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Chemistry of Silepins and their Analogs Containing Group 14 Elements

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Dedicated to Professor Jan Bergman on the occasion of his 80th birthday, in appreciation of many outstanding contributions to the field of heterocyclic chemistry and for much patience and enthusiasm during our time in your research group.

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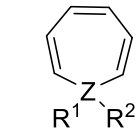
Abstract

The chemistry of silepins and related seven-membered heterocycles containing group 14 elements is reviewed.



Z = Si, Ge, Sn

Keywords: Silepins, germepins, stannepins, seven-membered heterocycles

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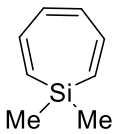
1. Introduction

While the certain classes of seven-membered heterocycles containing one heteroatom have been investigated in considerable detail,[1] such as the azepins,[2] oxepins[3] and thiepins,[4] some of their more exotic analogs featuring more unusual heteroatoms are still relatively scantily studied. This review aims at highlighting the key aspects of the chemistry and properties of seven-membered heterocycles containing group 14 elements, namely silicon, germanium and tin. These classes of compounds have for a long time been rather elusive, and useful synthetic methods for their construction have not been available until in the last decades, when modern synthetic tools became more readily accessible. In this account, the developments leading to the current level of knowledge are summarized. The emphasis is directed towards unsaturated systems, and the corresponding dihydro- and tetrahydro-derivatives are discussed only if relevant as key synthetic intermediates. Synthetic aspects are prioritized, although certain structural properties and applications of specific importance are also included in the discussion.

2. Silepins

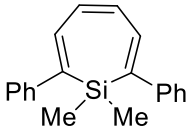
The silepin (or sila-2,4,6-heptatriene) ring system adopts a boat conformation, as deduced from NMR studies of its dimethyl derivative **1**. Its ^{1}H-NMR spectra remained unchanged over a wide temperature range (−122 °C to +30 °C), with the two methyl resonances as a singlet, indicating a rapid ring inversion.[5] For the much more sterically congested 9,9-dimethyl-9*H*-tribenzo[*b,d,f*]silepin, there was no line broadening observed for the two methyl resonances even at 200 °C, indicating a very rigid system in solution.[6] The boat conformation of the sila-2,4,6-heptatriene ring is also evident from several X-ray crystallographic studies.[6-13]



1

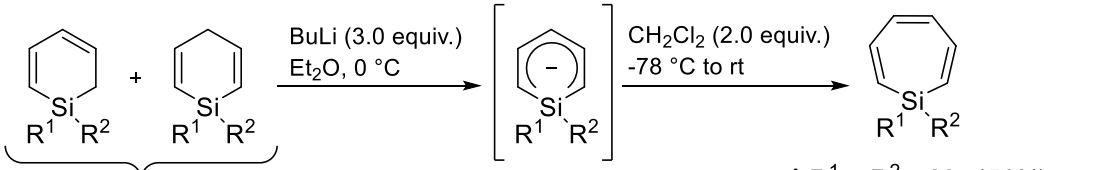
Simple, non-annulated silepins are relatively rare and only a limited number of examples are known. A tentatively assigned, fully substituted silepin was discussed at an early stage as a possible product from decomposition of a 7-silanorbornadiene derivative.[14] In a later contribution, the silepin **2** was prepared using an intricate and tedious route and was shown to cleanly produce *o*-terphenyl upon thermal pyrolysis at 250 °C via a postulated silacyclopropane intermediate.[15] Further examples have been identified as minor products from

photolysis of phenyldisilane derivatives with alkynes[16] or alkenes.[17,18] Although providing useful mechanistic insight into certain pathways leading to formation of silepins, none of these routes are however of any significant preparative use due to low isolated yields of products originating from complex reaction mixtures. As already indicated above, simple silepins undergo thermolysis with extrusion of silylene species leading to benzenoid aromatics,[15,19] but other, more complex degradation pathways are also known for silepins bearing various silyl-containing substituents.[16,20] Due to such degradation reactions, in combination other synthetic challenges and lack of suitable methods, considerable effort was required before synthetically useful approaches could be realized during later studies.

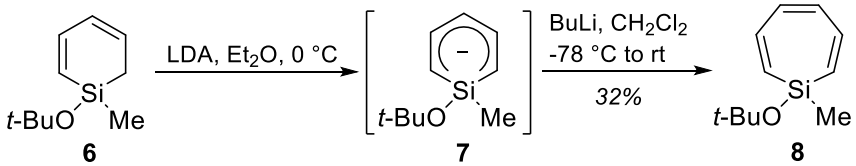


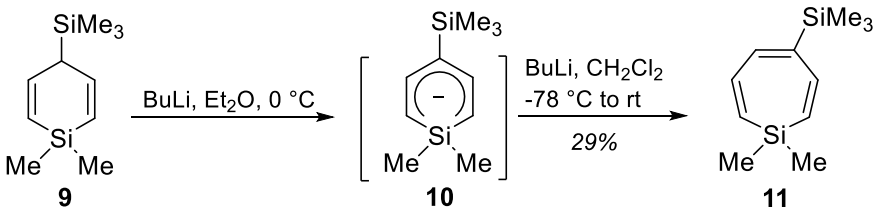
2

A rather direct method for synthesis of simple silepins was devised in the early nineties, relying on ring expansion of silacyclohexadienyl anions with chlorocarbene. For instance, isomeric mixtures of the silacyclohexadienes **3** were converted to the corresponding anionic intermediates **4**, which underwent reaction with chlorocarbene generated in situ from dichloromethane, providing the silepins **1** and **5** in moderate yields.[5]



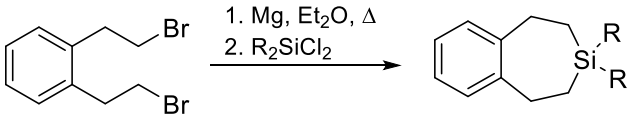
Likewise, metalation of the precursor **6** with LDA and subsequent exposure of the resulting anion **7** to butyllithium followed by dichloromethane resulted in formation of the silepin **8**, demonstrating further generality of this approach. In a further extension, the silacyclohexadiene **9** was treated with butyllithium producing the anionic intermediate **10**, which could be finally converted to the C-substituted silepin **11** in a similar manner. A detailed mechanistic investigation was also included in this important piece of work, providing explanations for the pathways leading to many of the observed products and side products.[5] Two structurally complex silepin-containing compounds have also been identified products from the reaction of a bulky N-heterocyclic silylene with boron trichloride, followed by a reduction effected by lithium metal, and finally ring expansion of a resulting silanorcaradienyl intermediate with methyl triflate or triethylamine hydrochloride.[21]





9 **10** **11**

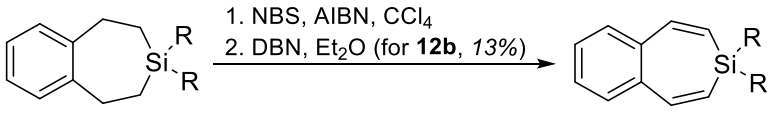
Fused silepins are more well-studied, and several different strategies for their construction are available. During extensive studies on compounds featuring C–Si bonds, a series of tetrahydrosilepins **12a–c** were obtained as products from the reactions of the Grignard reagent derived from the dibromide **13** with suitable silicon electrophiles.[22] In fact, this effort constitutes the first practical approach to structurally simple silepins.



