography on silica gel with hexane/CH₂Cl₂ (5/1 (v/v)) as eluent (Rᶠ = 0.43) to give 17 (863 mg, 4.35 mmol, 70% yield) as a yellow oil.

Method B (Scheme 6.3 (g)): To a solution of bisethynylbenzene (11) in THF (1.0 M, 10.0 mL, 10.0mmol) at −78 °C was added dropwise a solution of n-BuLi in hexane (1.6 M, 6.30 mL, 10.1 mmol, 1 eq.). The reaction mixture was stirred for 1 h and ClSiMe₃ (1.3 mL, 10.2 mmol, 1 eq.) was added portionwise. After another 1 h of stirring at −78 °C, the reaction mixture was allowed to warm to room temperature and the reaction was quenched by addition of two drops of water. The solution was concentrated in vacuo and the brown residue was diluted with Et₂O (25 mL) and H₂O (25 mL). The organic layer was separated and the aqueous layer was extracted with Et₂O (3 × 10 mL). The combined organic layers were washed with brine (10 mL), dried over MgSO₄, filtered and the solvents evaporated. The residue was subjected to column chromatography on silica gel with pentane/CH₂Cl₂ (6/1 (v/v)) as eluent to give double protected 1,2-bis(trimethylsilylthethyl)benzene (32, 830 mg, 3.14 mmol, 31% yield) as a colorless oil and a yellow oily fraction (350 mg) containing 32 / 17 / 11 in a molar ratio of 2/1/1.

Method C (Scheme 6.3 (h)): To a solution of 15 (300 mg, 1.00 mmol) and Pd(PPh₃)₄ (28.9 mg, 25.0 μmol, 2.5 mol%) in dry THF (10 mL) at 0 °C was added dropwise a solution of HC≡CMgBr in THF (0.5M, 5.00 mL, 2.50mmol, 2.5 eq.). The reaction mixture was stirred for 1 h at 0 °C, after which it was allowed to warm to room temperature. After 15 h of stirring at room temperature, the reaction was terminated by pouring the solution into an aqueous saturated NH₄Cl solution (15 mL). The aqueous layer was extracted with EtOAc (3 × 30 mL) and the combined organic layers were washed with


H₂O (10 mL) and brine (10 mL), dried over MgSO₄, filtered and concentrated in vacuo. The dry residue was subjected to column chromatography on silica gel with hexane/CH₂Cl₂ (5/1 (v/v)) with 1% NEt₃ as eluent (Rf = 0.43). The correct product was not isolated.

**1H NMR** (CDCl₃; 250.1 MHz): δ (ppm) = 7.43 – 7.51 (m, 2H, H⁻¹); 7.22 – 7.32 (m, 2H, H⁺¹); 3.29 (s, 1H, ≡C); 0.27 (s, 9H, Si(CH₃)₃). **13C NMR** (CDCl₃; 62.90 MHz): δ (ppm) = 132.8 (s, C⁴); 132.5 (s, C³); 128.5 (s, C²); 125.5 (s, C¹); 103.6 (s, ArC≡CSi); 99.4 (s, ArC≡CSi); 82.4 (s, ArC≡CH); 81.6 (s, ArC≡CH); 0.4 (s, Si(CH₃)₃).

**Bis(2-(trimethylsilylethynyl)phenyl)ethynyl-sulfide (18a)**

A solution of LiN(SiMe₃)₂ in hexane (1.0 M, 2.40 mL, 2.40 mmol, 1.2 eq.) was added dropwise to a solution of 17 (397 mg, 2.00 mmol) in THF (40 mL) at 0 °C. The light yellow solution was stirred at 0 °C for 2 h. Then a solution of S(SO₂Ph)₂ (377 mg, 1.20 mmol, 0.6 eq.) in THF (60 mL) was added dropwise to the reaction mixture at 0 °C. The resulting yellow suspension was stirred at 0 °C for 1 h and then allowed to warm to room temperature. After 2.5 h of stirring, H₂O (100 µL) was added to the reaction mixture, which was then concentrated in vacuo. The residue was diluted with hexane (80 mL) and H₂O (80 mL). The organic layer was separated and the aqueous layer was extracted with hexane (3 × 30 mL). The combined organic layers were washed with brine (40 mL) and dried over MgSO₄, filtered and concentrated in vacuo. The residue was subjected to column chromatography on silica gel with hexane/CH₂Cl₂ (9/1 (v/v)) with 1% NEt₃ as eluent (Rf = 0.15) to give 18a (217 mg, 509 µmol, 51% yield) as a slightly yellow viscous oil.

**1H NMR** (CDCl₃; 250.1 MHz): δ (ppm) = 7.41 – 7.47 (m, 4H, H⁻¹); 7.22 – 7.30 (m, 4H, H⁺¹); 0.26 (s, 18H, Si(CH₃)₃). **13C NMR** (CDCl₃; 62.90 MHz): δ (ppm) = 132.33 (s, C³); 132.30 (s, C⁴); 128.9 (s, C²); 128.5 (s, C¹); 126.5 (s, C³); 125.7 (s, C²); 103.3 (s, C≡CSi); 99.9 (s, C≡CSi); 93.8 (s, C≡CS); 76.3 (s, C≡CS); 0.4 (s, Si(CH₃)₃). **HR-MS (EI)**: calcd. for C₂₆H₂₆Si₂S [M]+: 426.1294, found: 426.1286. m/z (%): 426.0 [M]+ (7); 411.0 [M – CH₃]+ (88); 353.1 [M – Si(CH₃)₃]+ (100). **IR (KBr)**: ν (cm⁻¹) = 3062 (w); 3026 (w); 2957 (m); 2161 (s, C≡C); 1471 (m); 1443 (m); 1275 (w); 1250 (s); 1200 (m); 1097 (m); 1034 (w); 951 (w); 883 (m); 857 (s); 843 (s); 757 (s); 703 (w); 640 (m); 513 (m).

**Bis(2-(trimethylsilylethynyl)phenyl)ethynyl-diisopropyl-silane (18b)**

A solution of LiN(SiMe₃)₂ in hexane (1.0 M, 4.80 mL, 4.80 mmol, 1.2 eq.) was added dropwise to a solution of 17 (793 mg, 4.00 mmol) in THF (80 mL) at 0 °C. The resulting light yellow solution was stirred for 2 h, and then a solution of (i-Pr)₂SiCl₂ (430 µL, 4.80 mmol, 0.6 eq.) in THF (80 mL) was
added dropwise to the reaction mixture at 0 °C. The resulting yellow suspension was stirred at 0 °C for 2 h and then allowed to warm to room temperature. The reaction mixture was stirred for a further 15 h, and then concentrated in vacuo. The residue was diluted with hexane (100 mL) and H₂O (100 mL). The organic layer was separated and the aqueous layer was extracted with hexane (3 × 30 mL). The combined organic layers were washed with brine (40 mL), dried over MgSO₄, filtered and concentrated in vacuo. The residue was subjected to column chromatography on silica gel with hexane/CH₂Cl₂ (5/1 (v/v)) with 1% NEt₃ as eluent (Rf = 0.18) to give 18b (673 mg, 1.32 mmol, 66% yield) as a colorless viscous oil. 

