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Cyclopropylstannanes: synthesis and applications

Marina Rubina and Vladimir Gevorgyan*

Department of Chemistry, University of Illinois at Chicago, 845 West Taylor Street, Chicago, IL 60607-7061, USA

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1. Introduction

Cyclopropylstannanes are very versatile building blocks for synthetic organic chemistry (vide infra) and thus substantial attention has been paid by the synthetic community to development of efficient and selective methods for preparation of these useful synthons. Surprisingly, synthetic applications of cyclopropylstannanes have never been reviewed. The present review, although not comprehensive, highlights, in our judgment, the most important work on synthesis and chemistry of cyclopropylstannanes. Section 1 describes practical synthetic methods towards

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* Corresponding author. Tel.: +1-312-355-3579; fax: +1-312-355-0836; e-mail address: vlad@uic.edu

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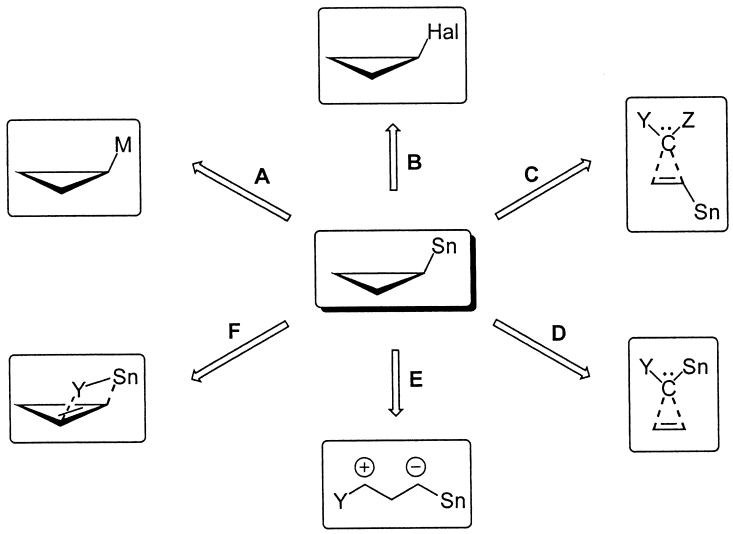


Figure 1.

cyclopropylstannanes, the most important of which are summarized in Figure 1. They involve reactions of cyclopropylmetals (Li, Mg) with tin electrophiles (A); displacement of cyclopropyl halides with stannyllithium reagents (B); addition of carbenoid species to vinylstannanes (C); addition of stannylcarbenoids to alkenes (D); 1,3-cyclization reactions (E); and addition of tin entities across the double bond of cyclopropenes (F).

Section 2 illustrates applications of cyclopropylstannanes in organic synthesis (Fig. 2). This includes tin–metal exchange reactions (G); tin–halogen exchange reactions (H); direct electrophilic destannylation (I); transition metal-catalyzed cross-coupling reactions (J); oxidative homocoupling reactions (K); and α-elimination of 1-halocyclopropylstannanes (L).

In addition, preparation and synthetic applications of related compounds, cyclopropenylstannanes, are also discussed (Section 2.6). Finally, miscellaneous synthetic schemes are summarized at the end of each chapter.

2. Synthesis

2.1. From cyclopropyl-containing precursors

2.1.1. Direct deprotonation of cyclopropane. Direct deprotonation of unsubstituted cyclopropane has not been documented, which can be attributed to its rather low C–H acidity (pK_a~46).[1] However, introduction of electron-withdrawing groups increases acidity of the geminal C–H and thereby allows for deprotonation with strong bases. Thus, sulfoxide **1** was successfully deprotonated with LDA in tetrahydrofuran followed by trapping with a tin electrophile to produce **3** in 78% yield (Scheme 1).[2]

Analogously, α-stannylsulfone **6** was prepared in 58% yield by deprotonation of **4** with *n*-butyllithium followed by reaction with tributyltin chloride (Scheme 2).[3,4]

Optically active **9** was prepared from the corresponding carbamate **7** via deprotonation with *sec*-butyllithium followed by addition of trimethyltin chloride, in 43%

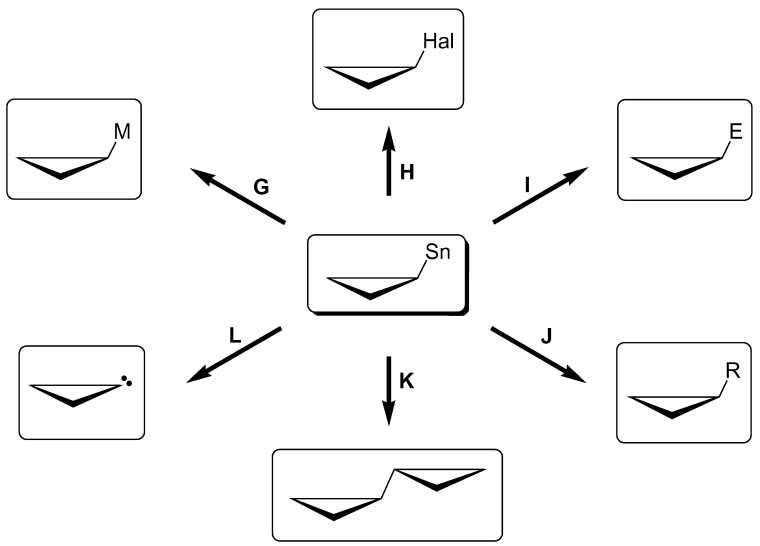
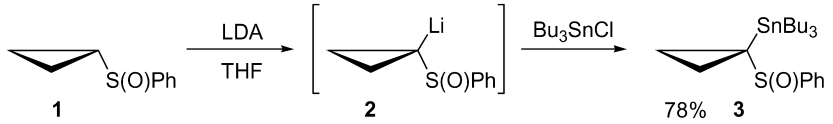
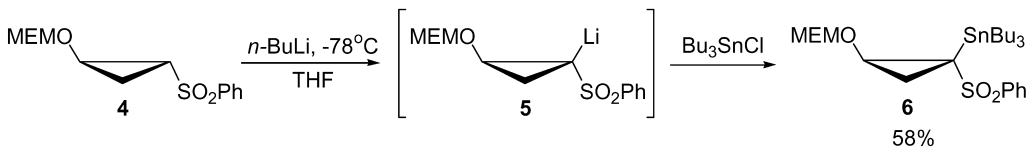


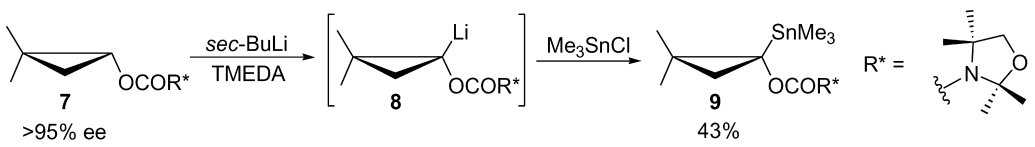
Figure 2.



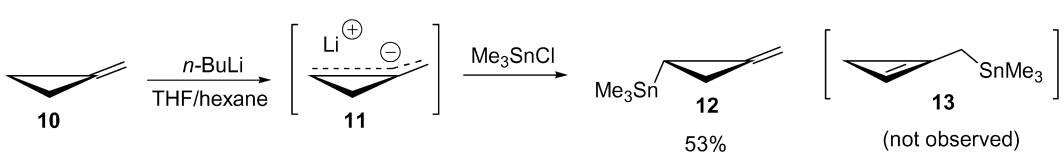
Scheme 1.



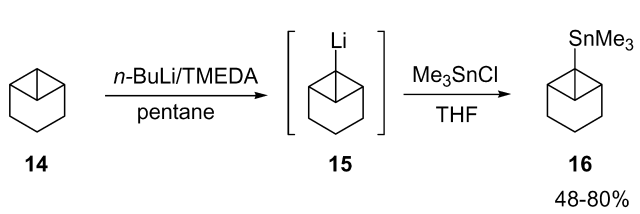
Scheme 2.



Scheme 3.



Scheme 4.



Scheme 5.

yield (Scheme 3).[5] Cyclopropyllithium anion, which is configurationally stable at −78 °C, gives rise to cyclopropylstannane with complete preservation of configuration at C-1.[5]

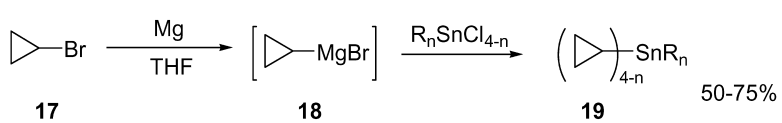
Methylenecyclopropane **10** represents another example of a cyclopropane with rather acidic protons (Scheme 4).[6] Deprotonation of **10** with *n*-BuLi generates 1,2-dimethanoallylic anion **11**, which is quenched with trimethyltin chloride at the more hindered site to afford methylenecyclopropane **12**, thereby avoiding formation of the rather more strained cyclopropene species **13**, which would form through alternative quenching at the less hindered *exo*-methylene terminus.

Compound **16** was synthesized by taking advantage of the high acidity of a bridgehead proton in the very strained bicyclobutane **14**. Metalation of the latter with *n*-butyllithium followed by addition of Me_3SnCl afforded **16** in moderate to good yields (Scheme 5).[7,8]

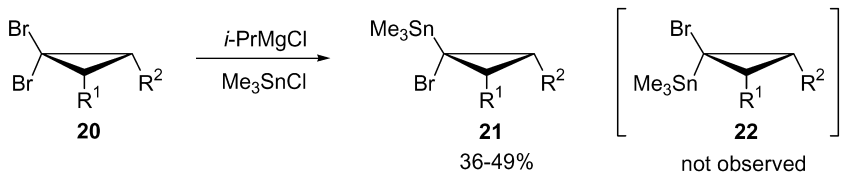
It is worth mentioning that, despite a few successful examples of direct deprotonation of cyclopropanes, the synthetic utility of this method is limited to substrates with enhanced C–H acidity.

2.1.2. Halogen–metal–tin exchange at halocyclopropanes. *Cyclopropylstannanes via halogen–magnesium exchange*. Efficient selective synthesis of cyclopropylstannanes via halogen–magnesium exchange was first demonstrated in the early 60s. This procedure allowed for synthesis of a number of cyclopropylstannanes in good yields from readily available bromide **17** (Scheme 6).[9]

Highly stereoselective monostannation of *gem*-dibromocyclopropanes was achieved via halogen to magnesium exchange with a Grignard reagent (Scheme 7).[10,11] The reaction proceeds with perfect steric control from the least hindered face. Subsequent treatment of the resulting cyclopropylmagnesium species with trimethyltin chloride at −70 °C produces only cyclopropylstannane **21** with the trimethyltin group *anti*- to the present substituent in the ring. Although the yields are moderate, this approach can serve as



Scheme 6.