13

12a R = Me (*38%*)
12b R = Ph (*58%*)
12c R = Cl (*63%*)

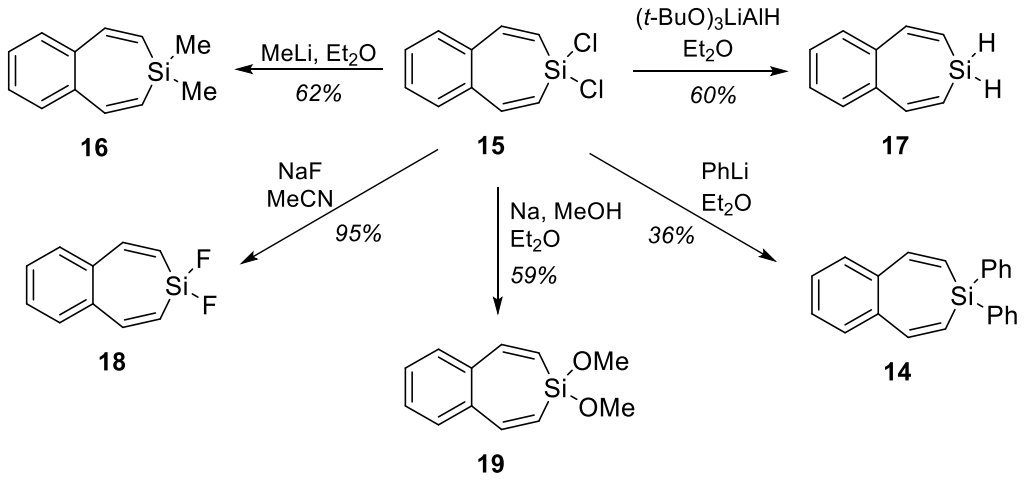
The tetrahydro-products above can serve as intermediates for further silepins. For example, the diphenyl derivative **12b** underwent initial benzylic bromination with NBS, followed by dehydrobromination in low yield induced by DBN, providing the fused silepin **14**.[19] The bromination of corresponding dichloro-derivative **12c** was followed by a thermal conversion to the product **15** in approximately 60% yield.[23] In contrast, attempts involving the dimethyl compound **12a** failed at the bromination stage as a result of decomposition into 1,2-divinylbenzene and dibromodimethylsilane.[22]



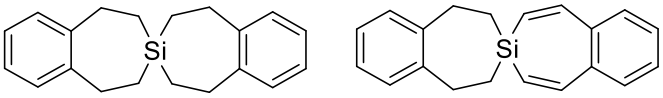
12b R = Ph
12c R = Cl

14 R = Ph
15 R = Cl

Birkofer reported that treatment of the dichloro-compound **15** with methyllithium in diethyl ether afforded 3,3-dimethyl-3*H*-benzo[*d*]silepin **16**, whereas reduction with tris-(*tert*-butoxy)lithium aluminium hydride provided the unstable parent fused silepin **17**.[24] A further demonstration of the synthetic utility of compound **15** was provided by the same group, as substitution with fluoride or methoxide gave the products **18** and **19**, respectively, whereas exposure of **15** to 2.2 equiv. of phenyllithium in diethyl ether provided an alternative synthesis of the diphenyl derivative **14**. The use of ca 1.3 equiv. of phenyllithium allowed isolation of the corresponding product where only one of the two available chlorine atoms in **15** had been displaced.[25]

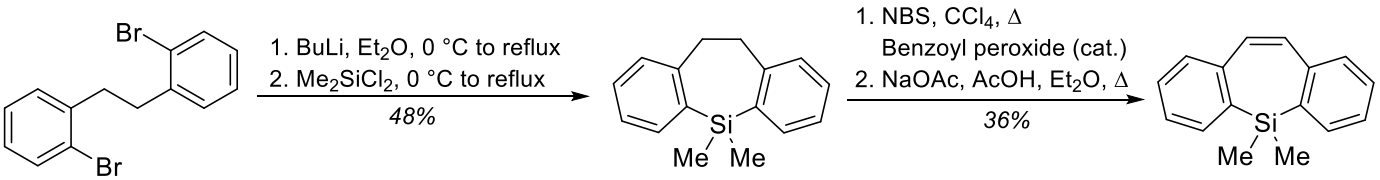


By combining previously used structural motifs, the Grignard reagent obtained from the dibromide **13** was allowed to react with the dichloro-compounds **12c** or **15**, providing modest yields of the products **20** and **21**, respectively, each featuring two spirocyclic 7-membered rings incorporating silicon as the pivotal element.[26] A spirocyclic, densely substituted silepin has also been reported as a product in high yield from the reaction of the lithium salt of tetramethylsilole anion with diphenylcyclopropenone.[27]



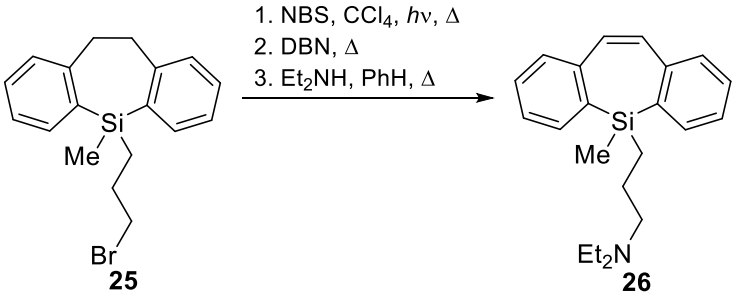
20 **21**

As is evident from some examples above, fused silepins are more stable than structurally simple derivatives of the parent heterocycle and have consequently been studied in more detail. This is particularly true for the dibenzo[*b*,*f*]silepins, which are featured in a number of studies investigating their synthesis and structure. The first examples of this class emerged already in the early seventies and are still occasionally revisited almost fifty years later. In one of the early efforts, metalation of the symmetrical dibromide **22**, and subsequent quench of the resulting dianion with dichlorodimethylsilane, provided the previously known intermediate **23** in a low yield of 16%,[28] followed by dehydrogenation using DDQ in refluxing toluene to give the target dibenzo[*b*,*f*]silepin **24** in 23% yield.[29] Meanwhile, an independent, very similar approach relied on a double benzylic bromination of compound **23**, with a final reductive step using zinc and acetic acid affording the product **24** in a comparatively higher overall yield of 14% from **22**.[30] In yet another contribution contemporary to the two previously mentioned, the conversion of **22** into **23** was effected much more efficiently in 48% yield. The target **24** could eventually be obtained after a radical bromination and subsequent dehydrobromination. A similar sequence was utilized for the synthesis of the corresponding analogue bearing two phenyl substituents on the silicon atom, featuring a dehydrobromination with DBN as the base. However, a serious drawback was the very low yield of the ring-forming step (5%).[31]



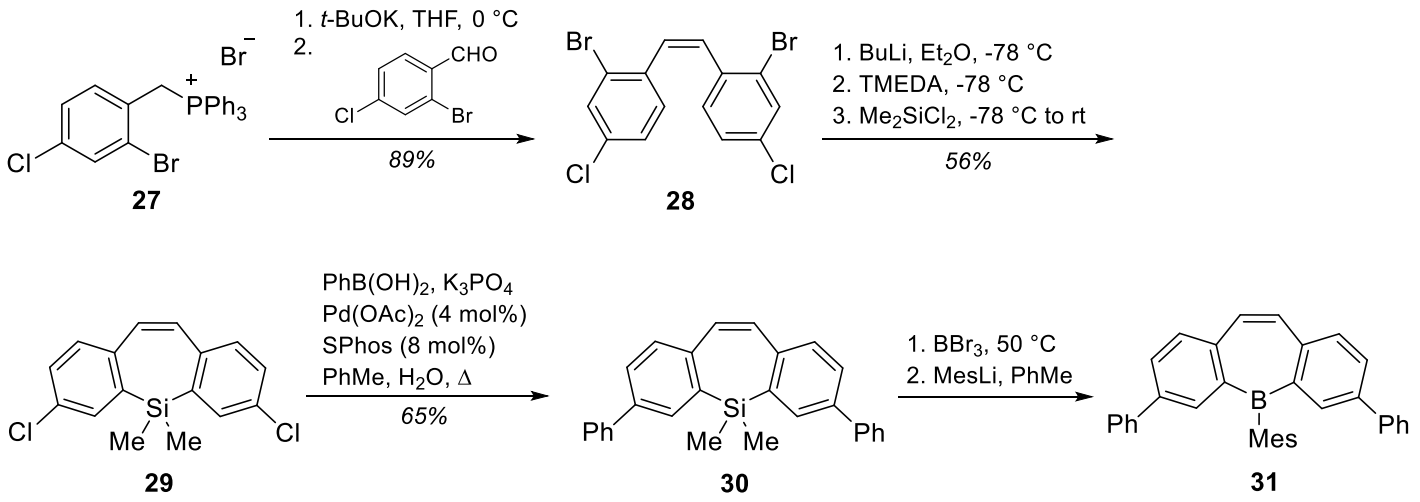
22 **23** **24**

The scope of the strategy discussed above was extended for preparation of further dibenzo[*b,f*]silepins[32] and later also towards silipramine and other members of this ring system featuring alkylamino substituents at the silicon center.[33] In the latter study, a dilithio-derivative of **22** was generated and allowed to react with a variety of chlorosilanes, leading to for instance the intermediate **25** in 52% yield. The sequence was continued with a benzylic bromination and dehydrobromination, and finally a substitution reaction with diethylamine leading to the product **26**, which was eventually isolated as its hydrochloride salt, albeit in a low overall yield which was not specified in detail.[33] The intermediacy of dilithio-derivatives has also been suggested as a rationale for the observed exchange of tellurium in benzo[*b*]tellurepins leading to the corresponding benzo[*b*]silepins or benzo[*b*]stannepins in modest yields.[34]