**1H NMR** (CDCl₃; 250.1 MHz): δ (ppm) = 7.42 – 7.56 (m, 4H, H₃,6); 7.19 – 7.31 (m, 4H, H₄,5); 1.12 – 1.30 (m, 14H, Si(CH₃)₂); 0.24 (s, 18H, Si(CH₃)₃).

**13C NMR** (CDCl₃; 62.9 MHz): δ (ppm) = 133.4 (s, C₆); 133.1 (s, C₃); 128.6 (s, C⁴); 128.3 (s, C⁵); 126.3 (s, C₂); 125.8 (s, C¹); 105.5 (s, C≡Si(i-Pr)₂); 103.6 (s, C≡CSiMe₃); 99.0 (s, C≡C≡SiMe₃); 92.3 (s, C≡CSi(i-Pr)₂); 18.4 (s, Si(CH(CH₃)₂)₂); 13.0 (s, Si(CH(CH₃)₂)₂); 0.4 (s, Si(CH₃)₃). 

**29Si NMR** (CDCl₃; 79.5 MHz): δ (ppm) = –22.7 (s, Si(i-Pr)₂); –17.3 (s, SiMe₃). 

**IR** (KBr): ν (cm⁻¹) = 2954 (w); 2867 (w); 2160 (s, C≡C); 1475 (m); 1441 (m); 1250 (m); 1227 (w); 1202 (w); 1098 (w); 1037 (w); 996 (m); 873 (s); 845 (s); 795 (s); 758 (s); 665 (m); 642 (m). 

**HR-MS** (EI): m/z = 508.2425 [M]⁺ (calculated for C₃₂H₄₀Si₃: 508.2438).

### Bis(2-ethylphenyl)ethynyl-sulfide (12a)

An aqueous solution of NaOH (2 M, 4.00 mL, 8.00 mmol, 20 eq.) was added to a solution of 18a (195 mg, 421 μmol) in MeOH (8 mL) and Et₂O (4 mL) at room temperature. The brown solution was stirred for 2 h, after which Et₂O (20 mL) and 2 M HCl aq. (20 mL) were added. The organic layer was separated and the aqueous layer was extracted with Et₂O (3 × 10 mL). The combined organic layers were washed with brine (15 mL), dried over MgSO₄, filtered and concentrated in vacuo. The residue was subjected to column chromatography on silica gel with hexane/CH₂Cl₂ (5/1 (v/v)) as eluent (Rf = 0.10) to give 12a (106 mg, 375 μmol, 89% yield) as a yellow oil.

**1H NMR** (CDCl₃; 250.1 MHz): δ (ppm) = 7.46 – 7.52 (m, 4H, H₃,6); 7.28 – 7.32 (m, 4H, H₄,5); 3.33 (s, 2H, C≡C).

### Bis(2-ethylphenyl)ethynyl-diisopropyl-silane (12b)

Finely powdered K₂CO₃ (24.0 mg, 180 μmol, 0.5 eq.) was added to a solution of 18b (179 mg, 352 μmol) in MeOH (3.4 mL) and THF (0.6 mL) at room temperature. The light yellow suspension was vigorously stirred for 40 min and then diluted with Et₂O (15 mL) and H₂O (15 mL). The organic layer was separated and the aqueous layer was extracted with Et₂O (2 × 7 mL). The combined organic layers were washed with H₂O (5 × 10 mL), dried over MgSO₄, filtered and concentrated in vacuo.
The residue was subjected to column chromatography on silica gel with hexane/CH₂Cl₂ (4/1 (v/v)) as eluent (R_f = 0.35) to give **12b** (106 mg, 291 μmol, 83% yield) as a white solid.

**^1H NMR** (CDCl₃; 250.1 MHz): δ (ppm) = 7.45 – 7.58 (m, 4H, H₃,6); 7.23 – 7.33 (m, 4H, H₄,5); 3.29 (s, 2H, ≡C–H); 1.08 – 1.32 (m, 14H; Si(CH(C₃H₃)₂)₂). **^13C NMR** (CDCl₃; 62.90 MHz): δ (ppm) = 133.0 (s, C₆); 132.9 (s, C₃); 128.8 (s, C₄,5); 126.5 (s, C₁); 125.6 (s, C₂); 105.3 (s, Ar≡CSi); 92.6 (s, Ar≡C≡Si); 82.5 (s, ArC≡CH); 81.8 (s, ArC≡CH); 18.2 (s, Si(CH(C₃H₃)₂)₂); 13.0 (s, Si(CH(CH₃)₂)₂). **^29Si NMR** (CDCl₃; 79.5 MHz): δ (ppm) = 22.6 (s, Si(i-Pr)₂).

**IR** (KBr): ν (cm⁻¹) = 2951 (m); 2860 (w); 2365 (w); 2161 (s, C≡C); 1474 (m); 1439 (m); 1319 (w); 1254 (w); 1220 (w); 1191 (w); 1094 (w); 999 (m); 954 (w); 880 (w); 848 (s); 766 (s); 744 (s); 676 (m); 661 (s); 628 (s); 528 (w); 511 (w); 481 (m).

**HR-MS** (El): m/z = 364.1637 [M⁺] (calculated for C₂₆H₂₄Si: 364.1647).

**Attempted cyclization of 12a with PhPCl₂**

A solution of LiN(SiMe₃)₂ in hexane (1.0 M, 750 μL, 750 μmol, 2 eq.) was added dropwise to a solution of **12a** (106 mg, 375 μmol) in THF (8 mL) at room temperature. The dark red solution was stirred for 4 h and then cooled to 0 °C. A solution of PhPCl₂ (51.0 μL, 380 μmol, 1 eq.) in THF (12 mL) was added dropwise to the reaction mixture at 0 °C. The resulting dark brown suspension was stirred at room temperature for 15 h. **^3¹P NMR** analysis of the reaction mixture showed a single peak at δ(³¹P) = –60.5 ppm. The solution was concentrated in vacuo and the dry residue was extracted with Et₂O (20 mL). The Et₂O solution was concentrated in vacuo and the residue was washed with dry pentane (20 mL). Various crystallization attempts (from CH₂Cl₂/pentane, CH₂Cl₂, THF, CDCl₃/pentane, Et₂O/pentane) gave nothing but an insoluble blue solid. Neither the molecular ion peak of **8a** in GC-MS, nor the correct **¹³C NMR** chemical shifts were detected.