Scheme 7.

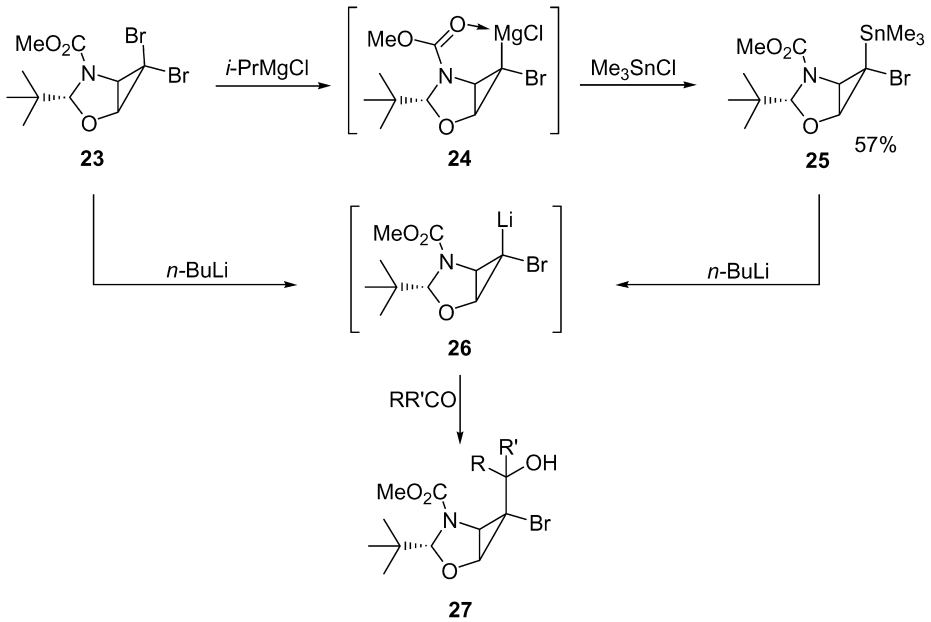
a complementary method to one involving lithium reagents, which allows for preparation of *syn*-isomers **22** (see below).

Seebach discovered directed monometalation of *gem*-dibromocyclopropane with isopropylmagnesium chloride in the oxazolidine series (Scheme 8).[12] The *syn*-magnesium carbanion was stabilized by the carbamate moiety in **24** providing a high degree of stereocontrol. Transmetalation of **24** with trimethyltin chloride afforded stannylated product **25** in 57% yield. Configuration of **25** was unambiguously confirmed by its conversion into lithium derivative **26** followed by trapping with an electrophile. The resulting product **27** had the same configuration as the compound obtained directly from **23** using organolithium reagent (Scheme 8).

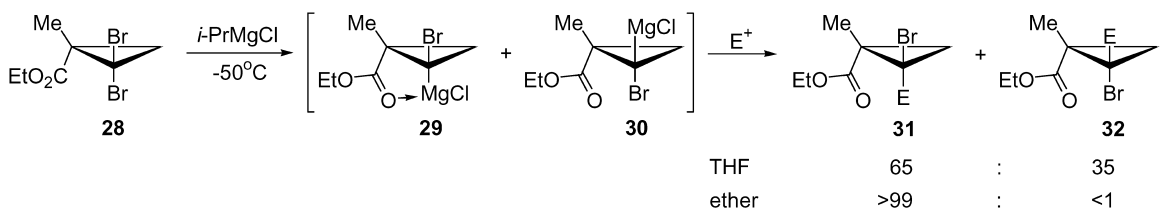
Knochel found an analogous directing effect of an ester group in the dibromo-cyclopropylcarboxylate series (Scheme 9).[13] Remarkably, it was shown that at low temperatures bulky isopropylmagnesium chloride did not compromise the stability of an ester group. Interestingly, the chelating effect of an ester group depended strongly upon the solvent used. Thus, treatment of dibromide **28** with the Grignard reagent in THF produced a mixture of isomeric cyclopropylmagnesium chlorides **29** and **30** in a 65:35 ratio as determined by the distribution of **31** and **32**, the products obtained after trapping of **29** and **30** with electrophiles. In contrast, analogous reaction performed in diethyl ether displayed perfect chelation control and proceeded in a highly diastereoselective fashion producing *cis*-magnesium species **29** exclusively. The latter can be selectively trapped by a number of electrophiles (Scheme 9).[13]

Knochel has also demonstrated that 2-iodocyclopropane-carboxylate **33** when treated with *i*-PrMgCl affords *cis*-**34**, which exhibited remarkable stability as a result of the chelating effect of the ester group (Scheme 10). Cyclopropylmagnesium chloride **34** reacted directly with a series of electrophiles, including Me_3SnCl, to form **35** in good yields.[13]

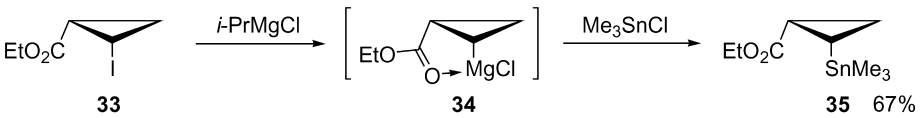
Cyclopropylstannanes via halogen to lithium exchange.



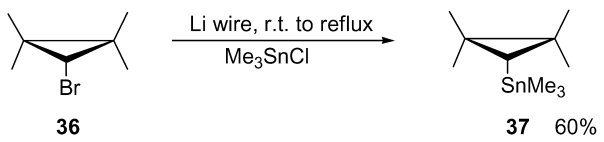
Scheme 8.



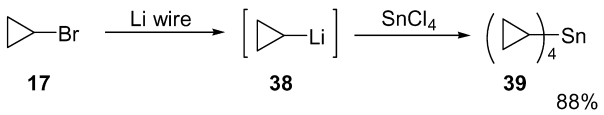
Scheme 9.



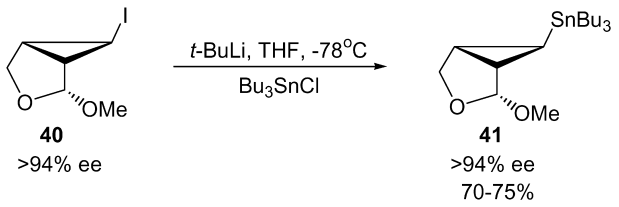
Scheme 10.



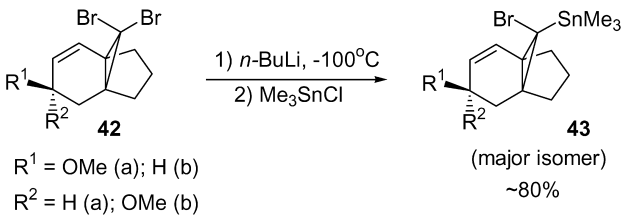
Scheme 11.



Scheme 12.



Scheme 13.



Scheme 14.

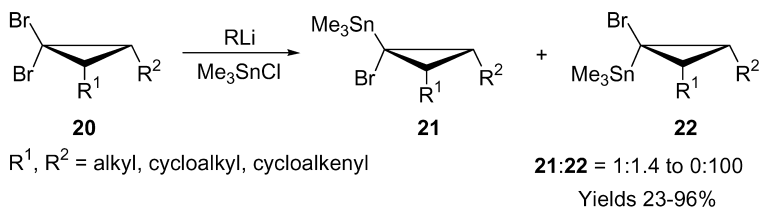
Halogen–lithium–tin exchange can be effected using lithium metal or a variety of alkyllithium reagents. The intermediate cyclopropyllithium species display higher stability when the reaction is carried out in diethyl ether, even at elevated temperatures, which allows for good yields of corresponding products. Thus, readily available cyclopropyl bromide **36** undergoes smooth tin–lithium exchange when reacted with lithium wire or lithium dispersion in diethyl ether (Scheme 11).[14] The half-life of the resulting tetramethylcyclopropyllithium in ether at room temperature was determined to be 38 h. Corresponding stannylated product **37** was isolated in good yield after addition of trimethyltin chloride (Scheme 11).

Likewise, tetracyclopropyltin **39** was prepared in very good yield by treatment of **17** with Li wire at 0 °C followed by reaction with $SnCl_4$ (Scheme 12).[15]

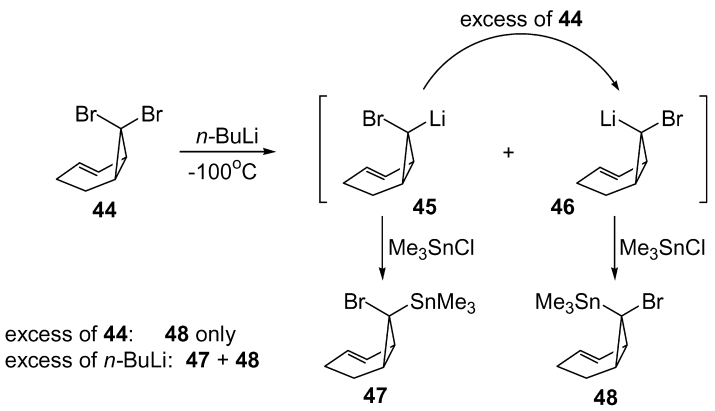
Halogen–lithium exchange with organolithium reagents is a much milder method as the reactions rapidly proceed at temperatures as low as −100 °C. This method allows for easy access to configurationally defined lithiated cyclopropanes, which can stereoselectively be functionalized with variety of electrophiles. Thus, optically active iodocyclopropane **40**, obtained from allylic diazoacetate using Doyle's protocol,[16] readily underwent consecutive iodine to lithium exchange and trapping with tin electrophile to provide **41** in good yield (Scheme 13).[17] Possible epimerization due to the chelating effect of methoxy substituent was not observed in this case, as detected by NMR analyses of the crude reaction mixtures. This indicates that the intermediate cyclopropyl anion retained its configuration under the above-mentioned reaction conditions (Scheme 13).