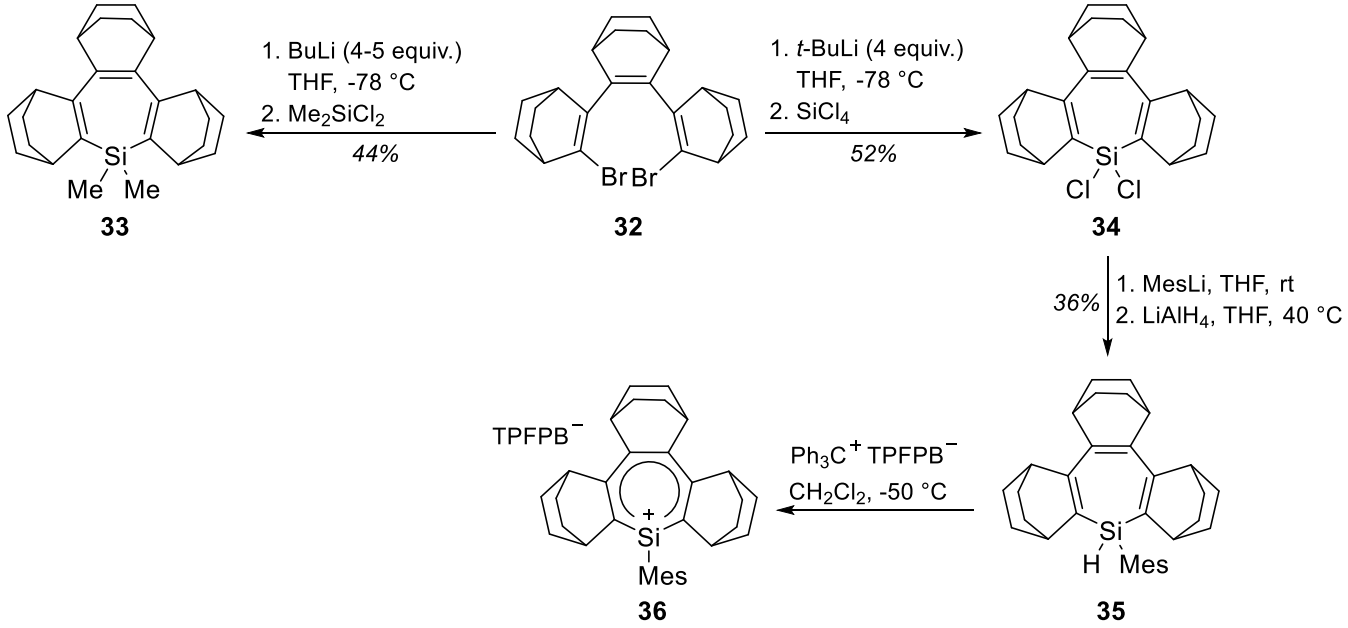
25 **26**

Many years later, more efficient and versatile methods for construction of fused silepins became available. Following a strategy used for synthesis of condensed stannepins (Cf. Section 4), the phosphonium salt **27** participated in a Wittig reaction with 2-bromo-4-chlorobenzaldehyde affording the (*Z*)-stilbene derivative **28**. Subsequent halogen-metal exchange employing the combination butyl lithium and TMEDA, followed by cyclization employing dichlorodimethylsilane, provided the key intermediate **29**, which served as a coupling partner in Suzuki coupling reactions rendering, among others, the product **30** in good overall yield. This chemistry also worked efficiently for synthesis of the dibenzo[*b,f*]silepin **24**, as well as a number of systems isomeric to the product **30** and its analogues instead bearing substituents in *para* position to the silicon center. In addition, it was demonstrated that transmetallation with BBr_3 followed by reaction with mesityllithium provides access to the corresponding borepin **31**, although no yield was reported for this transformation.[9] Likewise, thieno-fused silepins have also been prepared recently by halogen–lithium exchange followed by reaction with dichlorodimethylsilane. The resulting products served as precursors to borepinium ions.[35]



27 **28** **29** **30** **31**

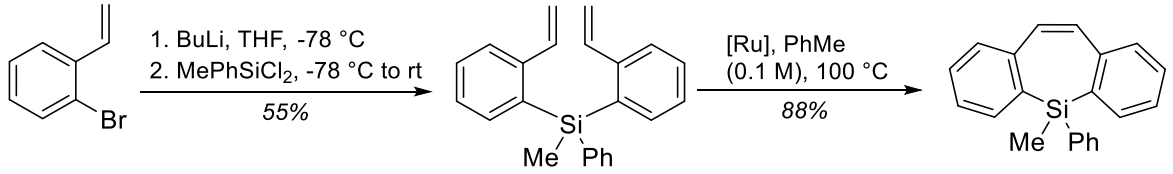
During studies of silepins featuring bulky cyclic motifs, treatment of the linear trimer of bicyclo[2.2.2]octene **32**[36] with 4–5 equivalents of butyllithium, followed by reaction with dichlorodimethylsilane afforded compound **33** in moderate yield.[13] Further derivatives bearing various combinations of substituents (e.g. H, Me, *t*-Bu) at the silicon center, including the system **34**, were later prepared using this methodology. The silepin **34** served as starting material for the corresponding difluoro- and dimethoxy derivatives via reactions with excess ZnF_2 or methanol, respectively.[12] Furthermore, introduction of the sterically demanding mesityl group at the silicon by treatment of **34** with mesityllithium was followed by reduction with $LiAlH_4$, providing the product **35**, a precursor to the first example of a cyclic π-conjugated silylium ion, which was characterized in solution as the silatropylium salt **36** generated from **35** and triphenylmethyl tetrakis(pentafluorophenyl)borate (TPFPB) in dichloromethane at −50 °C.[37,38]



33 **32** **34** **35** **36**

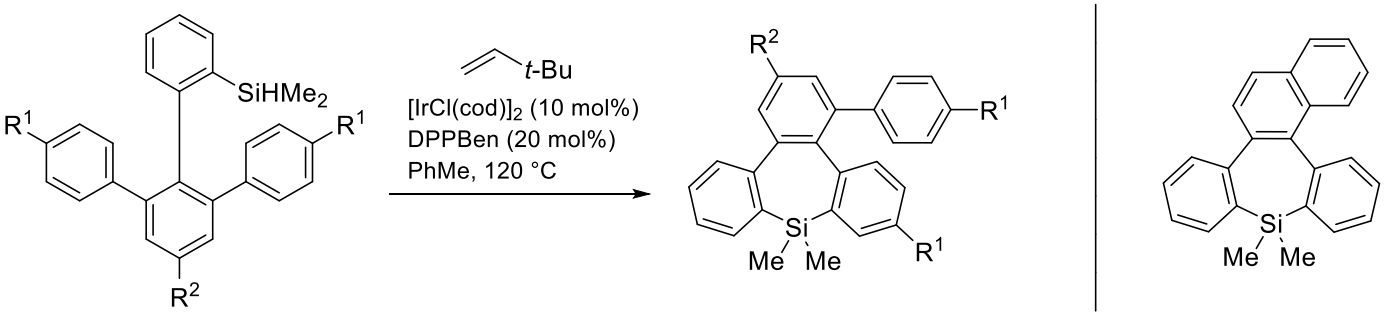
Several approaches to fused silepins rely on final formation of the C3–C4 bond for crafting the heterocyclic core. In a study that also encompassed synthesis of other seven-membered heterocycles containing one heteroatom, among others germepins and stannepins, ring-closing metathesis was employed as the key transformation. In a representative example, the required starting material **37** for the cyclization step was

obtained by metalation of 2-bromostyrene, followed by quench with suitable electrophiles to install the heteroatom. The desired product **38** could then be accessed by ring-closing metathesis using the second generation Hoveyda–Grubbs catalyst in toluene solution (0.1 M with respect to substrate). A similar synthesis of some C-substituted analogues, 1,1-dimethyldibenzo[*b,f*]germepin (Section 3), whereas a similar annulation to the corresponding fused stannepin system **24** required higher dilution conditions (0.002 M) in order to avoid formation of self-condensation macrocyclic side-products.[39] In a later report from another group, this strategy was used for preparation of additional new substituted dibenzo[*b,f*]silepins, dibenzo[*b,f*]germepins, and dibenzo[*b,f*]stannepins.[40]