**Attempted cyclization of 12b with MesPCl₂**

A solution of LiN(SiMe₃)₂ in hexane (1.0 M, 300 μL, 300 μmol, 2.2 eq.) was added dropwise to a solution of **12b** (49.0 mg, 130 μmol) in THF (3 mL) at 0 °C. The yellow solution was stirred for 2 h at 0 °C, and then a solution of MesPCl₂ (41.0 mg, 160 μmol, 1.2 eq.) in THF (26 mL) was added. The resulting brown solution was stirred at room temperature for 17 h. **^3¹P NMR** analysis of the reaction mixture showed a single peak at δ(³¹P) = –81.2 ppm. The solution was concentrated in vacuo, affording a brown oil, which was not further purified.
Bisethynyl-phenyl-phosphine sulfide (21a)

Method A (scheme 6.5 (a) and (b)): To a solution of Me₂SiC≡CH (1.48 mL, 10.5 mmol, 2.1 eq.) in THF (22 mL) was added dropwise over a period of 1 h a solution of EtMgBr in THF (0.5 M, 22.0 mL, 11.0 mmol) at 0 °C, prepared from Mg (291 mg, 12.0 mmol, 2.4 eq.) and EtBr (820 μL 11.0 mmol, 2.2 eq.). Stirring was continued for 1 h, after which the solution was added dropwise over a period of 1 h to a solution of PhPCl₂ (679 μL, 5.00 mmol) in THF (20 mL) at 0 °C. The resulting yellow solution was stirred for 2.5 h and subsequently warmed to room temperature. To this solution containing PhP(C≡C≡SiMe₃)₂ (δ(31P) = −60.0 ppm) S₈ (256 mg, 1.00 mmol, 0.2 eq.) was added and the reaction mixture was stirred for 48 h at 50 °C. The solution was washed with a saturated NH₄Cl solution (aq, 10 mL) and H₂O (10 mL) and extracted with Et₂O (3 × 25 mL). The organic layers were dried over MgSO₄, filtered through a pad of silica and concentrated in vacuo, to give PhP(S)(C≡C≡SiMe₃)₂ (21a; δ(31P) = −9.7 ppm). The orange oil was dissolved in THF (20 mL) and H₂O (0.5 mL). Bu₄NF on silica (1 μmol/mg, 50.0 mg, 50.0 μmol, 1 mol%) was added portionwise and stirring was continued for 12 h. The reaction mixture was filtered and the solvent removed in vacuo. The dry residue was subjected to column chromatography on silica gel with hexane/EtOAc (9/1 to 4/1 (v/v)) as eluent (Rf = 0.20) to give 21a (330 mg, 1.74 mmol, 35% yield) as a yellow powder.

Method B (Scheme 6.5 (c)): To a solution of PhPCl₂ (679 μL, 5.00 mmol) in THF (20 mL) at 0 °C was added dropwise a solution of HCC≡CMgBr in THF (0.50 M, 22.0 mL, 11.0 mmol, 2.2 eq.) over a period of 1 h at 0 °C. During the addition, the color of the reaction mixture changed from colorless to brown. Stirring was continued for 2 h at 0 °C, giving PhP(≡C≡CH)₂ (δ(31P) = −60.2 ppm). At room temperature, S₈ (256 mg, 1.00 mmol, 0.2 eq.) was added and the reaction mixture was stirred for 24 h at 50 °C. H₂O (360 mL, 20.0 μmol, 4 eq.) was added to destroy the remaining Grignard reagents. The solution was diluted with Et₂O (40 mL), filtered and concentrated in vacuo. The dry residue was subjected to column chromatography on silica gel with hexane/EtOAc (1/1 (v/v)) as eluent (Rf = 0.90) to give 21a (440 mg, 2.31 mmol, 46% yield) as a yellow powder.

1H NMR (20a; CDCl₃; 250.13 MHz): δ (ppm) = 8.10 (dd, 3J₉₈ = 17.1 Hz, 3J₉₉ = 6.4 Hz, 2H, H²,⁶); 7.57 (s, 3H, H₃,₄,₅); 0.29 (s, 9H, Si(CH₃)₃). 31P NMR (20a; CDCl₃; 101.26 MHz): δ (ppm) = −9.7 (s).

Mp (21a) = 66.5 − 67.5 °C. 1H NMR (21a; CDCl₃; 250.13 MHz): δ (ppm) = 8.13 (ddd, 3J₉₈ = 17.5 Hz, 3J₉₉ = 8.0 Hz, 4J₉₈ = 1.6 Hz, 2H, H²,⁶); 7.55 − 7.69 (m, 3H, H₃,₄,₅); 3.42 (d, 3J₉₈ = 11.0 Hz, 2H, ≡CH). 13C NMR (21a; CDCl₃; 100.62 MHz): δ (ppm) = 133.0 (d, 4JCP = 4.0 Hz, C₄); 130.9 (d, 1JCP = 116.7 Hz, C¹); 130.4 (d, 3JCP = 14.1 Hz, C₃,₅); 128.9 (d, 2JCP = 15.1 Hz, C²,₆); 77.6 (d, 1JCP = 168.0 Hz, P≡C); 93.3 (d, 2JCP = 31.2 Hz, ≡CH). 31P NMR (21a; CDCl₃; 101.26 MHz): δ (ppm) = −9.7 (s). IR (21a; neat): ν (cm⁻¹) = 3262 (w);
3231 (m); 2962 (w); 2053 (s, C≡C stretch); 1478 (w); 1439 (m); 1390 (w); 1313 (m); 1232 (w); 1186 (w); 1105 (m); 1017 (w); 998 (w); 715 (m); 682 (s, P=S stretch).

**Bisethynyl-mesityl-phosphine sulfide (21b)**

*Method A (scheme 6.5 (a) and (b)):* To a solution of Mes₃Si≡CH (3.36 mL, 24.0 mmol, 2.2 eq.) in THF (40 mL) was added dropwise over a period of 1 h at 0 °C a solution of EtMgBr in THF (0.63 M, 40.0 mL, 25.2 mmol), prepared from Mg (663 mg, 27.3 mmol, 2.5 eq.) and EtBr (1.82 mL 25.0 mmol, 2.3 eq.). Stirring was continued for another hour at 0 °C, after which the solution was added dropwise over a period of 1 h to a solution of MesPCl₂ (2.78 g, 11.00 mmol, 1 eq.) in THF (40 mL) at 0 °C. The reaction mixture was stirred for 2.5 h and subsequently warmed to room temperature. To this solution containing MesP(C≡SiMes₃)₂ S₈ (610 mg, 2.38 mmol, 0.22 eq.) was added and the reaction mixture was stirred for 40 h. The solvent was removed *in vacuo* and the dry residue redissolved in Et₂O (40 mL), washed with a saturated NH₄Cl solution (aq) and H₂O. The organic layer was dried over MgSO₄, filtered through a pad of silica and concentrated *in vacuo*. The crude product was not isolated.

*Method B (Scheme 6.5 (c)):* To a solution of MesPCl₂ (700 μL, 5.00 mmol) in THF (20 mL) was added dropwise a solution of HClMgBr in THF (0.50 M, 30.0 mL, 15.0 mmol, 3 eq.) over a period of 1 h at 0 °C. During the addition, the color of the reaction mixture changed from colorless to brown. Stirring was continued for 24 h, after which S₈ (256 mg, 1.00 mmol, 0.2 eq.) was added and the reaction mixture was stirred for another 48 h at 50 °C. The reaction was quenched with a saturated NH₄Cl solution (aq). The aqueous layer was extracted with CH₂Cl₂ and the combined organic layers were dried over MgSO₄, filtered and concentrated *in vacuo*. The dry residue was subjected to column chromatography on silica gel with hexane/EtOAc (9/1 to 2/1 (v/v)) as eluent (Rf (2/1) = 0.70) and the product was further purified by crystallization from cooling a hexane/EtOAc (19/1 (v/v)) solution, giving 21b (1.28 g, 5.51 mmol, 50% yield) as orange crystals.