A number of reports document the reaction of *gem*-dibromocyclopropanes with *n*-butyllithium followed by trapping with trimethyltin chloride (Schemes 14 and 15). In contrast to the analogous reaction with Grignard reagents, formation of *syn*-trimethylstannylcyclopropane **22** was observed predominantly or exclusively depending on the amount of *n*-BuLi used. Although the reasons for this are not completely understood, perfect facial selectivity was observed only when no excess of *n*-BuLi was present in the reaction;[11,18,19] otherwise, mixtures of *syn*- and *anti*-products were obtained.[20–23]

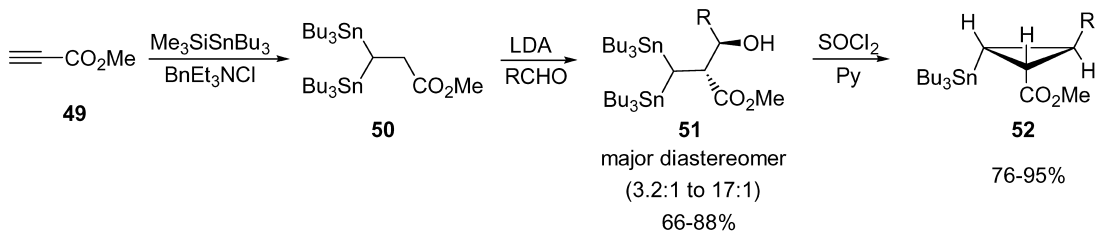
Thus, Warner demonstrated that when excess dibromide **44** was treated with *n*-BuLi, the initially formed carbanion **45** rapidly transformed into the isomeric **46**, which upon quenching with Me_3SnCl produced stannane **48** as the sole product. However, treatment of **44** with excess *n*-BuLi (1.3 equiv.) resulted in incomplete conversion of **45** into **46** and both cyclopropylstannanes **47** and **48** were formed (Scheme 16). Based on the above observations it was concluded that transformation **45** to **46** is a thermodynamically driven process.[24]



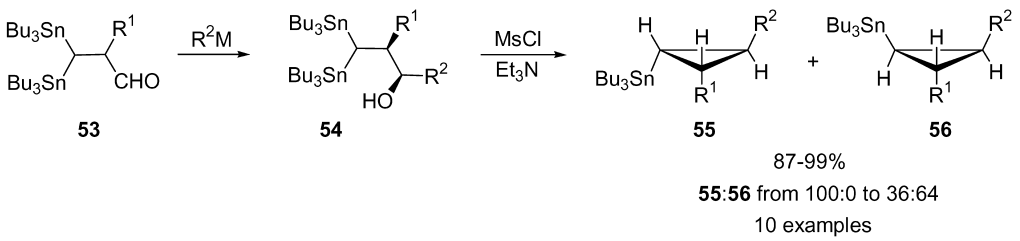
Scheme 15.



Scheme 16.



Scheme 17.



Scheme 18.

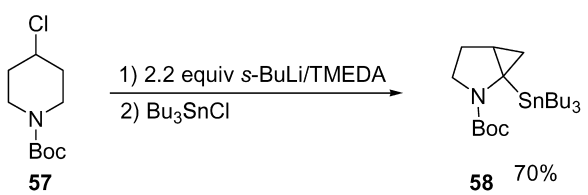
2.2. 1,3-Cyclization reactions

Functionalized cyclopropylstannanes are also accessible via 1,3-cyclization reactions of open chain precursors. This reaction requires substrates possessing both anion-stabilizing and good leaving groups, separated by a chain of three carbon atoms. Two different modes of 1,3-cyclization have been employed for synthesis of cyclopropylstannanes: (a) incorporation of the tin moiety into open-chain precursor, and (b) trapping of cyclopropylmetal species, obtained via 1,3-cyclization, with a tin electrophile.

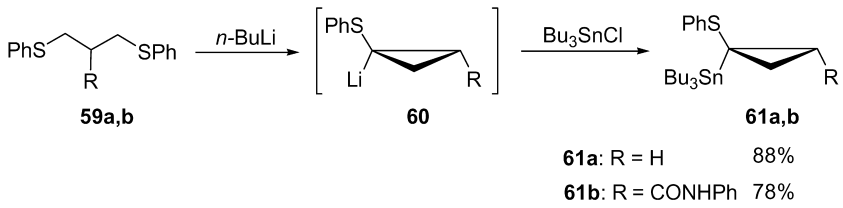
Mori has developed an efficient method for synthesis of bis(tributylstannyl)propionate **50**, an attractive versatile synthon, via sequential silastannation–desilylation of methyl propiolate **49** (Scheme 17).[25] Propionate **50** obtained by this method has been effectively employed for the construction of a series of 1,2,3-trisubstituted cyclopropyl derivatives.[26] Thus, the α-anion, generated from **50** by treatment with LDA, underwent a diastereoselective cross-aldol reaction with an aldehyde to form **51**. Treatment of the major diastereomer of **51** with $SOCl_2$ in the presence of pyridine triggered a destannylative cyclization to produce cyclopropylstannane **52** as single isomer in good to very high yields (Scheme 17).

Alternatively, bis(tributylstannyl)propionate **50** can be converted into aldehyde **53** via alkylation followed by subsequent reduction with DIBAL-H.[27] Aldehyde **53** upon treatment with organometallic reagents gives alcohol **54**, which under mesylation conditions undergoes destannylative 1,3-cyclization to form isomeric cyclopropanes **55** and **56** in very high yields. In most cases **55** was formed as a major diastereomer (Scheme 18).[27]

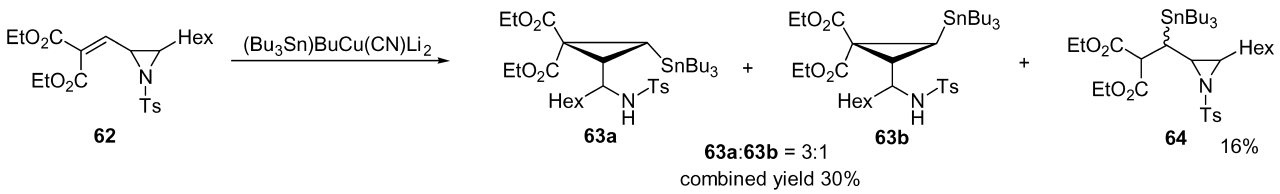
A lithiation–intramolecular cyclization reaction of *N*-Boc-4-chloropiperidine **57** with excess *s*-BuLi was reported by Beak.[28] The first equivalent of *s*-BuLi causes intramolecular nucleophilic substitution leading to bicyclic pyrrolidine, from which selective deprotonation by second equivalent of base followed by trapping with Bu_3SnCl affords **58** in good yield (Scheme 19).[28]



Scheme 19.



Scheme 20.



Scheme 21.

Treatment of bis(phenylthio)propane **59a** with 2 equiv. of *n*-BuLi followed by the addition of Bu_3SnCl afforded α-stannyl cyclopropyl sulfide **61a** (Scheme 20, R=H, 88%).[29] Similarly, trisubstituted **61b** was obtained through cyclization of **59b** in 78% yield.[30] This easy and straightforward approach was only applied to the synthesis of geminally thio-substituted cyclopropylstannanes (Scheme 20).

The Michael-addition initiated ring closure (MIRC) reaction is a powerful approach for construction of highly substituted cyclopropane derivatives;[31] however, when applied to synthesis of cyclopropylstannanes, suffers from poor yields and low facial selectivity. Thus, vinylaziridine **62** was treated with a stannylcuprate reagent affording diastereomeric cyclopropylstannanes **63a**,**b** in a mixture with non-cyclized Michael addition product **64** (Scheme 21).[32]

2.3. Addition of carbenes and carbenoids to olefins

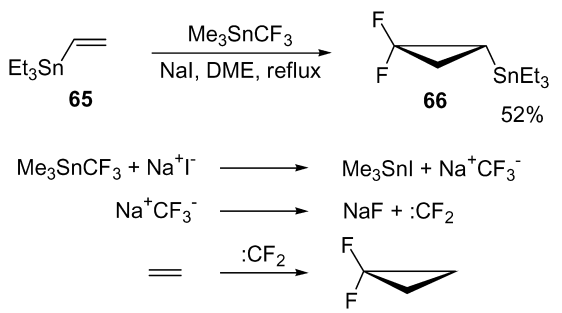
Addition of carbenes to olefins is arguably one of the most powerful methods for the construction of the three-membered ring. This methodology has been applied to the synthesis of cyclopropylstannanes using two different strategies. The first approach involves [2+1] cycloaddition of vinylstannanes and carbenoid species (tin resides at C2 unit). The second utilizes the analogous addition of tin-containing carbenes to olefins (tin resides at C1 unit).

2.3.1. Addition of dihalocarbenes to vinylstannanes. Generally, synthesis of cyclopropylstannanes via addition of dihalocarbenes to vinyltin derivatives cannot be considered as a reliable method, as it often provides low to moderate yields. There were only few reports documenting rather efficient conversion of unsubstituted vinyltin compounds into dihalocyclopropylstannanes. The success in these cases was achieved by applying very mild conditions (non-basic, non-nucleophilic, and non-Lewis-acidic) for generation of carbene species. The dihalocarbenes react smoothly with vinylstannanes **65** and **67**, producing reasonable yields of difluoro- and dichloro-cyclopropylstannanes **66** and **68**, respectively (Schemes 22 and 23).[33,34]

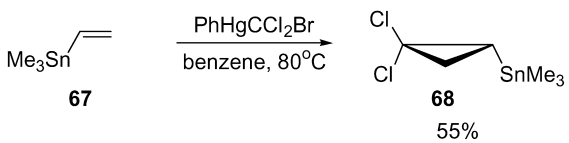
Normally, standard Zn-assisted procedures for addition of carbenoids to alkenes are not successful when applied to vinylstannanes which do not possess a directing group. These rather sensitive substrates were shown to undergo very sluggish cyclopropanation providing poor yields of corresponding cyclopropanes. The main reason for such inefficiency is zinc halide, generated in situ in this reaction. It causes redistribution of alkyl groups at the tin moiety between the starting vinyltrialkyltin and a product, leading to complicated mixtures of tetraalkylstannanes.[9,35]

2.3.2. Simmons–Smith reaction. In contrast to moderately efficient additions of carbenoid species to vinyltin derivatives which do not possess directing/activating groups (see above), allylic alcohols possessing tin substituents undergo smooth Simmons–Smith cyclopropanation[36] in both stoichiometric and catalytic fashion.