37 **38**

A set of fused silepins, among others the systems **39a–b**, has been obtained via an iridium-catalyzed C–H/Si–H coupling reaction starting from the precursors **40a–b** with $[IrCl(cod)]_2$ as the catalyst and 1,2-bis(diphenylphosphino)benzene (DPPBen) as ligand, and required the presence of a bulky alkene as a hydrogen acceptor for optimal results. With a substrate bearing two *meta*-substituted benzene rings, the cyclization proceeded efficiently and selectively at the less hindered site, while a substrate featuring a central naphthalene core gave a respectable yield of the product **41**.[11] In this context, it should be noted that the closely related system 9,9-dimethyl-9*H*-tribenzo[*b,d,f*]silepin has been reported long time ago as a minor product from the reaction of 1,2-dichlorobenzene with chloromethoxydimethylsilane and sodium in refluxing toluene,[41] and a few years later also in very low yield (3.5%) from a dilithiated terphenyl derivative and dichlorodimethylsilane.[6]

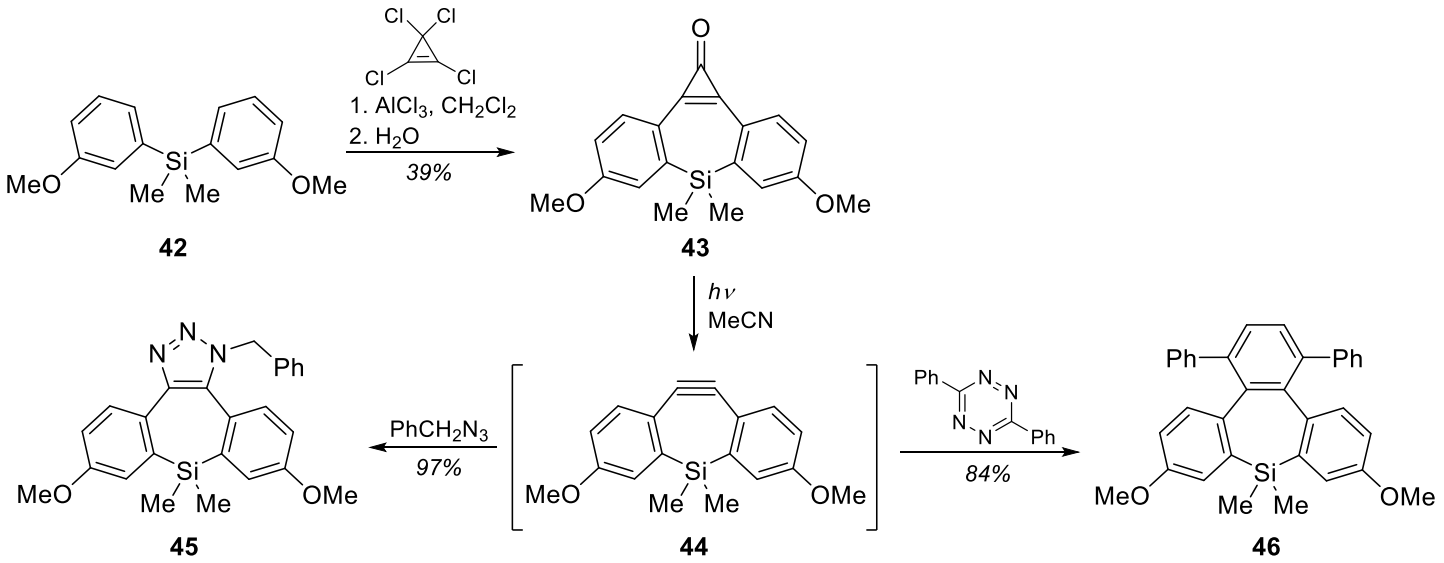


40a R^1 = Cl, R^2 = H
40b R^1 = H, R^2 = Me

39a R^1 = Cl, R^2 = H (*67%*)
39b R^1 = H, R^2 = Me (*90%*)

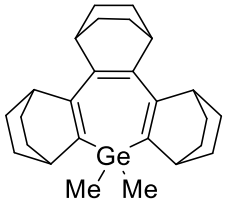
41

The silane **42**, which is readily available by metalation of 3-bromoanisole with butyllithium and subsequent quench with dichlorodimethylsilane, constituted a starting point in an approach to fused silepins. After a reaction with tetrachlorocyclopropene, followed by in situ hydrolysis, the strained ring system **43** was obtained in moderate overall yield. This key intermediate served as a precursor to the alkyne **44** intermediate, which underwent a copper-free click reaction with benzyl azide to provide the triazole-fused silepin **45** in excellent yield, or participated in a reverse electron demand Diels–Alder cycloaddition with for instance 3,6-diphenyltetrazine, affording the product **46**.[42]



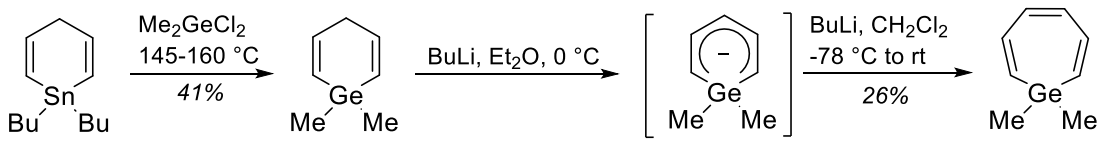
3. Germepins

The germepins (or 1-germacyclohepta-2,4,6-trienes) are the least studied members of this series. As in the case of silepins, structurally simple germepins are quite rare, but several examples of fused derivatives have been studied in some detail. The crystal structures of the germepin **47** featuring three fused bicyclo[2.2.2]octene motifs was compared to its sila- and stanna-analogs, demonstrating that the central seven-membered ring of all members of the series adopts a boat conformation, and the structure becomes more deeply folded with increasing size of the heteroatom in order to release the inner angle strain.[13] The fragmentation of some dibenzo[*b,f*]germepin derivatives in electron impact mass spectrometry has also been discussed.[43]

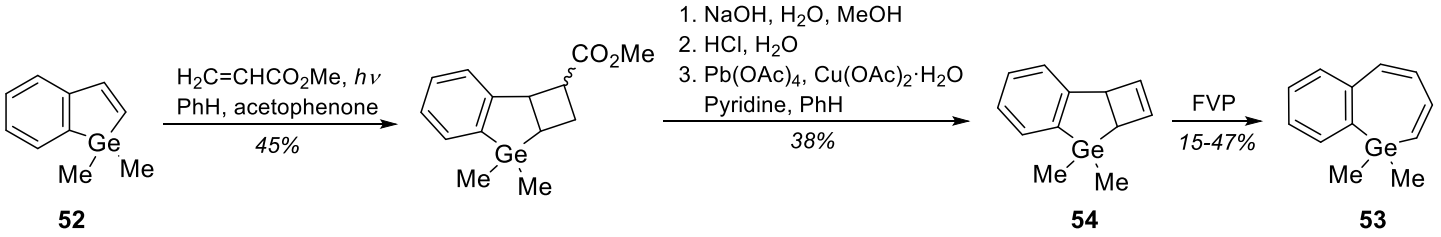


47

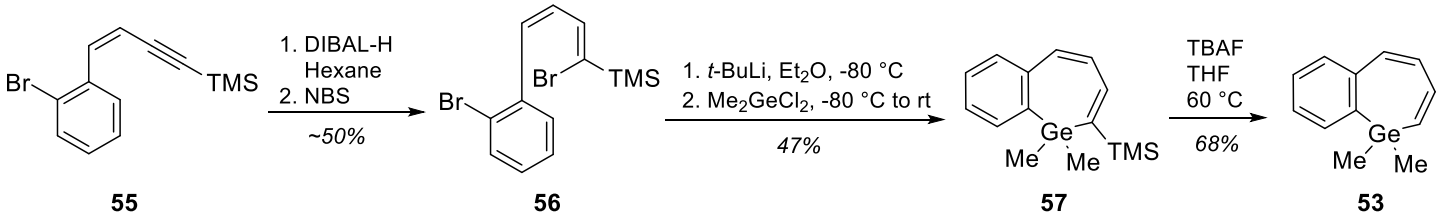
Heating of the stannacyclohexadiene **48** with dichlorodimethylgermane at 145-160 °C led to a disproportionation reaction providing the germacyclohexadiene **49** after vacuum distillation. In similarity to the findings during studies of its silicon analogues, the germacyclohexadienyl anion **50** could be generated by deprotonation with 3.5 equivalents of butyl lithium. Finally, a ring expansion was effected upon addition of dichloromethane to the reaction mixture, providing a modest yield of the germepin **51**.[44] In a later study, the kinetics and mechanism of the thermal decomposition of the 1-germacyclohepta-2,4,6-triene **51** was studied. Upon heating in toluene-d_8, compound **51** undergoes thermolysis into benzene and dimethylgermylene, which was trapped by 2,3-dimethyl-1,3-butadiene, resulting in the easily detected product 1,1,3,4-tetramethyl-1-germacyclopent-3-ene.[45]