**1H NMR** (CDCl₃; 250.13 MHz): δ (ppm) = 6.97 (d, 4JHP = 5.5 Hz, 2H, H₃S₅); 3.48 (d, 3JHP = 10.8 Hz, 2H, ≡CH₂); 2.87 (s, 6H, o-CH₃ (Mes)); 2.34 (s, 3H, p-CH₃ (Mes)). **13C NMR** (CDCl₃; 100.62 MHz): δ (ppm) = 142.1 (d, 1JCP = 3.3 Hz, C⁻); 141.0 (d, 1JCP = 12.6 Hz, C⁻); 131.2 (d, 3JCP = 13.1 Hz, C⁻); 126.0 (d, 1JCP = 110.1 Hz, C¹); 92.6 (d, 3JCP = 30.0 Hz, ≡CH); 79.3 (d, 1JCP = 163.3 Hz, PCE); 23.4 (d, 3JCP = 8.4 Hz, o-CH₃ (Mes)); 20.9 (d, 5JCP = 1.4 Hz, p-CH₃ (Mes)). **31P NMR** (CDCl₃; 101.26 MHz): δ (ppm) = −16.4 (s).
**Bis(2-(trimethylsilyl)ethynyl)phenyl]ethynyl-phenyl-phosphine sulfide (19a)**

**Method A (scheme 6.4 (f)):** A solution of LiN(SiMe₃)$_2$ in hexane (1.0 M, 540 μL, 540 μmol, 2.4 eq.) was added dropwise to a solution of 17 (90.0 mg, 454 μmol, 2 eq.) in dry THF (10 mL) at 0 °C. After 1 h of stirring, PhPCl$_2$ (30.8 μL, 227 μmol) was added dropwise over a period of 15 min, while the reaction was kept at 0 °C. After another 1 h of stirring, the solution was allowed to warm to room temperature, after which S$_8$ (14.1 mg, 55.0 μmol, 0.24 eq.) was added. The reaction mixture was stirred for 15 h and, after which $^{31}$P NMR analysis showed a single peak at $\delta(^{31}\text{P}) = 122.2$ ppm. The reaction was quenched with water and the aqueous layer was extracted with Et$_2$O (3 × 40 mL), the combined organic layers dried over MgSO$_4$, filtered and concentrated in vacuo. The residue was subjected to column chromatography on silica gel with hexane/EtOAc (1/0 to 5/1 (v/v)) with 1% NEt$_3$ as eluent. The correct product was not isolated.

**Method B (Scheme 6.5 (d)):** A solution of n-BuLi in hexane (1.6 M, 1.80 mL, 2.88 mmol, 2.04 eq.) was added dropwise to a solution of 21a (260 mg, 1.41 mmol) in THF (14 mL). The resulting yellow solution was stirred for 3 h, after which a solution of 14 (733 mg, 2.89 mmol, 2.05 eq.) in THF (5 mL) was added dropwise at –78 °C. The reaction mixture was stirred for 1 h at –78 °C and then allowed to warm to room temperature. Stirring was continued for 20 h, after which the reaction was quenched with H$_2$O (10 mL). The aqueous layer was extracted with CH$_2$Cl$_2$ (3 × 30 mL). The combined organic layers were dried over MgSO$_4$, filtered and concentrated in vacuo. The residue was subjected to column chromatography on silica gel with hexane/CH$_2$Cl$_2$ (1/0 to 1/3 (v/v)) as eluent. Two products were isolated, which were found to be the starting materials.

**Method C (Scheme 6.5 (e)):** See Table 6.2. for the reaction conditions used. 15 (150 mg, 500 μmol, 2 eq.), 21a (47.6 mg, 250 μmol), Pd(OAc)$_2$ (2.21 mg, 10.0 μmol, 4 mol%), PPh$_3$ (10.5 mg, 20.0 mmol, 8 mol%) and Cul (3.80 mg, 20.0 mmol, 8 mol%) were suspended in the right solvent system (5 mL) and placed under N$_2$ (and H$_2$). The reaction mixture was stirred at the correct temperature for 72 h. After cooling the

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Chapter 6: P,S-, P,Si- and P,B-macrocycles

mixture down to room temperature, H₂O (25 mL) and CH₂Cl₂ (25 mL) were added. The aqueous layer was extracted with CH₂Cl₂ (3 × 10 mL) and the combined organic layers were washed with H₂O (10 mL), dried over MgSO₄, filtered and concentrated in vacuo. The residue was subjected to column chromatography on silica gel with hexane/EtOAc (10/1 (v/v)) as eluent. None of the applied conditions gave the correct product.

Method D (Scheme 6.6 (h)): A suspension of 21a (29.7 mg, 50.0 μmol), HCC≡CSiMe₃ (19.6 mg, 200 μmol, 4 eq.), Pd(OAc)₂ (560 mg, 2.50 μmol, 5 mol%), PPh₃ (2.62 mg, 5.00 mmol, 10 mol%) and CuI (1.90 mg, 5.00 mmol, 10 mol%) in THF (4 mL) and NEt₃ (1 mL) was stirred for 24 h at 50 °C. The mixture was washed with H₂O (10 mL) and the aqueous layers were extracted with CH₂Cl₂ (3 × 10 mL). The combined organic layers were dried over MgSO₄, filtered and concentrated in vacuo. The residue was subjected to column chromatography on silica gel with hexane/EtOAc (3/1 (v/v)) as eluent. The correct product was not formed and unreacted 21a was isolated.

(2-Ethynylphenyl)trimethylsilane (22)

A solution of n-BuLi in hexane (1.6 M, 26.3 mL, 42.0 mmol, 2.1 eq.) was added dropwise to a solution of ethynylbenzene (2.04 g, 20.0 mmol) in THF (15 mL) at −40 °C. After completion of the addition, the reaction was cooled to −70 °C, and a solution of t-BuOK (3.37 g, 30.0 mmol, 1.5 eq.) in THF (15 mL) was added. Stirring was continued for 30 min, and then the reaction mixture was warmed to 0 °C. Another portion of t-BuOK (898 mg, 8.00 mmol, 0.4 eq.) in THF (5 mL) was added and the reaction mixture was recooled to −40 °C. ClSiMe₃ (6.48 g, 60.0 mmol, 3 eq.) was added and the solution was warmed to room temperature. A solution of KOH in MeOH (2 M, 30.0 mL, 60.0 mmol, 3 eq.) was added, after which the reaction mixture was stirred for 2 h at 50 °C. The solution was extracted with pentane (3 × 25 mL) and the organic layer washed with H₂O (30 mL) and a 2 M HCl solution (aq, 20 mL). The combined organic layers were dried over MgSO₄, filtered and concentrated in vacuo. The residue is distilled (0.1 mbar, 50 °C) to give 22 (1.42 g, 12.7 mmol, 63% yield) as a colorless oil.

¹H NMR (CDCl₃; 250.13 MHz): δ (ppm) = 7.55 – 7.49 (m, 2H, H₄,5); 7.31 – 7.27 (m, 2H, H₃,6); 3.20 (s, 1H, ≡CCH); 0.41 (s, 9H, Si(CH₃)₃).