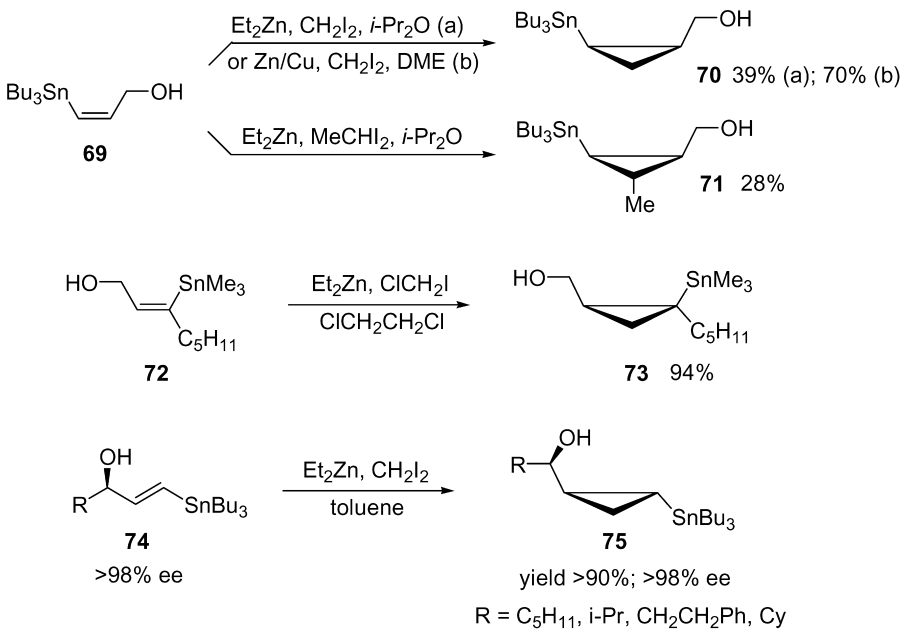
A series of di- and trisubstituted tin-containing cyclopropylcarbinols **70**, **71**, and **73** have been synthesized employing different variations of 'traditional' Et_2Zn–dihalomethane combinations (Scheme 24).[37–41] Optically active cyclopropylstannane **75** has been efficiently



Scheme 22.



Scheme 23.



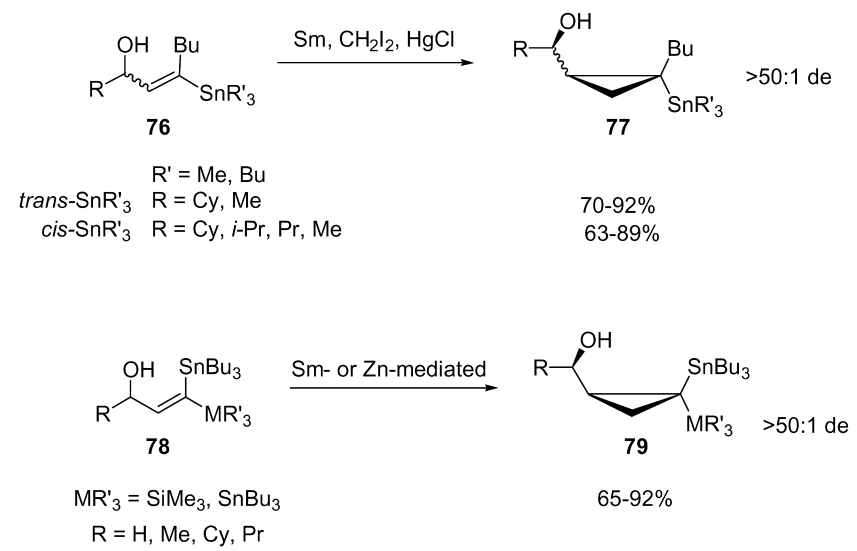
Scheme 24.

synthesized via highly diastereoselective cyclopropanation of chiral allylic alcohol **74** (Scheme 24).[37]

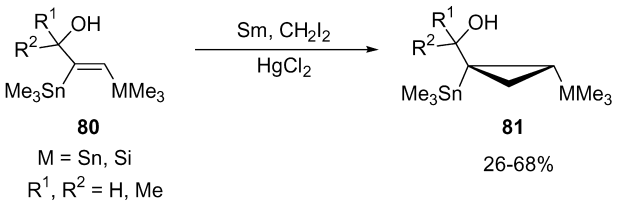
Cyclopropanation involving Sm carbenoids have been extensively studied by Lautens.[42–48] Usually generated from Sm/Hg amalgam or samarium iodide and dihalomethane, these carbenoids are often a more efficient alternative to the reactions with Zn reagents.[36] Somewhat disadvantageous is that Sm-promoted cyclopropanation often requires a large excess of Sm reagent to achieve high conversions, and yields can be non-reproducible with different Sm batches. A practical alternative to the Hg activator was found to be TMSCl, which sometimes improves stereoselectivity of the reaction and makes it less sensitive to the Sm source (Scheme 25).

It was demonstrated that olefins bearing silicon and/or tin substituents undergo highly diastereoselective cyclopropanation in the presence of Sm. High selectivity in this reaction was observed for *Z*- di- or trisubstituted olefins, whereas disubstituted *E*-alkenes provided moderate selectivity. For a few substrates, a comparison with other cyclopropanating procedures was made.[44] While secondary allylic alcohol **78** (MR'_3=$SiMe_3$) bearing a cyclohexyl substituent reacted smoothly in the presence of Sm metal, the reaction with Zn/Cu couple resulted in predominant destannylation, and SmI_2 produced no reaction at all. In contrast, primary allylic alcohol **78** (MR'_3=$SiMe_3$, R=H) reacted smoothly in the presence of samarium iodide. This indicates that SmI_2-mediated cyclopropanation is much more sensitive to steric effects than when metallic Sm is used. Attempted dichlorocyclopropanation of this substrate using chloroform and NaOH produced the corresponding allyl chloride only.

Although the Sm method has been shown to be very efficient



Scheme 25.



Scheme 26.

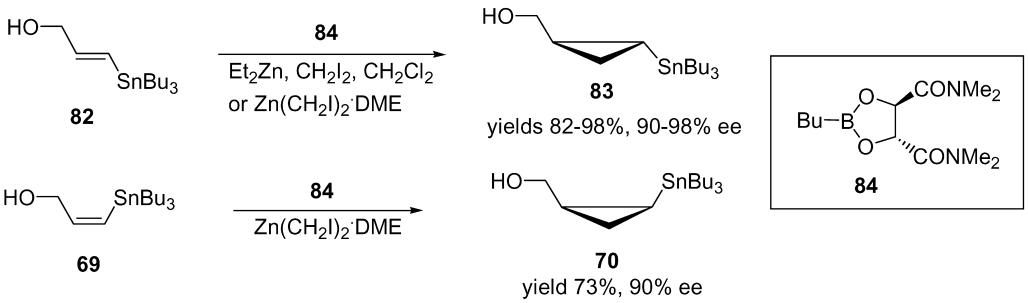
for 1,1-distannyl- or silastannylalkenes, it was only partially applicable to the 1,2-disubstituted substrates, as shown by Mitchell.[49] Even though primary alcohols **80** give acceptable yields of the products, this method fails when steric demands in the starting olefin increase. Secondary alcohols produced the corresponding products in very low yields, whereas tertiary analogs did not react at all (Scheme 26).

Asymmetric cyclopropanation reaction using stoichiometric amount of chiral dioxaborolane, discovered by Charette,[31] was effectively applied to the synthesis of tin-containing cyclopropylmethanols.[50–54] Both *trans*- and *cis*-alkenylstannanes were employed with similar efficiency, producing *trans*- (**83**) and *cis*-cyclopropylstannylmethanols (**70**), respectively, in high yields and enantiomeric excess (Scheme 27).

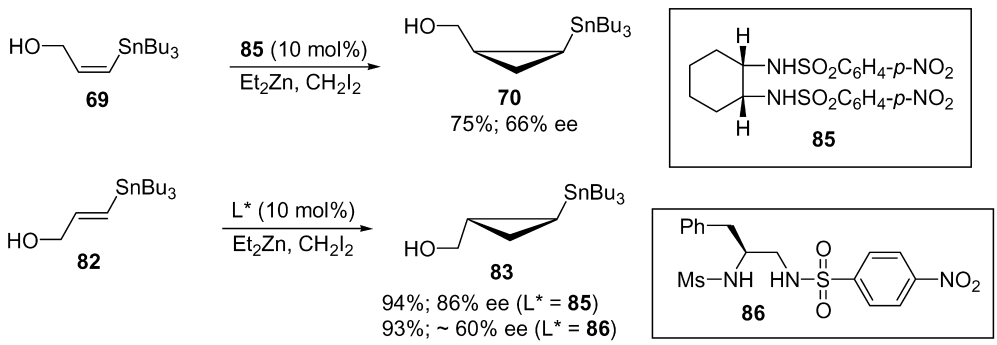
Catalytic enantioselective cyclopropanation of allylic alcohols developed by Kobayashi was also extended to the synthesis of optically active cyclopropylstannanes. As in the case with other substituents, reaction with *trans*-alkene **82** produced **83** with higher enantiomeric excess (86%), compared to the analogous reaction with *cis*-isomer **69**, which afforded the corresponding cyclopropylstannane **70** with moderate ees only (66%, Scheme 28).[55] Disulfonamide ligand **86** reported by Imai displayed poorer enantiomeric induction in the reaction with *trans*-alkene **82** (~60% ee) (Scheme 28).[56]

2.3.3. Rh-Catalyzed addition of carbenoid species. Asymmetric intramolecular cyclopropanation of olefins via the Rh-catalyzed decomposition of diazoesters represents a very powerful approach to optically active cyclopropanes.[57] Excellent functional group compatibility and mild reaction conditions resulted in extensive application of this method in organic synthesis. Doyle demonstrated that using this methodology, chiral cyclopropylstannanes **88** can be obtained in good yield and very high degrees of enantioselectivity (Scheme 29).[16,58]

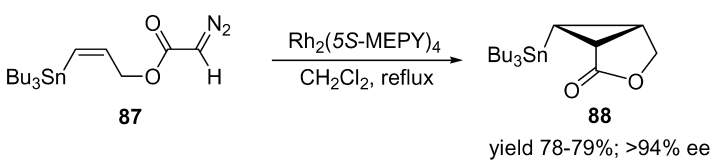
2.3.4. Addition of tin-containing carbenes to olefins. It should be mentioned that synthesis of cyclopropylstannanes via addition of tin-containing carbenes and carbenoids to olefins has proved less efficient compared to the methods described above, involving addition to vinyltins. Additional



Scheme 27.



Scheme 28.



Scheme 29.

α-carbanion stabilization by stannyl group allowed for preparation of rather stable tin-containing carbenoid species **90**, which was obtained in high yields from bis(diazoacetate) **89** and when reacted with isobutene under photolytic conditions gave cyclopropyltin derivative **91** in moderate yield (Scheme 30).[59]

Insertion of metalated carbenes into olefins was further investigated on series of differently substituted alkenes.[60] Generally, trimethylstannyl diazoacetate **92** provided rather poor yields of the corresponding cyclopropylstannanes **94** except for the case with isobutene (70%, Scheme 31).