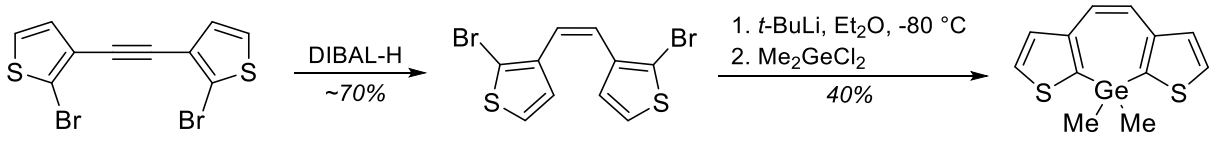
The germole **52** was selected as a starting point for accessing the benzo[*b*]germepin **53** in a rather intricate sequence featuring flash vacuum pyrolysis (FVP). A regioselective cycloaddition of **52** with methyl acrylate, followed by saponification and decarboxylation provided the intermediates **54**, which produced the target ring system **53** along with naphthalene (formed by thermal decomposition of **53**) upon exposure to various FVP-conditions. Likewise, related silepins could also be obtained in this manner starting from suitable silole derivative.[46,47]



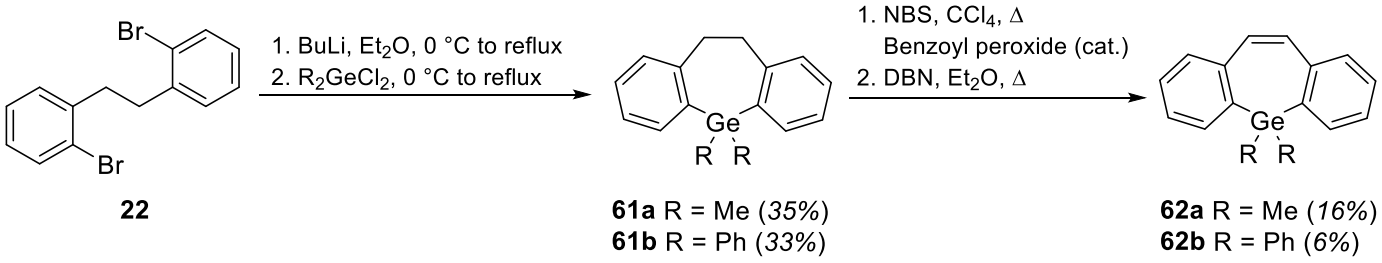
A different strategy to the system **53** was realized by initial reduction and bromination of compound **55** (available in three steps from *o*-bromocinnamic acid) which gave the (*Z,Z*)-diene **56** along with its (*Z,E*)-stereoisomer. Subsequent metalation using *tert*-butyllithium, followed by treatment with dichlorodimethylgermane provided the fused germepin **57**, which was finally converted to the target product **53** by cleavage of the TMS-group. The approach also proved to be applicable to preparation of the corresponding stannepin derivative, as well as related products incorporating group 15 and 16 heavier elements.[48]



In an approach to an extensive set of thieno-fused seven-membered heterocycles incorporating group 14, 15 and 16 elements, reduction of the alkyne **58** with DIBAL-H provided the common precursor **59**, which underwent bromine-metal exchange, followed by cyclization with suitable electrophiles, leading for instance to the fused germepin **60**. Likewise, isomeric systems featuring the two thiophene motifs fused via their 3,4-positions was accessed in a similar manner.[49]



Following an strategy used for preparation of dibenzo[*b,f*]silepins (Section 2), the bibenzyl derivative **22** could be converted to the dihydrodibenzo[*b,f*]germepins **61a–b** in modest yields, and further to the unsaturated systems **62a–b**. A similar sequence targeting stannepins failed at the corresponding dihydro-derivative stage, as attempted bromination/dehydrobromination failed, leading to ring cleavage products.[50]

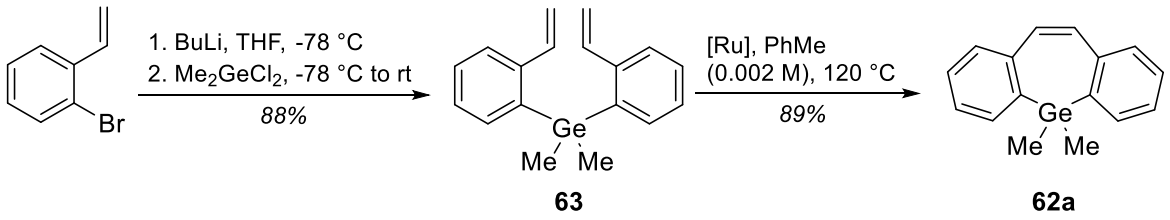


22

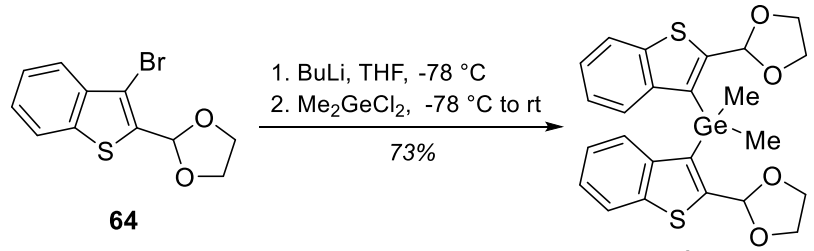
61a R = Me (*35%*)
61b R = Ph (*33%*)

62a R = Me (*16%*)
62b R = Ph (*6%*)

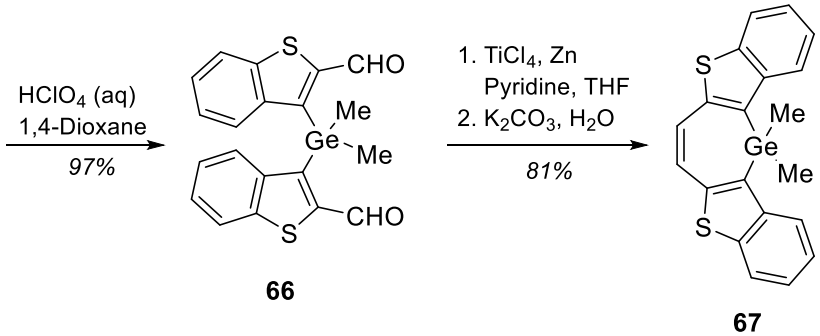
Metalation of 1-bromo-2-ethenylbenzene and subsequent reaction with dichlorodimethylgermane provided an excellent yield of compound **63**, which served as a precursor to the fused germepin **62a** via a final ring-closing metathesis step employing the second-generation Hoveyda–Grubbs catalyst in toluene. For the best outcome, the reaction required low dilution conditions (0.002 M) and elevated temperature.[39] The scope of this strategy was expanded further by the preparation of a few substituted derivatives of **62a** in a later study.[40]



63 **62a**



64 **65**



66 **67**

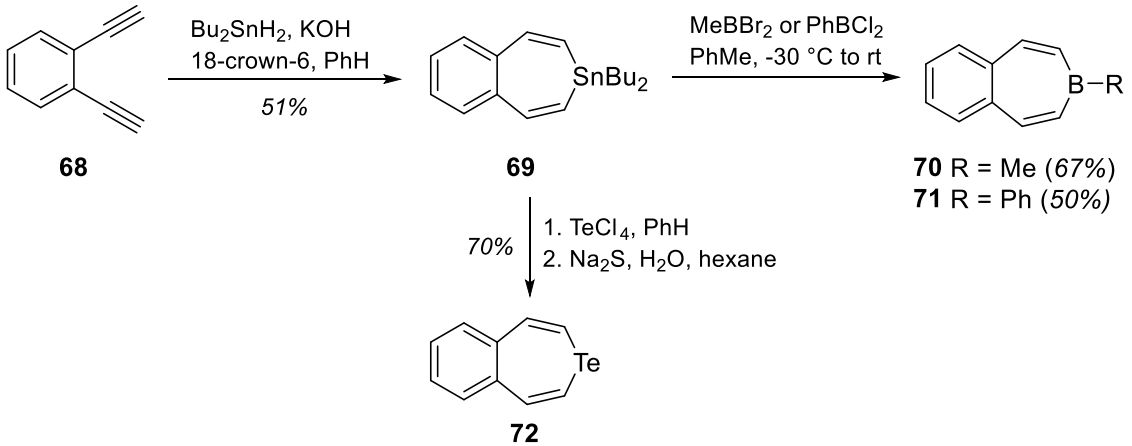
Following an adaptation of a strategy developed for synthesis of fused thiepins,[51,52] the readily available masked benzo[*b*]thiophene-2-carbaldehyde **64** was subjected to a directed metalation reaction, followed by

quenching with dichlorodimethylgermane, affording the symmetrical intermediate **65** in good yield. Subsequent deprotection of the aldehyde motifs proceeded smoothly, giving the dialdehyde **66**, which was finally cyclized under McMurry-conditions to the target germepin system **67**. When the germanium electrophile was replaced by Me_2SiCl_2, the route also proved useful for construction of the corresponding sila-analog.[53]