Bis(2-(trimethylsilyl)phenyl)ethynyl-phenyl-phosphine sulfide (23a)

Method A (Scheme 6.6 (b)): A solution of EtMgBr in THF (0.84 M, 2.5 mL, 2.10 mmol), prepared from Mg (53.5 mg, 2.20 mmol, 2.2 eq.) and EtBr (153 μL 2.10 mmol, 2.1 eq.), was added dropwise to a solution of 22 (349 mg, 2.00 mmol, 2 eq.) at 0 °C. Stirring was continued for 1 h at 0 °C, after which a solution of PhPCl₂ (179 mg, 1.00 mmol) in THF (5 mL) was added at 0 °C. The reaction mixture was stirred for 12 h, and simultaneously allowed to warm to room temperature. ³¹P NMR analysis of the
reaction mixture showed the presence of PhP(C≡C(o-SiMe₃Ph))₂ (δ(³¹P) = −60.8 ppm). Subsequently, S₈ (130 mg, 500 μmol, 0.2 eq.) was added and the solution is stirred for 48 h. The solvents were evaporated in vacuo, the residue was diluted with Et₂O (10 mL), filtered and concentrated in vacuo. The dry residue was subjected to column chromatography on silica gel with hexane/EtOAc (20/1 (v/v)) as eluent. The correct product was not isolated.

**Method B (Scheme 6.6 (c))**: A solution of 22 (192 mg, 1.10 mmol, 2.2 eq.), PhPCl₂ (67.9 μL, 500 μmol), NEt₃ (630 μL, 4.50 mmol, 9 eq.) and CuI (9.52 mg, 50.0 μmol, 10 mol%) in toluene (10 mL) was stirred for 24 h at room temperature, giving PhP(C≡C(o-SiMe₃Ph))₂ (δ(³¹P) = −60.4 ppm). Subsequently, S₈ (25.7 mg, 100 μmol, 0.2 eq.) was added and the reaction mixture was stirred for 25 h at 50 °C. The solution was washed with H₂O (3 × 15 mL) and extracted with CH₂Cl₂ (3 × 15 mL). The combined organic layers were dried over MgSO₄, filtered and concentrated in vacuo. The dry residue was subjected to column chromatography on silica gel with hexane/EtOAc (1/1 (v/v)) as eluent (Rₛ = 0.90) to give 23a (126 mg, 258 μmol, 52% yield) as a yellow solid.

**¹H NMR** (CDCl₃; 250.13 MHz): δ (ppm) = 8.03 (dd, ³JHP = 17.0 Hz, ³JHH = 6.5 Hz, 2H, H³⁻⁶ (PPh)); 7.44 – 7.33 (m, 7H, H³⁻⁵ (Ar) + H³⁻⁴⁻⁵ (PPh)); 7.24 – 7.16 (m, 4H, H³⁻⁴⁻⁵ (Ar)); 0.15 (s, 18H, Si(CH₃)₃). **³¹P NMR** (CDCl₃; 101.26 MHz): δ (ppm) = −9.3 (s).

**1-Ethynyl-2-iodobenzene (25)**

To a solution of 15 (1.50 g, 5.00 mmol) in Et₂O (50 mL) and MeOH (100 mL) was added a solution of NaOH in H₂O (2.0 M, 25 mL, 50 mmol, 10 eq.). The reaction mixture was stirred for 1 h at room temperature, and subsequently extracted with CH₂Cl₂ (3 × 75 mL). The organic layers were washed with H₂O (2 × 75 mL), dried over MgSO₄, filtered and concentrated in vacuo, giving 25 (1.02 g, 4.47 mmol, 89% yield) as a colorless liquid.

**¹H NMR** (CDCl₃; 250.13 MHz): δ (ppm) = 7.72 (d, ³JHH = 7.5 Hz, 1H, H³); 7.38 (d, ³JHH = 7.5 Hz, 1H, H⁴); 7.17 (t, ³JHH = 7.5 Hz, 1H, H⁵); 6.89 (t, ³JHH = 7.5 Hz, 1H, H⁶); 3.29 (s, 1H, H⁷).[²⁸]

**Bis(2-iodophenyl)ethynyl-phenyl-phosphine sulfide (24a)**

**Method A (Scheme 6.6 (f))**: A solution of EtMgBr in THF (0.50 M, 5.50 mL, 2.75 mmol), prepared from Mg (72.9 mg, 3.00 mmol, 2.6 eq.) and EtBr (180 μL 2.75 mmol, 2.2 eq.), was added dropwise to a solution of 25 (513 mg, 2.25 mmol, 2 eq.) in THF (2.5 mL) at −78 °C. Stirring was continued for 1 h, during which the reaction mixture was allowed to warm to 0 °C. This solution was added dropwise to a solution of PhPCl₂ (153 μL, 1.13 mmol) in THF (5 mL) at 0 °C. The reaction mixture was stirred for 16 h, during which the reaction mixture was allowed to warm to room temperature, to give PhP(C≡C(o-IPh))₂ (δ(³¹P) = −60.5 ppm). Subsequently, S₈ (146 mg,
570 μmol, 0.5 eq.) was added and the solution is stirred for 24 h at 50 °C. H₂O (50.0 μL, 2.78 μmol, 2.5 eq.) was added to destroy the remaining Grignard reagents. The mixture was diluted with Et₂O (10 mL), filtered and concentrated in vacuo. The dry residue was subjected to column chromatography on silica gel with hexane/EtOAc (1/3 (v/v)) with 1% NEt₃ as eluent (Rᵢ = 0.10), to give 24a (60.0 mg, 100 μmol, 4% yield) as a yellow solid.

**Method B (Scheme 6.6 (g))**: A solution of 25 (250 mg, 1.10 mmol, 2.2 eq.), PhPCl₂ (67.9 μL, 500 μmol), NEt₃ (630 μL, 4.50 mmol, 9 eq.) and CuI (9.52 mg, 50.0 μmol, 10 mol%) in toluene (10 mL) was stirred for 24 h at room temperature, giving PhP(C≡C(o-IPh))₂ (δ(31P) = –62.0 ppm). Subsequently, S₈ (25.7 mg, 100 μmol, 0.2 eq.) was added and the reaction mixture was stirred for 48 h at room temperature. The solution was washed with H₂O (10 mL) and extracted with CH₂Cl₂ (3 × 75 mL). The combined organic layers were dried over MgSO₄, filtered and concentrated in vacuo. The dry residue was subjected to column chromatography on silica gel with hexane/EtOAc (4/1 (v/v)) as eluent (Rᵢ = 0.20) to give 24a (198 mg, 333 μmol, 66% yield) as a yellow solid.

**1H NMR** (CDCl₃; 250.13 MHz): δ (ppm) = 8.18 (ddd, 3J_HP = 17.3 Hz, 3J_HH = 7.5 Hz, 4J_HH = 2.3 Hz, 2H, H₂(Ph)); 7.72 (d, 3J_HH = 7.8 Hz, 2H, H₁(Ar)); 7.46 – 7.50 (m, 5H, H₆(Ar) + H₃,4,5(PPh)); 7.21 (t, 3J_HH = 7.8 Hz, 2H, H₄(Ar)); 6.97 (t, 3J_HH = 7.8 Hz, 2H, H₅).