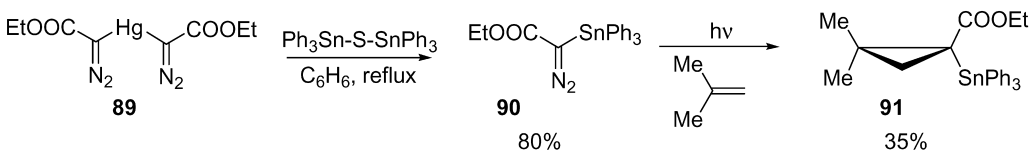
Poor yields were also obtained in the reaction of trimethylstannylcarbene **96** generated by treatment of chloromethyltrimethyltin **95** with LiTMP in cyclohexene–ether solution; norcarane **97** was isolated in 21% yield from a complex mixture of unidentified products (Scheme 32).[61]

α-Phosphinosubstituted cyclopropylstannane **99** was obtained in 55% yield as a mixture of diastereomers in the reaction of stannyl-containing carbenoids with acrylates (Scheme 33).[62]

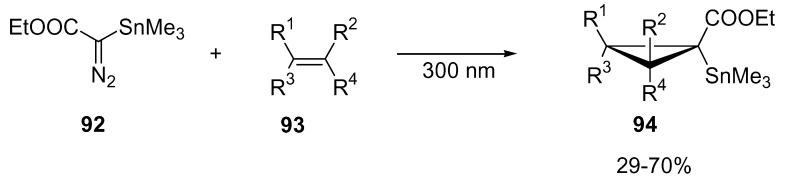
2.4. Addition of tin-containing entities across the double bond of cyclopropenes and methylenecyclopropanes

Addition of tin-containing species to the double bond of cyclopropenes and methylenecyclopropanes represents another very attractive and powerful approach to cyclopropylstannanes. Significant strain energy in unsaturated three-membered rings versus parent cyclopropanes is the reason for the high affinity of their double bonds towards various addition reactions.[63,64] This methodology has been realized in the synthesis of series of cyclopropylstannanes via radical-initiated or transition metal-catalyzed addition of tin hydrides and tin–metal species to the unsaturated precursors.

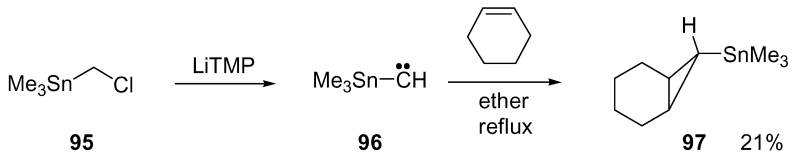
2.4.1. Addition of tin hydrides to cyclopropenes. Nakamura demonstrated that radical-initiated *trans*-addition



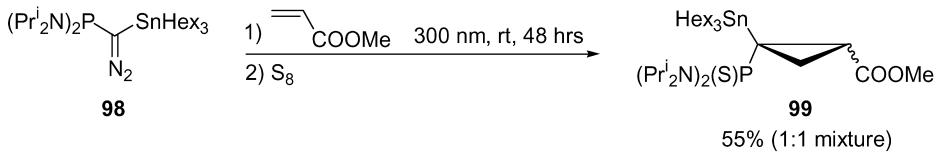
Scheme 30.



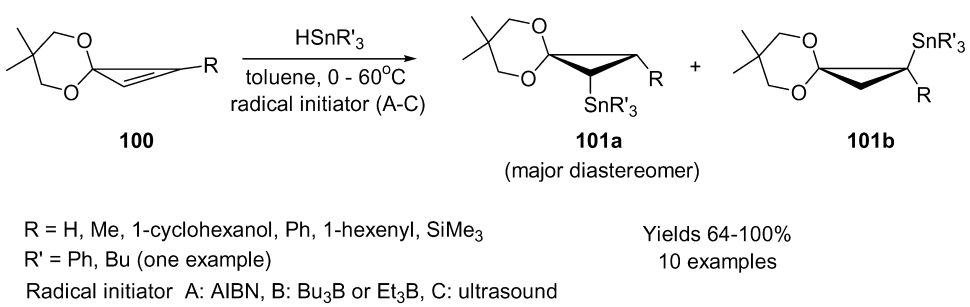
Scheme 31.



Scheme 32.



Scheme 33.



Scheme 34.

of tin hydrides (mostly triphenyltin hydride) across the double bond of cyclopropenone acetals proceeds smoothly to afford a variety of stannylcyclopropanone acetals in high yields (Scheme 34).[65,66] It was shown that the β-addition product, cyclopropylstannane **101a**, always formed as a major regioisomer and the regioselectivity depended on the size of an R group; however, mixtures of diastereomers of **101a** were observed (from 20:1 to 6:1 with *cis*-isomer being a major product).

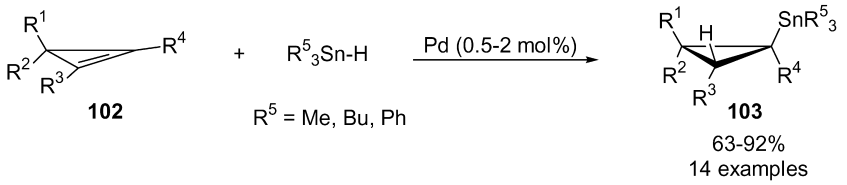
Transition metal-catalyzed hydrostannation of cyclopropenes. In contrast to the *trans*-selective radical-initiated hydrostannation, transition metal-catalyzed addition of tin species across the double bond of cyclopropenes proceeds highly *cis*-selectively to produce multisubstituted cyclopropane derivatives in very good yields (Scheme 35).[67] A number of transition metals (Ru, Rh, Pt, Pd) were shown to catalyze this reaction; however, palladium catalysts appeared to be superior over other metals: the reaction proceeded extremely fast at temperatures as low as −78 °C and allowed for efficient synthesis of up to pentasubstituted cyclopropylstannanes. Great functional group tolerance was demonstrated on substrates bearing ester, ether, silyl, and allyl functionalities. It was shown that the addition across the double bond of cyclopropene is generally controlled by steric factors and proceeds from the least hindered face regardless of the substituents at the tin atom (Me, Bu, Ph). Remarkably, alkoxymethyl substituents displayed a significant directing effect in the hydrostannation of 3,3-disubstituted cyclopropenes preferentially affording addition products with *syn* orientation of alkoxymethyl and tin substutuents.

2.4.2. Addition of ditin and silicon–tin species to cyclopropenes. De Meijere's protocol for silastannation of methylenecyclopropenes (see below) was adapted to sila- and stannastannation of 3,3-disubstituted cyclopropenes (Scheme 36).[67] Palladium acetate–*tert*-isooctyl isocyanide[68] (Walborsky's ligand) catalyst combination effected facile addition of the bimetallic species, which was shown to be entirely sterically controlled.

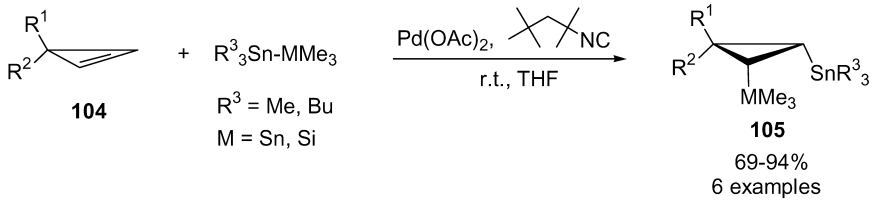
2.4.3. Addition of tin–metal species to methylenecyclopropanes. De Meijere showed that palladium acetate-catalyzed addition of silastannanes to bicyclopropylidene **106** proceeded smoothly in the presence of *tert*-isooctyl isocyanide complex to form stannyl bis-cyclopropanes **107** and **108** (Scheme 37).[69] It was shown that employment of palladium tetrakis ($Pd(PPh_3)_4$) in this reaction led to opening of cyclopropyl ring. Interestingly, disproportionation to form disilanes and distannanes occurred, when trimethylsila(trimethyltin) was employed (R=Me), resulting in formation and subsequent addition of hexamethylditin to the double bond to give **108** (Scheme 37).[69]

2.5. Miscellaneous

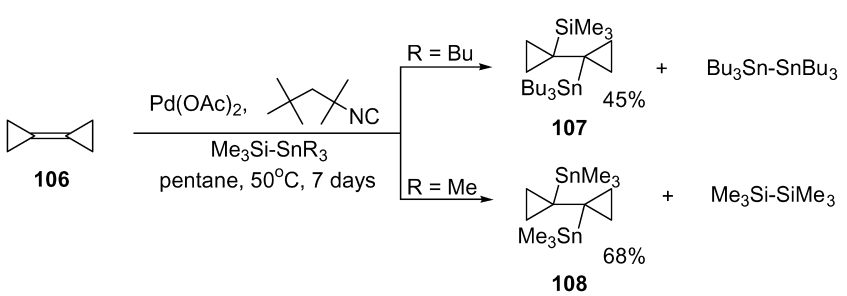
2.5.1. Kulinkovich reaction. A highly diastereoselective synthesis of cyclopropylstannanes using the Kulinkovich cyclopropanation reaction[70] was reported by Cha



Scheme 35.



Scheme 36.



Scheme 37.

(Scheme 38).[71] Cyclopropanation of carboxamides afforded higher yields than that of corresponding esters, which was explained by higher stability of amides toward nucleophilic attack by Grignard reagents. Furthermore, due to the high propensity of β-stannylcyclopropanols toward ring-opening, silyl protection was necessary to isolate these compounds. Interestingly, esters and carboxamides afforded *cis*- and *trans*-products, respectively, and the stereochemical outcome of this reaction for both esters and amides was opposite to that for alkyl-substituted olefins.[72,73] The reason for this effect remains unclear and is believed partly to originate from steric effect of the bulky tributyltin moiety. Overall, the method provides reasonable to good yields of amides **111**; however, the reaction with esters suffers from substantial formation of ring-opening products.

2.5.2. Substitution at cyclopropyl ring with tin nucleophiles. When optically active cyclopropylbromide **112** was treated with trimethylstannyllithium, two products, **113** and **114**, were obtained (Scheme 39).[74,75] The absolute configuration at C1 for both, **113** and **114**, remained unchanged with no racemization occurred. As a possible route to the formation of by-product **114**, the authors suggested involvement of the cyclopropyllithium intermediate **116**, which resulted from transition complex **115** via metal–halogen exchange. However, all attempts to prove the above assumption by trapping **116** with any other electrophiles failed.