4. Stannepins

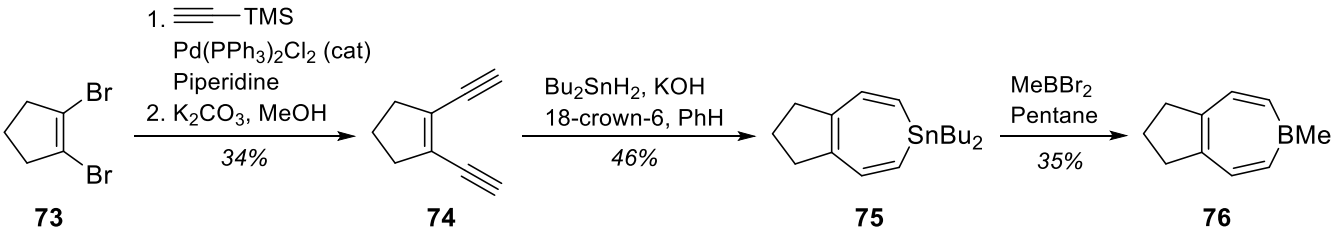
The stannepins are perhaps the most interesting analogs as they may serve as synthetic intermediates towards seven-membered heterocycles containing other elements, in particular borepins. In similarity to their sila- or germa-analogs, many stannepins are prone to degradation, but there are examples of fused derivatives which are sufficiently resistant towards oxidation or thermal decomposition to be useful in synthetic applications. In similarity to the silepins and germepins, the stannepin ring system exists in boat conformation in the solid state, which has been demonstrated by single crystal X-ray diffraction.[13,54,55]

In a pioneering paper, it was discovered that heating of 1,2-diethynylbenzene (**68**) with equimolar amounts of for instance diethyltin dihydride in benzene gives, among other products, low yields of benzo-fused stannepins.[56,57] As a later development, it was demonstrated that a base catalyzed hydrostannation of 1,2-diethynylbenzene (**68**) with dibutyltin dihydride provided the fused stannepin **69**.[58] In contrast to the thermally induced hydrostannation reactions,[56,57] this base catalyzed cyclization took place in better yield and with higher purity. The stannepin **69** could be further converted to the borepin **70**.[58] The fact that stannepins undergo conversion into borepins via metal-metal exchange reactions has been known since 1967 when Leusink and co-workers prepared the fused system **71** in approximately 50% yield via the reaction of **69** with dichlorophenylborane.[59] Later, Axelrad and Halpern isolated 3*H*-benzo[*d*]borepin-3-ol upon treatment of **69** with boron trichloride followed by hydrolysis.[60] The stannepin **69** has also been converted to benzo[*d*]tellurepin **72** in good overall yield by treatment with tellurium tetrachloride, followed by sodium sulfide.[61] Likewise, treatment of **69** with one equivalent of $SbCl_5$ leads to the formation of the corresponding *Sb*-chlorostibepin.[62] Additional examples of transmetallation reactions of stannepins leading to other seven-membered metalloid heterocycles are discussed below.



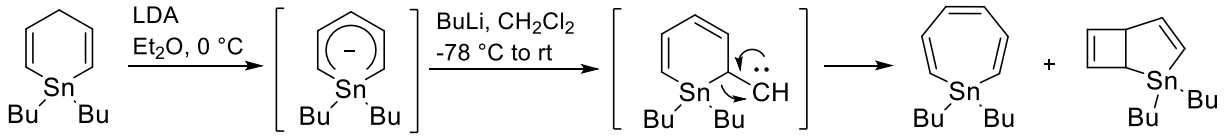
A related sequence involving a final conversion to borepins commenced with the Sonogashira coupling of the dibromoalkene **73** with (trimethylsilyl)acetylene followed by cleavage of the silyl unit to afford the unstable intermediate **74**, which was thereafter annulated under conditions outlined above to the stannepin **75**. The

rather labile product **75** could finally be converted to the air-sensitive borepin **76**.[63] The strategy has also been employed in later studies for synthesis of heterocycle-fused stannepins featuring thiophene or 1-methylpyrrole motifs *en route* to thieno[3,4-*d*]borepins,[64] thieno[2,3-*d*]borepins[65] and 5-methyl-1-phenylpyrrolo[3,4-*d*]borepin.[66]



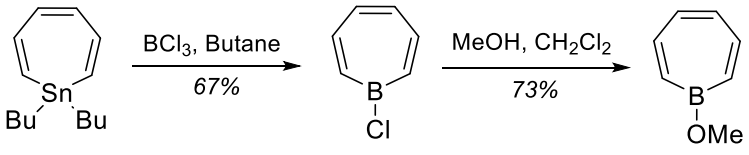
73 **74** **75** **76**

In an extension of the applicability of a direct approach to silepins,[5] it was demonstrated the corresponding tin- and germanium heterocycles may be accessed in similar manner. Generation of the stannacyclohexadiene anion **77** from **78** (available via hydrostannation of 1,4-pentadiyne) required the use of LDA, since it was anticipated that butyl lithium may cleave the tin-vinyl bond. Subsequent reaction of **77** with chlorocarbene derived from butyl lithium and dichloromethane provided the stannepin **79** in 33% yield. The key step in its formation was suggested to occur via a 1,2-migration of the stannyl group to the carbene centre in the intermediate **80**,[44] which would be in line with previous mechanistic studies of the corresponding route for silepin synthesis.[5] The synthesis of the stannepin **79** via this pathway is accompanied by formation of its bicyclic isomer **81**, which was characterized in a later study. Taking advantage of the fact that **79** is thermally labile, heating a mixture of compounds **79** and **81** to 100 °C for 21 h enabled simple isolation of pure **81** after full rearrangement of the present stannepin **79**.[67]



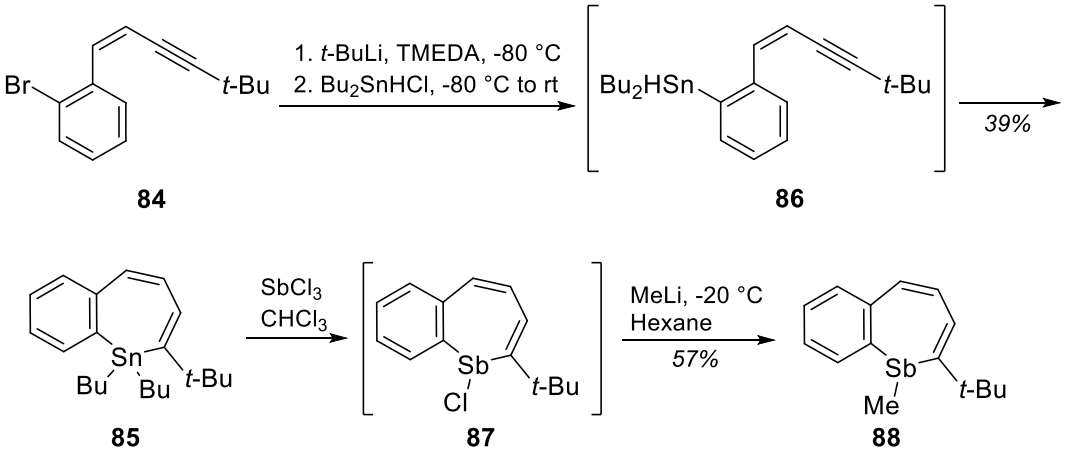
78 **77** **80** **79** (*33%*) **81**

As discussed above, stannepins attracted attention as synthetic intermediates for fused borepins due to their propensity to undergo tin-boron exchange reactions. This reactivity has for instance been utilized for the transformation of **79** into 1-chloroborepin **82**,[68,69] a precursor to 1-methoxyborepin **83**, as well as the sensitive parent heterocycle 1*H*-borepin itself.[68] The method was also later applied to the conversion of 1,1-dibutylstannepin **79** using dibromomethylborane into 1-methylborepin, which proved to be remarkably stable under certain conditions, as it resisted decomposition upon heating for 1.5 h in degassed carbon tetrachloride at 160 °C. However, a gradual decomposition into benzene was observed even at −20 °C in chloroform, which was attributed to the presence of trace amounts of acid.[70]