**31P NMR** (CDCl₃; 101.26 MHz) δ (ppm) = –8.7 (s).

**1-(Trimethylsilyl)ethynyl-2-(triphenylsilyl)ethynyl-benzene (26)**

A solution of 15 (150 mg, 500 μmol), HC≡CSiPh₃ (142 mg, 500 μmol, 1 eq.), Pd(OAc)₂ (2.25 mg, 10.0 μmol, 2 mol%), PPh₃ (5.25 mg, 20.0 μmol, 4 mol%) and Cul (3.81 mg, 20.0 μmol, 4 mol%) in THF (5 mL) and NEt₃ (1 mL) was stirred at room temperature for 24 h. The mixture was concentrated in vacuo and the residue was diluted with EtOAc (150 mL) and H₂O (150 mL). The mixture was washed with H₂O (2 × 100 mL) and the aqueous layers were extracted with CH₂Cl₂ (3 × 100 mL). The combined organic layers were dried over MgSO₄, filtered and concentrated in vacuo. The residue was subjected to column chromatography on silica gel with hexane as eluent (Rᵢ = 0.30) to give 26 (112 mg, 245 μmol, 50% yield) as a yellow oil.

**1H NMR** (CDCl₃; 250.13 MHz): δ (ppm) = 7.84 – 7.31 (m, 19H, H³,4,5,6 + Si(C₆H₅)₃); 0.14 (s, 9H, Si(CH₃)₃).

**1-(Triphenylsilyl)ethynyl-2-ethynyl-benzene (27)**

K₂CO₃ (34.6 mg, 250 μmol, 1 eq.) was added to a solution of 26 (114 mg, 250 μmol) in THF (10 mL) and MeOH (10 mL). The reaction mixture was stirred for 2 h at room temperature, and subsequently extracted with CH₂Cl₂ (3 × 10 mL). The organic layers were washed with
H₂O (20 mL), dried over MgSO₄ and concentrated in vacuo. The residue was analyzed by NMR spectroscopy, which showed that no reaction had taken place.

1-(Triisopropylsilyl)ethynyl-2-(trimethylsilyl)ethynyl-benzene (28)

A solution of 15 (450 mg, 1.50 mmol), HC≡CSi(i-Pr)₃ (319 mg, 1.75 mmol, 1.2 eq.), PdCl₂ (13.3 mg, 75.0 μmol, 5 mol%), PPh₃ (19.7 mg, 75.0 μmol, 5 mol%) and CuI (28.6 mg, 150 μmol, 10 mol%) in THF (5 mL) and NEt₃ (0.5 mL) was stirred at room temperature for 24 h. The mixture was concentrated in vacuo and the residue was diluted with EtOAc (150 mL) and H₂O (150 mL). The mixture was washed with H₂O (2 × 100 mL) and the aqueous layers were extracted with CH₂Cl₂ (3 × 100 mL). The combined organic layers were dried over MgSO₄, filtered and concentrated in vacuo. The residue was subjected to column chromatography on silica gel with hexane as eluent (Rf = 0.10) to give 28 (486 mg, 1.37 mmol, 91% yield) as yellow oil.

³¹H NMR (CDCl₃; 250.13 MHz): δ (ppm) = 7.52 (m, 3 JHH = 5.8 Hz, 4 JHH = 3.4 Hz, 2H, H₃,6); 7.28 (m, 3 JHH = 5.8 Hz, 4 JHH = 3.4 Hz, 2H, H₄,5); 1.21 (s, 21H, Si(CH(C₂H₃)₂)₃); 0.30 (s, 9H, Si(CH₃)₃).[37]

Bis(2-(triisopropylsilyl)ethynyl)-phenyl-ethynyl-phenyl-phosphine (30a)

A yellow solution of 29 (203 mg, 786 μmol, 2.1 eq.), PhPCl₂ (51.0 μL, 376 μmol), NEt₃ (300 μL, 2.15 mmol, 5.7 eq.) and CuI (7.24 mg, 38.0 μmol, 10 mol%) in toluene (15 mL) was stirred for 16 h at room temperature. The reaction mixture was diluted with pentane (20 mL) and filtrated through a pad of alumina. The filtrate was concentrated in vacuo and the dry residue was subjected to column chromatography on alumina with hexane as eluent (Rf = 0.28) to give 30a (126 mg, 187 μmol, 50% with respect to PhPCl₂) as a yellow solid, together with unreacted 29 (95.1 mg, 368 μmol, 47% yield).
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1H NMR (CDCl3; 400.13 MHz): \( \delta \) (ppm) = 7.94 (t, \( ^3J_{HH} \approx ^3J_{HH} = 8.0 \) Hz, 2H, \( H^2 \), PPh); 7.52 – 7.57 (m, 4H, \( H^3, H^4 \) (Ar)); 7.42 – 7.46 (m, 3H, \( H^3, H^4, H^5 \) (PPh)); 7.28 – 7.34 (m, 4H, \( H^4, H^5 \) (Ar)); 1.18 (s, 42H, \( Si(CH(CH_3)_2)_3 \)).

13C NMR (CDCl3; 125.80 MHz): \( \delta \) (ppm) = 133.3 (s, \( C^1 \) (PPh)); 132.6 (s, \( C^3 \) (Ar)); 132.2 (d, \( ^2J_{CP} = 21.9 \) Hz, \( C^2 \) (PPh)); 129.2 (s, \( C^4 \) (PPh)); 128.6 (d, \( ^3J_{CP} = 7.8 \) Hz, \( C^5 \) (PPh)); 128.5 (s, \( C^6 \) (Ar)); 127.8 (s, \( C^7 \) (Ar)); 126.3 (d, \( ^3J_{CP} = 1.4 \) Hz, \( C^1 \) (Ar)); 125.2 (d, \( ^4J_{CP} = 1.1 \) Hz, \( C^2 \) (Ar)); 104.74 (s, \( C = CSi \)); 104.67 (d, \( ^2J_{CP} = 7.6 \) Hz, \( C = CP \)); 95.8 (s, \( \equiv Si \)); 86.8 (d, \( ^1J_{CP} = 5.0 \) Hz, \( \equiv CP \)); 18.7 (s, \( Si(CH(CH_3)_2)_3 \)); 11.3 (s, \( Si(CH(CH_3)_2)_3 \)).

31P NMR (CDCl3; 161.98 MHz): \( \delta \) (ppm) = –59.9 (t, \( ^2J_{PH} = 8.9 \) Hz).

29Si NMR (CDCl3; 79.5 MHz): \( \delta \) (ppm) = –1.3 (s).

**HR-MS** (EI): \( m/z = 687.3602 \) [M(O) + H]° (calculated for \( C_{44}H_{56}OPSi_2 \) = 687.3607).

### Bis[2-(triisopropylsilylethynyl)phenyl]ethynyl-mesityl-phosphine (30b)

A yellow solution of 29 (640 mg, 2.48 mmol, 2.1 eq.), MesPCl2 (261 μL, 1.18 mmol), NEt3 (1.00 mL, 7.18 mmol, 6 eq.) and Cul (47.6 mg, 248 μmol, 20 mol%) in toluene (40 mL) was stirred for 48 h at room temperature. The reaction mixture was concentrated in vacuo and the dry residue was subjected to column chromatography on alumina with hexane as eluent (\( R_f = 0.29 \)) to give 30b (259 mg, 364 μmol, 31% with respect to MesPCl2) as a yellow solid, together with unreacted 29 (402 mg, 1.56 mmol, 63% yield).