The reaction of tributylstannyllithium with the magnesium salt of 1-ethoxycyclopropanol **118**, obtained form hemiacetal **117**, proceeded very slowly to afford a low yield of stannylcyclopropyl MOM ether **119** (Scheme 40). The authors explained the low efficiency of this reaction by competitive decomposition of the tributylstannyllithium reagent.[35]

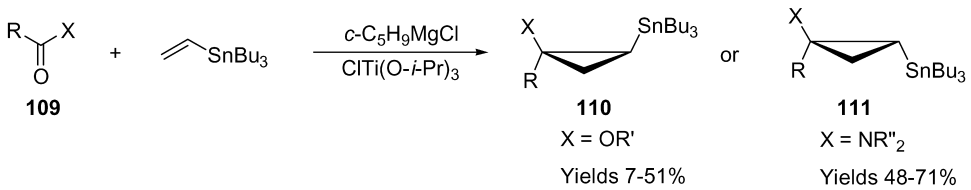
2.6. Cyclopropenylstannanes (synthesis and applications)

Cyclopropenes display comparable reactivity to that observed for terminal acetylenes, towards deprotonation reactions. The increased acidity of the olefinic protons in cyclopropenes is attributed to a high degree of *s*-character of the C–H bond, which results from significant ring strain.[76]

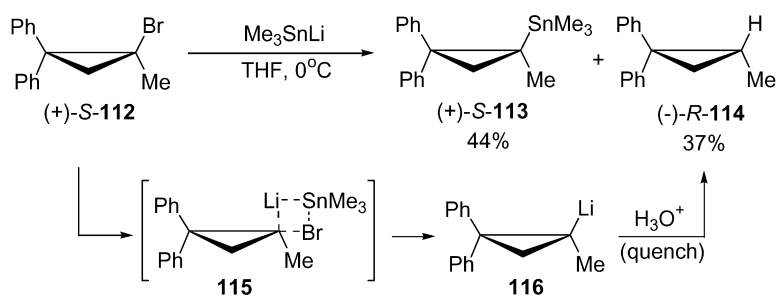
Thus, metalation of both olefinic carbon atoms in cyclopropene **120** by LDA followed by trapping with a metal electrophile afforded disilyl-, distannyl-, and digermylcyclopropenes **121a–c**. The yields of bis-silylcyclopropene **121a** obtained by this method was good, whereas preparation of tin (**121b**) and germanium (**121c**) analogs was less efficient (Scheme 41).[77] Low yields of **121b**,**c** were attributed to their low stability during isolation due to more labile C–Sn and C–Ge bonds in cyclopropenes.

Efficient monometalation of cyclopropenone acetal **122** was achieved by Nakamura by employment of 1 equiv. of *n*-BuLi at −70 °C in THF in the presence of HMPA (Scheme 42).[78] The latter was shown to be necessary for stabilization of cyclopropenyllithium **123**, and thus for obtaining higher yields of the products.

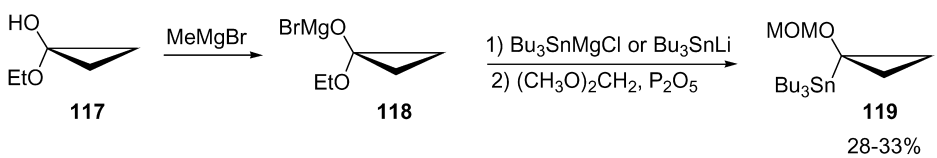
It was found that addition of allylzinc reagents to the stannyl cyclopropenone acetals (CPA), as well as to their silyl and germyl analogs, proceeded much faster than that to



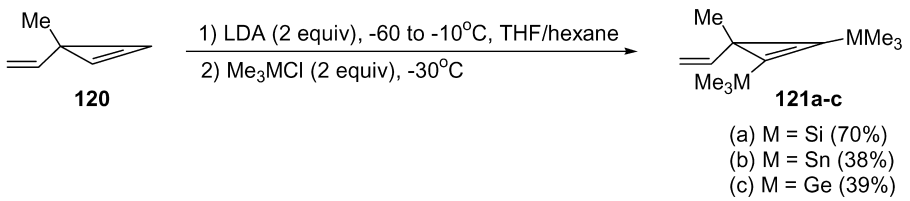
Scheme 38.



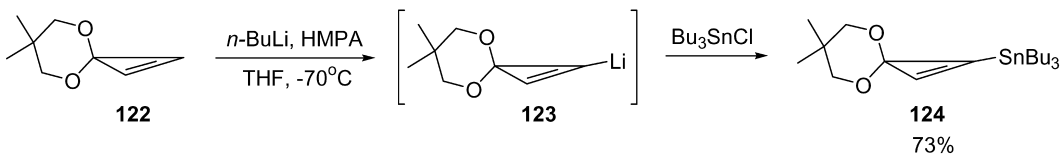
Scheme 39.



Scheme 40.



Scheme 41.

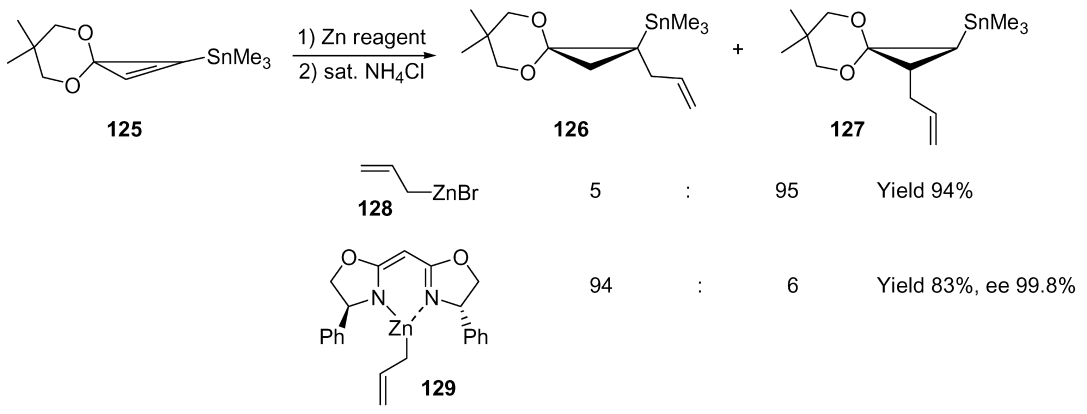


Scheme 42.

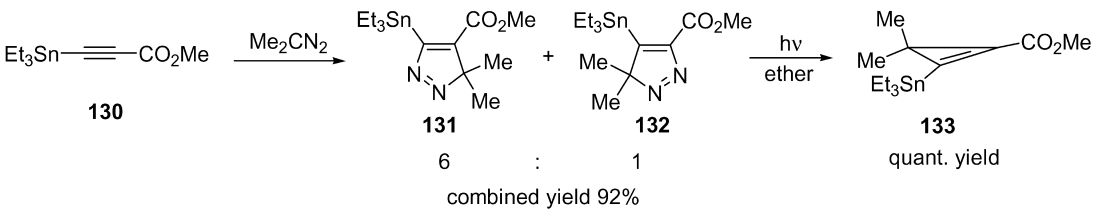
carbon-substituted CPAs (Scheme 43).[79] This observation is in agreement with previously obtained results on carbometalation of olefins.[80] Addition of allylzinc bromide to trimethylstannyl CPA provided a mixture of two regioisomers **126** and **127** in excellent yield with 95:5 selectivity favoring formation of the β-addition product **127**. The observed regioselectivity was attributed to electrostatic interactions between the Lewis acidic zinc atom and the partially negatively charged carbon atom adjacent to tin. However, the regioselectivity was completely reversed, favoring the geminal product **126**, when allylzinc reagent **129**, bearing a chiral bisoxazoline ligand, was used (Scheme 43). The opposite regioselectivity observed in this case was explained by unfavorable steric interactions between bulky bisoxazoline ligand and trimethyltin substituent. High yields, and very good regioselectivity, taken together with excellent enantioselectivity obtained in the reaction with **129**, makes it a very useful method for the synthesis of allyl-substituted (trimethylstannyl)cyclopropanone acetals.

Guillerm reported a single example of dipolar [2+3] cycloaddition of diazopropane to methyl triethylstannylpropiolate (Scheme 44).[81] The reaction proceeds in very high yield to form isomeric pyrazolines, which undergo extrusion of nitrogen upon irradiation to produce (triethylstannyl)cyclopropenyl carboxylate **133** in quantitative yield.

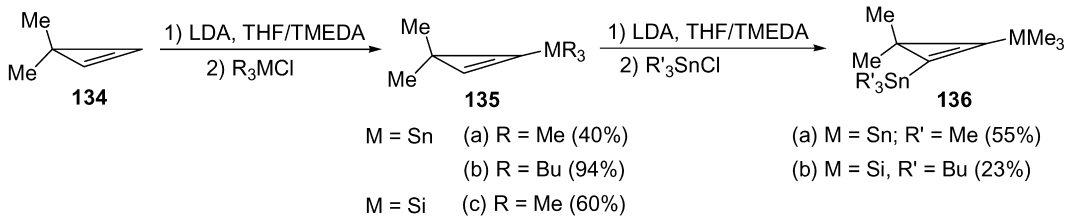
De Meijere reported synthesis of mono- (**135**) and dimetalated cyclopropenes (**136**) using sequential deprotonation/electrophile trapping (Scheme 45).[82–84] It was recognized that use of LDA as the deprotonating agent allows to avoid undesirable addition of alkyllithium reagent across the double bond of cyclopropene. Lower yields obtained for monometalated compounds **135a** and **135c** are probably due to volatility of these products (Scheme 45).[82]



Scheme 43.



Scheme 44.



Scheme 45.

Cyclopropenylstannane **136b** was tested in the Stille cross-coupling reaction with various halides and triflates (Scheme 46). However, good results were obtained only in the reactions with phenyl iodide (98%) and bromide (63%), whereas employment of triflates proved inefficient.[84] A two-fold coupling of phenyl iodide with distannane **138** afforded diphenylcyclopropene **139**, albeit in low yield (Scheme 46).