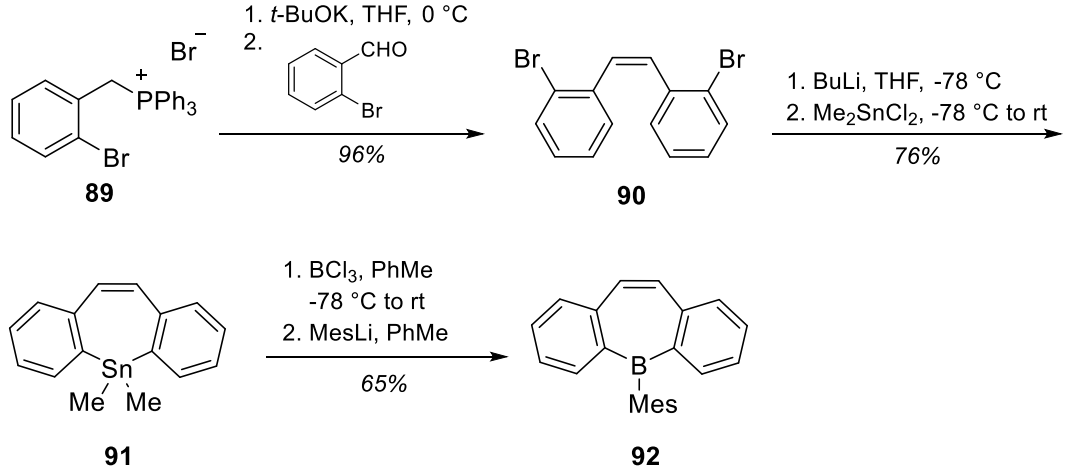


79 **82** **83**

Compound **84** served as a starting material for the benzo[*b*]stannepin **85**, which was accessed via a halogen–metal exchange, followed by reaction with dibultylchlorostannane, and formation of the resulting intermediate **86** via a *7-endo-dig* cyclization. It was also demonstrated that compound **85** can be converted to the unstable stibepin **87** and further to the isolable methyl substituted derivative **88**.[71,72]

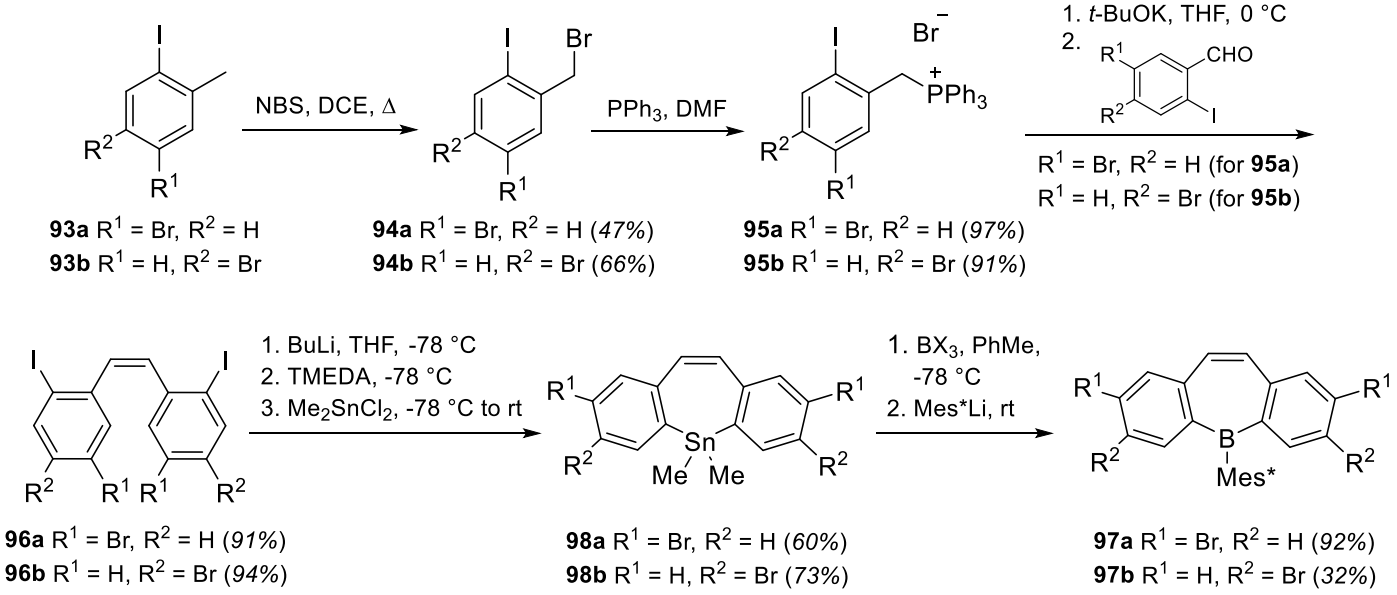


In an example serving as an illustration of an approach involving benzo[*b,f*]stannepins as synthetic intermediates, the phosphonium salt **89** underwent a Wittig reaction with 2-bromobenzaldehyde affording the (*Z*)-alkene **90**. A double metalation employing butyllithium, followed by treatment with dichlorodimethylstannane, gave the stannepin **91** in good yield. The sequence was concluded by installation of the boron center using boron trichloride, followed by substitution of the final chlorine atom with a mesityl unit, providing the target product **92**.[73] Two extended systems were also prepared successfully following this procedure,[73] paving the way for further developments. In contrast, during another study it was reported that all attempts failed to effect a transmetallation with aluminium in the stannepin **91** under various conditions, and the target aluminepin could only be accessed by lithiation of **90** followed by cyclization with dichloroethylaluminum.[74]

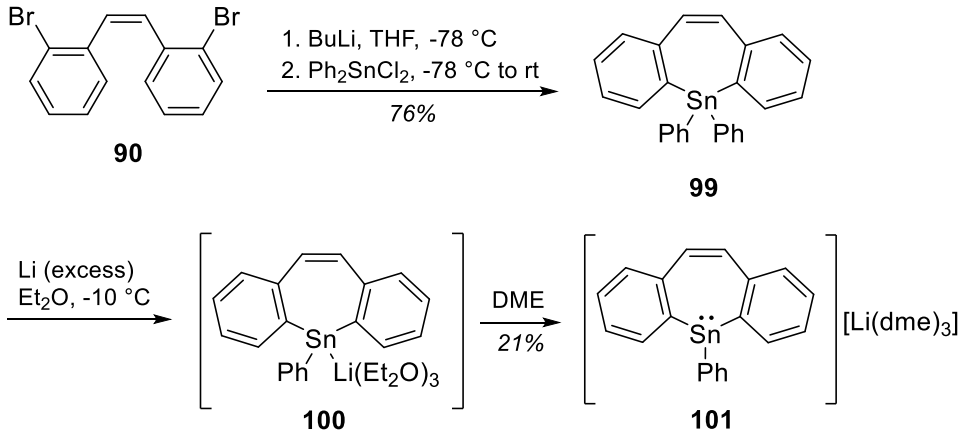


The availability of halogenated derivatives of heterocycle **91**[75,76] as synthetic intermediates has provided new opportunities for construction of structurally more advanced borepin derivatives applicable in standard cross coupling techniques. Treatment of the halogenated toluene derivatives **93a**–**b** with NBS gave the intermediates **94a**–**b**, which were in turn converted to the corresponding phosphonium salts **95a**–**b**. Subsequent

Wittig olefination provided the symmetrically substituted (*Z*)-stilbenes **96a**–**b**, finally leading to the target borepins **97a**–**b** via the stannepins **98a**–**b**.[75]