1H NMR (CDCl3; 400.13 MHz): \( \delta \) (ppm) = 7.47 – 7.53 (m, 4H, \( H^3, H^4 \) (Ar)); 7.25 – 7.31 (m, 4H, \( H^4, H^5 \) (Ar)); 6.97 (d, \( ^4J_{HH} = 3.3 \) Hz, 2H, \( H^3, H^4 \) (Mes)); 2.88 (s, 6H, o-CH3 (Mes)); 2.34 (s, 3H, p-CH3 (Mes)); 1.14 (s, 21H, \( Si(CH(CH_3)_2)_3 \)); 1.13 (s, 21H, \( Si(CH(CH_3)_2)_3 \)).

13C NMR (CDCl3; 125.80 MHz): \( \delta \) (ppm) = 144.8 (d, \( ^2J_{CP} = 20.1 \) Hz, \( C^2 \) (Mes)); 140.6 (d, \( ^4J_{CP} = 1.3 \) Hz, \( C^4 \) (Mes)); 132.7 (s, \( C^3 \) (Ar)); 132.5 (d, \( ^4J_{CP} = 2.4 \) Hz, \( C^5 \) (Ar)); 129.6 (d, \( ^3J_{CP} = 5.8 \) Hz, \( C^5 \) (Mes)); 128.2 (s, \( C^5 \) (Ar)); 127.8 (s, \( C^4 \) (Ar)); 125.7 (d, \( ^3J_{CP} = 1.8 \) Hz, \( C^1 \) (Ar)); 125.6 (d, \( ^4J_{CP} = 1.8 \) Hz, \( C^2 \) (Ar)); 125.5 (d, \( ^1J_{CP} = 1.3 \) Hz, \( C^1 \) (Mes)); 104.9 (s, \( C = CSi \)); 103.9 (d, \( ^1J_{CP} = 11.3 \) Hz, \( C = CP \)); 95.5 (s, \( \equiv Si \)); 87.5 (d, \( ^1J_{CP} = 3.8 \) Hz, \( \equiv CP \)); 23.2 (d, \( ^3J_{CP} = 18.9 \) Hz, o-CH3 (Mes)); 21.2 (s, p-CH3 (Mes)); 18.7 (s, \( Si(CH(CH_3)_2)_3 \)); 11.3 (s, \( Si(CH(CH_3)_2)_3 \)).

31P NMR (CDCl3; 161.98 MHz): \( \delta \) (ppm) = –82.3 (s). 29Si NMR (CDCl3; 79.5 MHz): \( \delta \) (ppm) = –1.3 (s).

### Bis[2-(triisopropylsilylethynyl)phenyl]ethynyl-(2,4,6-tri-tert-butylphenyl)-phosphine (30c)

A yellow solution of 29 (530 mg, 2.05 mmol, 2.1 eq.), Mes*PCl2 (0.25 M in Et2O, 4.00 mL, 1.00 mmol), NEt3 (850 μL, 6.10 mmol, 6.1 eq.) and Cul (19.0 mg, 100 μmol, 10 mol%) in toluene (40 mL) was stirred for 48 h at room temperature. 31P NMR analysis showed that the reaction did not proceed, as the major signal was at \( \delta^{31P} = 152.3 \) ppm, corresponding to Mes*PCl2. Thus, additional Cul catalyst (19.0 mg, 100 μmol, 10 mol%) was added, the reaction was heated to 60°C
and stirred for another 72 h. The $^{31}$P NMR spectrum showed a minor signal at $\delta^{(31P)} = -87.2$ ppm. The reaction mixture was concentrated in vacuo and the dry residue was subjected to column chromatography on alumina with pentane to pentane/CH$_2$Cl$_2$ (1/1 (v/v)) as eluent. None of the isolated fractions contained 30c.

**Bis(2-ethynylphenyl)ethynyl-phenyl-phosphine (31a)**

To a solution of 30a (120 mg, 179 µmol) and degassed H$_2$O (10.0 µL, 180 µmol, 1 eq.) in THF (7 mL) was added Bu$_4$NF in THF (1 M, 18.0 µL, 180 µmol, 10 mol%) dropwise over a period of 5 min. The orange reaction mixture was stirred for 1 h, after which the reaction was diluted with pentane (15 mL) and degassed H$_2$O (15 mL). The organic layer was washed with degassed H$_2$O (3 × 15 mL), dried over MgSO$_4$$_2$, filtered and concentrated in vacuo in the presence of silica gel (250 mg). Hexane was washed through this pad of silica gel to remove the silyl side-product, and then hexane/CH$_2$Cl$_2$ (3/1 (v/v)) was used as eluent ($R_f = 0.57$), to give 31a (56.0 mg, 156 µmol, 87% yield) as a white solid.

$^1$H NMR (CDCl$_3$; 250.13 MHz): $\delta$ (ppm) = 7.95 – 8.01 (m, 2H, $H^{2,6}$ (PPh)); 7.49 – 7.53 (m, 4H, $H^{4,4}$ (Ar)); 7.42 – 7.46 (m, 3H, $H^{3,4,5}$ (PPh)); 7.26 – 7.33 (m, 4H, $H^{4,5}$ (Ar)); 3.26 (s, 2H, $\equiv CH$). $^{31}$P NMR (CDCl$_3$; 161.98 MHz): $\delta$ (ppm) = –60.8 (s). $^{29}$Si NMR (CDCl$_3$; 79.5 MHz): $\delta$ (ppm) = –1.5 (s).

**Bis((2-ethynylphenyl)ethynyl)mesityl-phosphine (31b)**

To a solution of 30b (130 mg, 182 µmol) and degassed H$_2$O (10.0 µL, 180 µmol, 1 eq.) in THF (7 mL) was added Bu$_4$NF in THF (1 M, 18.0 µL, 180 µmol, 10 mol%) dropwise over a period of 5 min. The orange reaction mixture was stirred for 1 h, after which the reaction was diluted with pentane (15 mL) and degassed H$_2$O (15 mL). The organic layer was washed with degassed H$_2$O (3 × 15 mL), dried over MgSO$_4$$_2$, filtered and concentrated in vacuo in the presence of silica gel (250 mg). Hexane was washed through this pad of silica gel to remove the silyl side-product, and then hexane/CH$_2$Cl$_2$ (3/1 (v/v)) was used as eluent ($R_f = 0.46$), to give 31b (60.0 mg, 150 µmol, 82% yield) as a white solid.