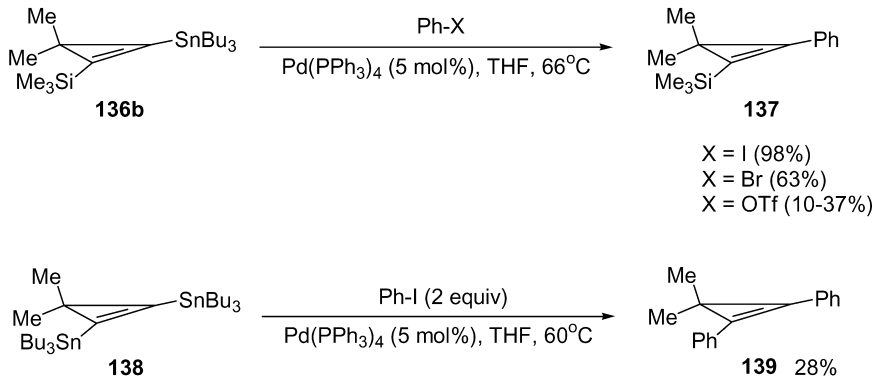
3. Applications

3.1. Transformations with preservation of the cyclopropyl ring

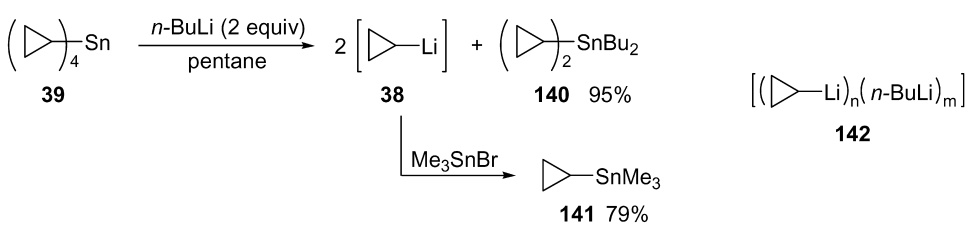
3.1.1. Reactions involving tin–lithium exchange. To date, among all applications, the tin–lithium exchange reaction represents the most important and most extensively used transformation of cyclopropylstannanes. Facile transmetalation with organolithium reagents at temperatures as low as −100 °C makes cyclopropylstannanes a convenient precursor of reactive stereodefined (vide infra) cyclopropyllithium species. A few features of this transformation are worth emphasizing. First, while tributyltin group can undergo smooth tin–lithium exchange at geminally unsubstituted and substituted cyclopropylstannanes, transmetalation of the trimethyltin group of the latter proved unsuccessful. Second, *syn*-oriented directing groups, such as alkoxymethyl- or carbonyl-containing substituents, facilitate transmetalation; however, generally, bulky *syn*-substituents significantly impede or completely suppress tin–lithium exchange. The resulting cyclopropyllithium species are normally configurationally stable at temperatures as high as 0 °C, however, partial or complete epimerization can occur at this temperature if an *anti*-oriented directing substituent is present at the cyclopropyl ring.

The very first experiments on tin–lithium exchange on cyclopropyl series was performed by Seyferth in early 60s (Scheme 47).[15,85] Solid cyclopropyllithium **38** was obtained via reaction of tetracyclopropylstannane **39** with 2 equiv. of *n*-BuLi in pentane. Cyclopropyllithium **38**, which precipitated from the reaction mixture, was treated with trimethyltin bromide to provide cyclopropyltrimethylstannane **141** in 79% yield. In all reactions performed, isolated solid cyclopropyllithium contained small amounts of *n*-BuLi, which upon quenching with Me_3SnBr produced $BuSnMe_3$ (2–4%). The presence of *n*-BuLi in the cyclopropyllithium precipitate was explained by the formation of mixed organolithium polymer of type **142**.

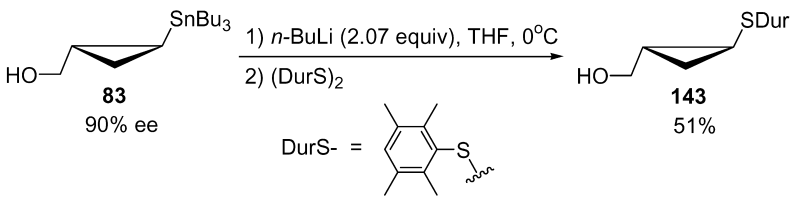
Lithiodestannylation of **83** was performed to introduce an arylthio-substituent in the cyclopropyl ring (Scheme 48).[52,54]



Scheme 46.



Scheme 47.

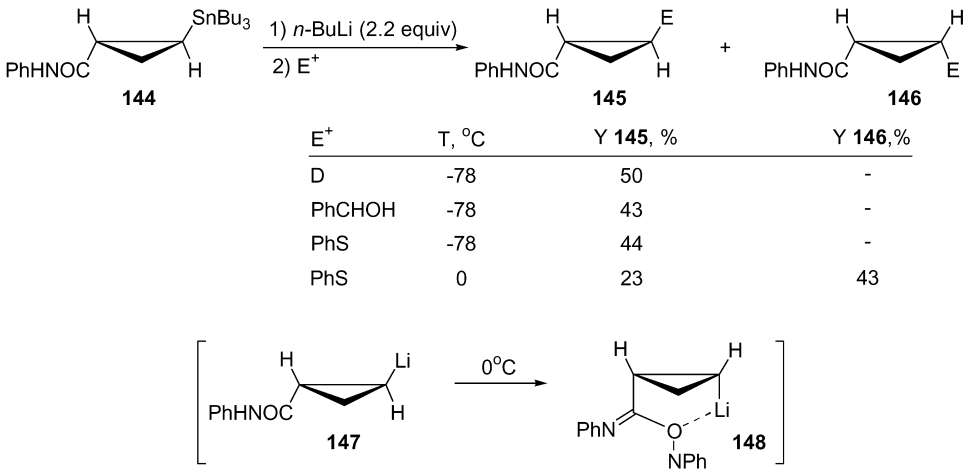


Scheme 48.

Interestingly, although the reaction of **83** was carried out at 0 °C, no epimerization occurred in this case despite the presence of the potentially directing hydroxymethyl substituent.

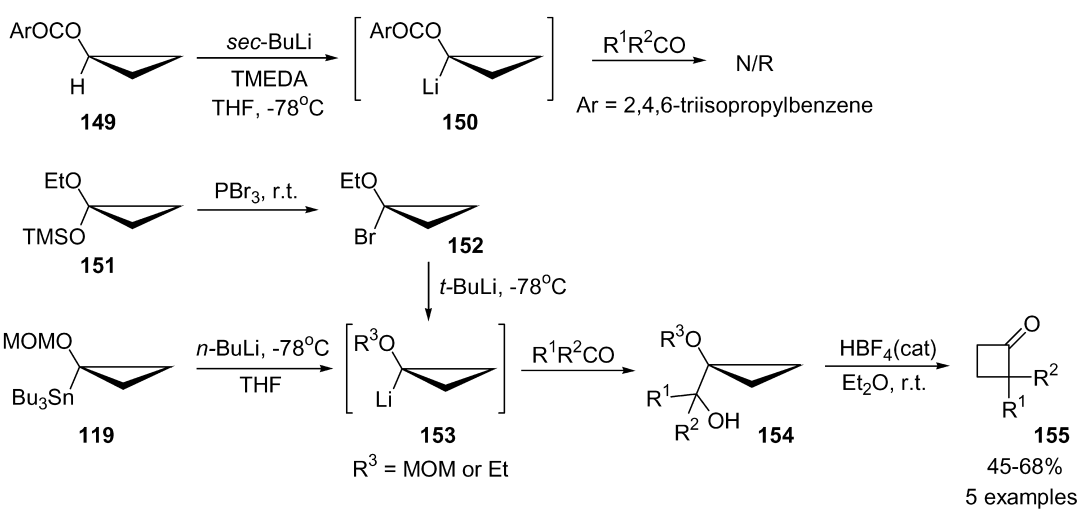
In contrast, Tanaka demonstrated that tin–lithium exchange with **144** proceeds with retention of configuration at low temperature; however, when warmed up to 0 °C, *trans*-**147** isomerizes into *cis*-cyclopropyllithium to form stabilized lithium chelate species **148** (Scheme 49). Experiments involving optically active **144** revealed that tin–lithium exchange performed at −78 °C did not compromise either of the chiral centers of the molecule.[86]

Gadwood investigated various approaches to generation of (1-alkoxycyclopropyl)lithium reagents en route to cyclobutanone derivatives **155** (Scheme 50).[35] Three methods have been explored: deprotonation of hindered cyclopropyl benzoates, halogen–metal exchange of α-haloethers, and transmetalation of alkoxycyclopropylstannanes. Direct deprotonation of cyclopropylbenzoate **149** can be easily accomplished with *sec*-BuLi/TMEDA, but the derived organolithium compound did not react with ketones, probably due to steric hindrance. In contrast, easily available 1-bromoethoxycyclopropane **152** has been found to be a convenient precursor for reactive (1-alkoxycyclopropyl)lithium reagents. Metal–halogen exchange between **152** and *t*-BuLi occurred rapidly at low temperature, and the resulting organolithium compound **153** reacted cleanly with a variety of aldehydes and ketones. Likewise, cyclopropylstannane **119** also underwent transmetalation smoothly, leading to desired lithium intermediate **153**. However, the

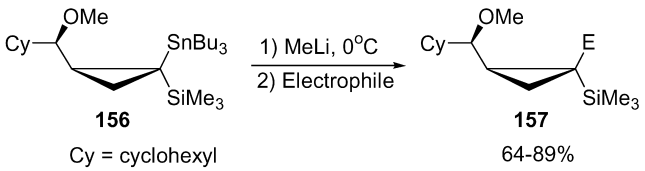


E^+	T, °C	Y **145**, %	Y **146**,%
D	-78	50	-
PhCHOH	-78	43	-
PhS	-78	44	-
PhS	0	23	43

Scheme 49.



Scheme 50.