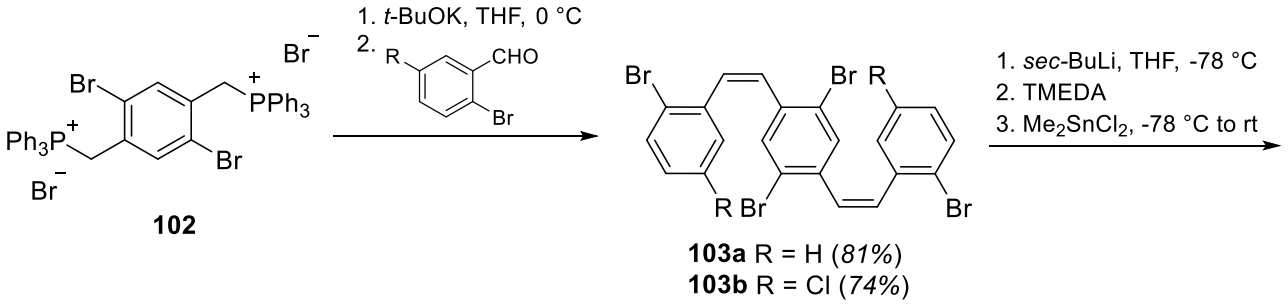


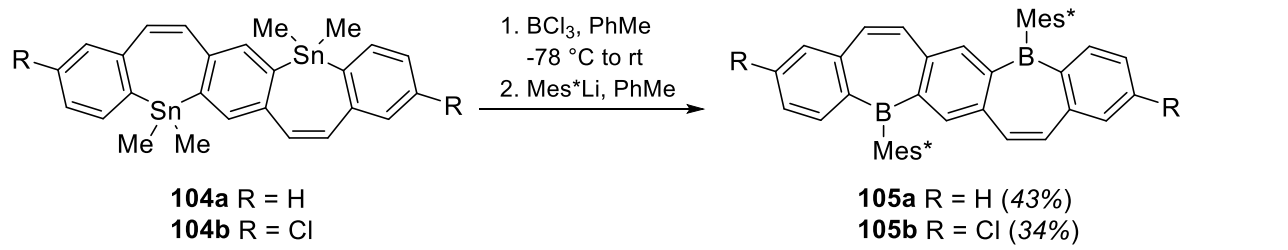
The chemistry outlined above has also been used recently during studies of a tin analogue of the cycloheptatrienyl anion. The stilbene **90** was metalated as outlined above, and the resulting dilithio-species was quenched with dichlorodiphenylstannane, affording the fused stannepin **99** in good yield. Subsequent reaction with lithium metal in ether gave the intermediate **100**, which could in turn be converted to the isolable solvent-separated ion pair structure **101** upon treatment with 1,2-dimethoxyethane.[55]



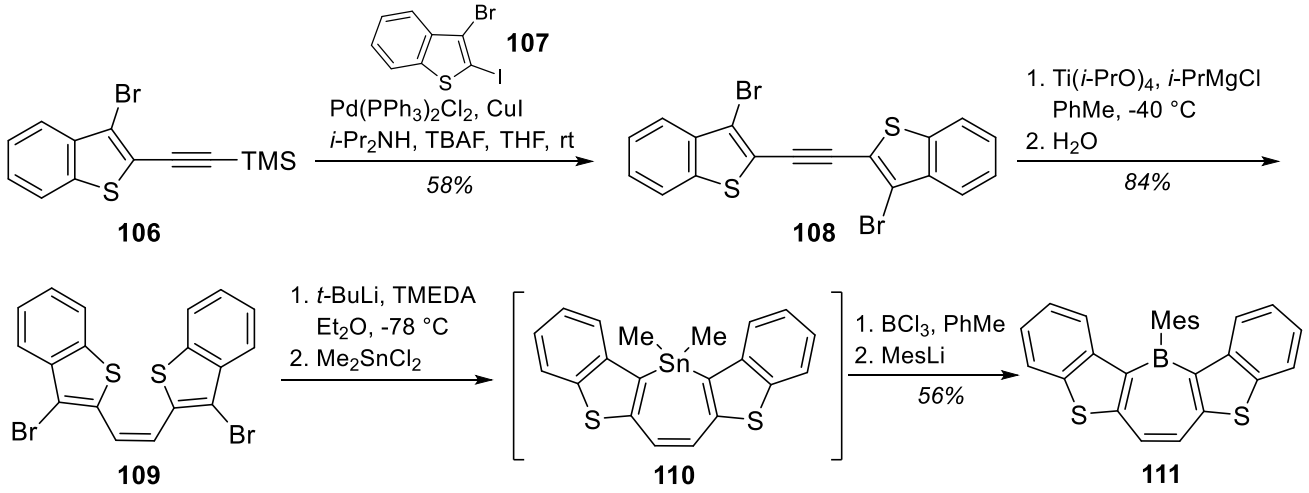
In a related approach towards fused pentacyclic borepins, double Wittig olefination of the bis(phosphonium) salt **102** (readily available in two steps from 1,4-dibromo-2,5-dimethylbenzene) with benzaldehyde derivatives gave the dienes **103a–b** displaying (*Z,Z*)-configuration. Subsequent lithiation, followed by reaction with dichlorodimethylstannane afforded the fused stannepins **104a–b** in respectable yields. Heteroatom exchange using boron trichloride, and a final substitution of the chlorine atoms with 2,4,6-tris-*tert*-butylphenyl (Mes*) motifs gave the target borepin derivative **105a–b**. The bulky substituents at the boron atom provided efficient stability towards oxidation or hydrolysis for convenient handling under ambient conditions.[76,77] A variation of this strategy also proved efficient for construction of isomeric fused pentacyclic systems having the borepin

cores oriented with the boron atoms *meta* to each other around the central benzene ring.[78] Dibenzo[*b,f*]stannepins with various substitution patterns have also been prepared by ring-closing metathesis in analogy to the methodology used for accessing silepins and germepins as discussed above (Sections 2 and 3).[39,40]

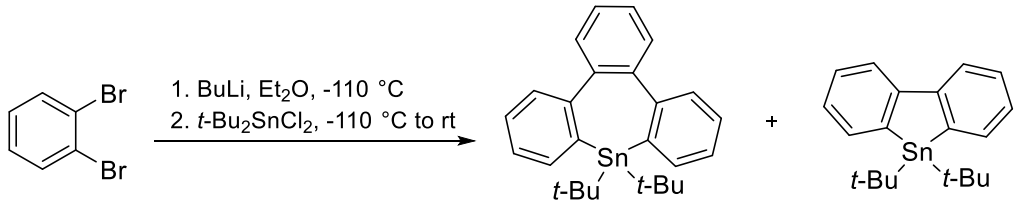




A variation relying on cyclization of dilithio-derivatives featuring the use of heterocyclic building blocks has also appeared. The thiophene derivatives **106** and **107** were subjected to in situ desilylation and Suzuki coupling affording compound **108**, followed by a selective titanium-mediated reduction of the alkyne unit providing the (*Z*)-alkene **109**. Halogen–metal exchange and quench with dichlorodimethylstannane gave the stannepin intermediate **110** (not isolated in pure form), which was finally converted to the target borepin system **111** employing a tin–boron exchange with BCl_3 and a final installation of the mesityl motif.[79]



The reaction of 1,2-dibromobenzene with equimolar amounts of butyllithium at low temperature led to formation of (2-bromophenyl)lithium while suppressing benzyne formation, and was followed by introduction of the electrophile *t*-Bu_2SnCl_2, giving a mixture of the fused stannepin **112** and the stannafluorene **113**, both of which could be isolated in low yields of 16% and 4%, respectively.[54]



112 (*16%*) **113** (*4%*)

6. Conclusions and Future Outlook

There have been considerable advances in the synthesis of silepins, germepins, and stannepins over the recent decades, and much information has been gathered on their structure, properties, and reactivity. The development has been driven by the availability of modern synthetic methods, in particular various metalation techniques and cross-coupling reactions, which have provided access to key building blocks and intermediates crucial for construction of more elaborate derivatives with specific properties. Although it has been noted that many structurally simple members of these classes of heterocycles undergo degradation, either thermally or due to oxidative conditions, structurally more complex systems with strategically positioned substituents or ring fusions appear to be relatively stable compounds. The current level of knowledge in this field lends support to the view that further studies may reveal new potentially useful aspects, relevant for instance in development of new functional materials (reflected in a recent review on luminescent borepins, silepins, and phosphepins),[80] provided that the stability issues associated with these classes of compound can be mitigated successfully. Nonetheless, the fact that some of the discussed systems serve as useful intermediates for other seven-membered heterocycles may also contribute to further developments.

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