$^1$H NMR (CDCl$_3$; 250.13 MHz): $\delta$ (ppm) = 7.38 – 7.44 (m, 4H, $H^{3,6}$ (Ar)); 7.18 – 7.26 (m, 4H, $H^{4,5}$ (Ar)); 6.90 (d, $^3$J$_{HF}$ = 3.3 Hz, 2H, $H^{3,5}$ (Mes)); 3.16 (s, 2H, $\equiv CH$); 2.83 (s, 6H, o-CH$_3$); 2.25 (s, 3H, $p$-CH$_3$). $^{13}$C NMR (CDCl$_3$; 100.62 MHz): $\delta$ (ppm) = 144.7 (d, $^2$J$_{CP}$ = 18.8 Hz, C$^{2,6}$ (Mes)); 140.7 (d, $^4$J$_{CP}$ = 1.5 Hz, C$^4$ (Mes)); 132.3 (s, C$^3$ (Ar)); 132.0 (d, $^3$J$_{CP}$ = 2.0 Hz, C$^5$ (Ar)); 129.4 (d, $^3$J$_{CP}$ = 5.9 Hz, C$^{3,5}$ (Mes)); 128.2 (s, C$^{4,5}$ (Ar)); 125.9 (d, $^4$J$_{CP}$ = 1.4 Hz, C$^2$ (Ar)); 125.2 (s, C$^1$ (Mes)); 124.7 (d, $^3$J$_{CP}$ = 2.4 Hz, C$^1$ (Ar)); 103.4 (d, $^2$J$_{CP}$ = 10.1 Hz, C$\equiv$CP); 87.5 (d, $^5$J$_{CP}$ = 3.0 Hz, C$\equiv$CH); 82.0 (d, $^1$J$_{CP}$ = 72.4 Hz, $\equiv$CP); 81.4 (s,
\[ \equiv \text{CH}; \ 23.2 \ (d, \ J_{CP} = 18.9 \text{ Hz, } \alpha-\text{CH}_{3}); \ 21.0 \ (s, \ p-\text{CH}_{3}). \]

**\(^{31}\text{P} \text{ NMR} \) (CDCl\(_3\); 161.98 MHz): \( \delta \ (\text{ppm}) = -83.0 \ (s). \)**

**HR-MS (EI):** \( m/z = 401.1454 \ [M + H]^{+} \) (calculated for C\(_{29}\)H\(_{22}\)P: 401.1459).

**Attempted cyclization of 31a with B(OMe)\(_3\)**

Li\( \text{N(SiMe}_{3}\)\(_2\) (1.0 M in hexane, 308 \( \mu \)L, 308 \( \mu \)mol, 2.2 eq.) was added dropwise to a solution of 31a (58.0 mg, 140 \( \mu \)mol) in THF (12 mL) at \(-78 \degree \text{C}. \) The yellow solution was stirred for 2 h at \(-78 \degree \text{C}, \) and a solution of B(OMe)\(_3\) (15.9 \( \mu \)L, 140 \( \mu \)mol, 1 eq.) in THF (4 mL) was added at \(-78 \degree \text{C}. \) The resulting brown solution was stirred for 21 h, while slowly allowed to warm to room temperature. In a separate flask, \( n-\text{BuLi} \) (1.6 M in hexane, 98.0 \( \mu \)L, 154 \( \mu \)mol, 1.1 eq.) was slowly added to a solution of MesBr (21.4 \( \mu \)L, 140 \( \mu \)mol, 1 eq.) in THF (5 mL) at \(-78 \degree \text{C}. \) The colorless solution was stirred for 1 h, while slowly allowed to warm to 0 \degree \text{C}. At that temperature, the solution was slowly added to the first flask. The combined solutions were stirred for another 4 h at room temperature, and one drop of degassed H\(_2\)O was added to quench any remaining reactive species. The solvents were removed in vacuo, and the crude product was analyzed by NMR.

**\(^{1}\text{H} \text{ NMR} \) (CDCl\(_3\); 400.13 MHz): \( \delta \ (\text{ppm}) = 7.15 - 7.55 \ (m)); \ 6.83 \ (d, \ J_{HP} = 7.2 \text{ Hz, } H_{3,5} \ (\text{Mes})); \ 2.30 \ (s, \ \alpha-\text{CH}_{3}); \ 2.26 \ (s, \ p-\text{CH}_{3}). \)**

**\(^{31}\text{P} \text{ NMR} \) (161.98 MHz): \( \delta \ (\text{ppm}) = -60.8 \ (s). \)**

**Attempted cyclization of 31b with B(OMe)\(_3\)**

Li\( \text{N(SiMe}_{3}\)\(_2\) (1.0 M in hexane, 330 \( \mu \)L, 330 \( \mu \)mol, 2.2 eq.) was added dropwise to a solution of 31b (60.0 mg, 150 \( \mu \)mol) in THF (5 mL) at \(-78 \degree \text{C}. \) The yellow solution was stirred for 2 h at \(-78 \degree \text{C}, \) and then a solution of B(OMe)\(_3\) (17.0 \( \mu \)L, 150 \( \mu \)mol, 1 eq.) in THF (2 mL) was added, still at \(-78 \degree \text{C}. \) The resulting brown solution was stirred for 24 h, while slowly allowed to warm to room temperature. NMR analysis of the reaction mixture showed signals at \( \delta^{(\text{P})} = -82.9 \ \text{ppm and } \delta^{(\text{B})} = 3.4 \ \text{ppm.} \) In a separate flask, \( n-\text{BuLi} \) (1.6 M in hexane, 103 \( \mu \)L, 165 \( \mu \)mol, 1.1 eq.) was slowly added to a solution of MesBr (23.0 \( \mu \)L, 150 \( \mu \)mol, 1 eq.) in THF (5 mL) at \(-40 \degree \text{C}. \) The colorless solution was stirred for 2 h, while slowly allowed to warm to 0 \degree \text{C}. At that temperature, the solution was slowly added to the first flask at 0 \degree \text{C}. The combined solutions were stirred for another 4 h at room temperature, and NMR analysis of the reaction mixture showed signals at \( \delta^{(\text{P})} = -83.0 \ \text{ppm and } \delta^{(\text{B})} = -2.0 \ \text{ppm.} \) Degassed H\(_2\)O (20 \( \mu \)L) was added to the reaction mixture, which was dried over MgSO\(_4\). The suspension was diluted with pentane (20 mL) and the solids were filtered off. The filtrate was concentrated in vacuo and subjected to column chromatography with hexane to hexane/CH\(_2\)Cl\(_2\) (3/1 (v/v)) as eluent. None of the isolated fractions contained 10b.
**Attempted cyclization of 31a with Si(i-Pr)₂Cl₂**

LiN(SiMe₃)₂ (1.0 M in hexane, 343 µL, 343 µmol, 2.2 eq.) was added dropwise to a solution of 31a (56.0 mg, 156 µmol) in THF (10 mL) at 0 °C. The yellow solution was stirred for 2 h at 0 °C, and then a solution of Si(i-Pr)₂Cl₂ (28.2 µL, 156 µmol, 1 eq.) in THF (2 mL) was added at 0 °C. The resulting grey solution was allowed to warm to room temperature and stirred for 20 h. H₂O (20 µL) was added to the reaction mixture, which was subsequently dried over MgSO₄, filtrated and concentrated in vacuo. NMR analysis of the brown residue showed signals at $\delta^{(31)P} = -58.2$ ppm and $-60.8$ ppm and $\delta^{(29)Si} = -1.78$ ppm and $-11.5$ ppm. The residue was extracted with pentane (20 mL) and CH₂Cl₂ (20 mL), the solids were filtered off and the filtrate was concentrated in vacuo and subjected to column chromatography with hexane to hexane/CH₂Cl₂ (2/1 (v/v)) as eluent. None of the isolated fractions contained 9a.

### 6.5. References