Scheme 51.

synthetic usefulness of this route is questionable due to the relative inaccessibility of starting cyclopropylstannane **119**.[35]

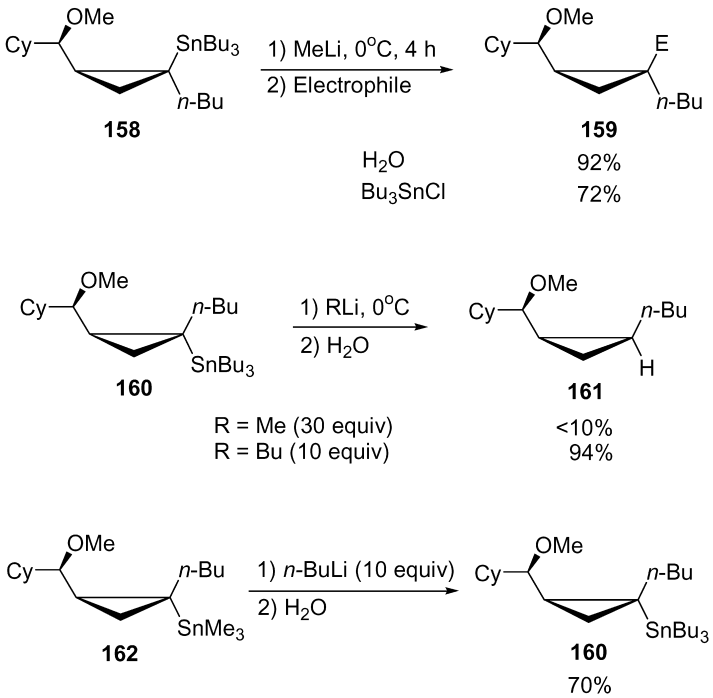
Lautens performed systematic studies on the tin–lithium exchange using a series of different geminal bimetallic cyclopropylstannanes (Scheme 51).[43,47,48] Investigation of solvent effect on the reaction rate revealed that the transmetalation of cyclopropylstannanes occurred extremely efficiently in a matter of a few minutes when THF or DME were used as solvents: only 1.05 equiv. of methyllithium were enough for complete rapid transmetalation in these solvents. Interestingly, the corresponding reactions in ether and hexane were unsuccessful. The analogous reaction with *n*-BuLi (30 equiv.) was complete only after 10 h in THF, and it was considerably slower in DME and did not proceed in Et_2O or hexane at all.[43] A number of electrophiles (R_3MCl (M=Sn, Si), CO_2, PhSSPh, CHO) were tested to demonstrate the synthetic utility of this reaction (Scheme 51). In most cases, good to high yields of corresponding functionalized cyclopropanes were obtained. Surprisingly, attempts to trap the resulting cyclopropyllithium species with TMSCl were unsuccessful.[43]

Replacement of a silyl moiety for an alkyl group has a significant effect on the transmetalation rate. Tin–lithium exchange of **158** required 4 h, versus bimetallic stannylsilylcyclopropane **156** which reacted in 25 min (Scheme 52). The authors suggest that the ability of the silyl group to stabilize an α-carbanion is responsible for the observed dramatic difference in the reaction rates of **156** versus **158**. The relative stereochemistry of the tributylstannyl group and alkoxymethyl substituent at C-2 was shown to have a significant influence on the rate of transmetalation. In contrast to smooth tin–lithium exchange of *Z*-stannylcyclopropane **158** with methyllithium, the isomeric *E*-**160** did not undergo transmetalation even with a large excess of MeLi. However, complete transmetalation was achieved with 10 equiv. of *n*-BuLi in THF (Scheme 52). To determine whether the less sterically hindered tin moiety would undergo transmetalation more readily than its tributylstannyl-substituted analog, the reaction with trimethylstannylcyclopropane **162** was attempted. No reaction of **162** with MeLi was observed; however, treatment of **162** with 10 equiv. of *n*-BuLi resulted in unexpected complete methyl to butyl group exchange at the tin moiety (Scheme 52).[43]

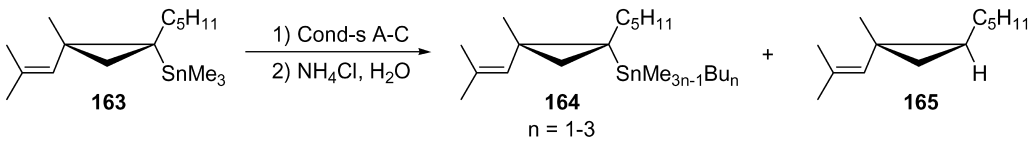
Analogously, lithiodestannylation of tetrasubstituted trimethylstannylcyclopropane **163** also proved unsuccessful (Scheme 53).[38] The reaction did not proceed in any conditions tried (methods A–C); instead, methyl to butyl substitution occurred leading to mixtures of products **164**.[38]

Sensitivity of tin–lithium exchange to facial steric hindrance was studied using diastereomeric cyclopropylstannanes **166** and **168** (Scheme 54). While the substrate bearing less bulky *cis*-methyl group underwent smooth transmetalation with *n*-BuLi at −30 °C,[87] more sterically hindered **168** with a *cis*-phenyl substituent did not undergo this reaction even at room temperature.[88]

Lautens has also found an interesting example of a retro-Brook type rearrangement[89] in cyclopropyl series: the silyl group underwent smooth 1,4-migration to C-1 of the cyclopropane under treatment of **169** with MeLi followed

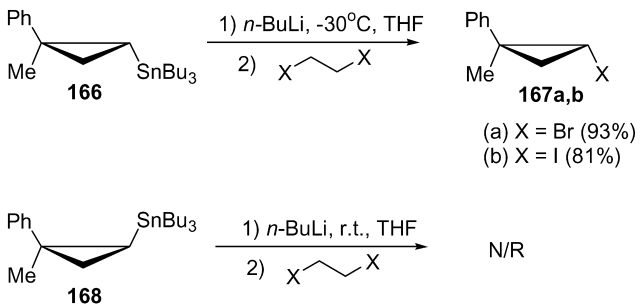


Scheme 52.



A: *n*-BuLi (2.05 equiv); **163** : **164** : **165** = 15 : 70 : 15
B: MeLi; N/R
C: *n*-BuLi (10 equiv); **164** (n = 3) : **165** = 75 : 5

Scheme 53.



Scheme 54.

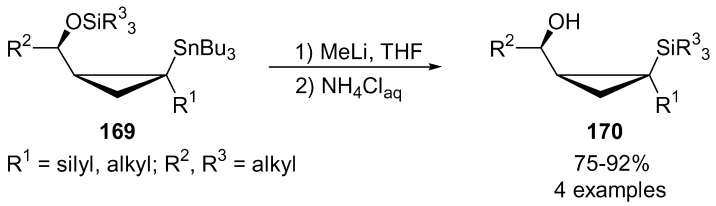
by hydrolytic workup (Scheme 55). Protonation of lithium alkoxide then provided a hydroxyl moiety, which can be used for further transformations.[43,47]

Another application of bimetallic cyclopropanes en route to cyclopropylidenes has been reported by Lautens. Tin–lithium exchange followed by trapping with electrophile and subsequent Peterson olefination afforded product **172** in unspecified yield (Scheme 56).[46]

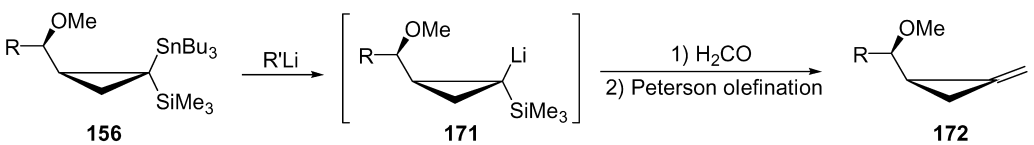
Optically active tributylstannylcyclopropyl synthons **173** were used as key intermediates in the synthesis of Dictyopterene A (**175**, Scheme 57).[53] Transmetalation—trapping with electrophile occurred smoothly in case of all three compounds, providing cyclopropylaldehydes **174** in good to very high yields (Scheme 57).

Mori investigated transmetalation of 1,2,3-trisubstituted cyclopropanes **176** and **178**, and subsequent trapping of the resulting cyclopropyllithium species with various electrophiles (Scheme 58).[26] It was shown that quenching with MeI proceeded smoothly affording a very high yield of the methylated product, whereas other electrophiles required addition of HMPA, still providing moderate to good yields of the products. The fact that cyclopropylstannane **176** also undergoes methylation producing **177** in high yield indicates that transmetalation tolerates *cis*-oriented alkoxymethyl substituents.

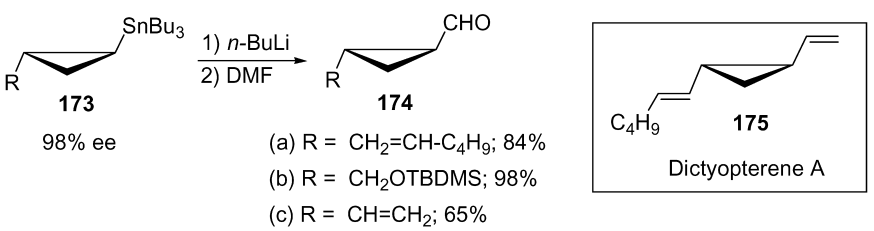
The extension of this methodology was demonstrated later by Mori in synthetic studies toward Ambruticin (Scheme 59).[27] Two alternative approaches to the required key intermediate **181** employing different flavors of the tin–lithium exchange motif at the cyclopropyl ring were explored. Thus, tributylstannylcyclopropane **180** was



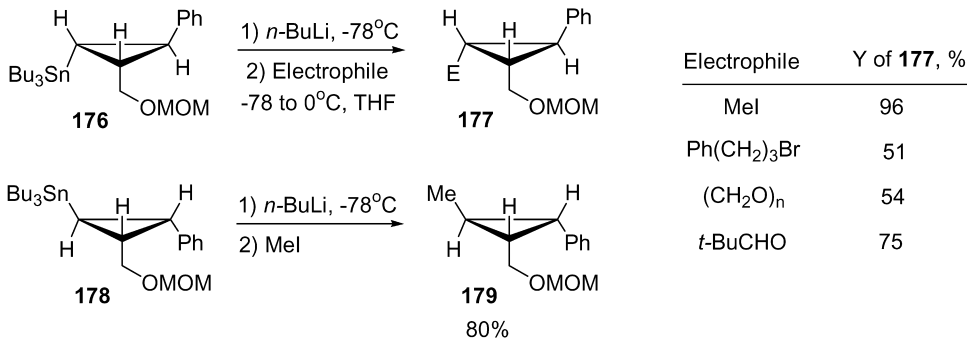
Scheme 55.



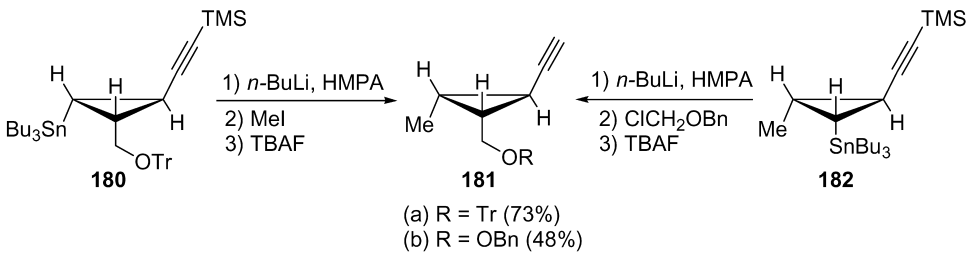
Scheme 56.



Scheme 57.



Scheme 58.

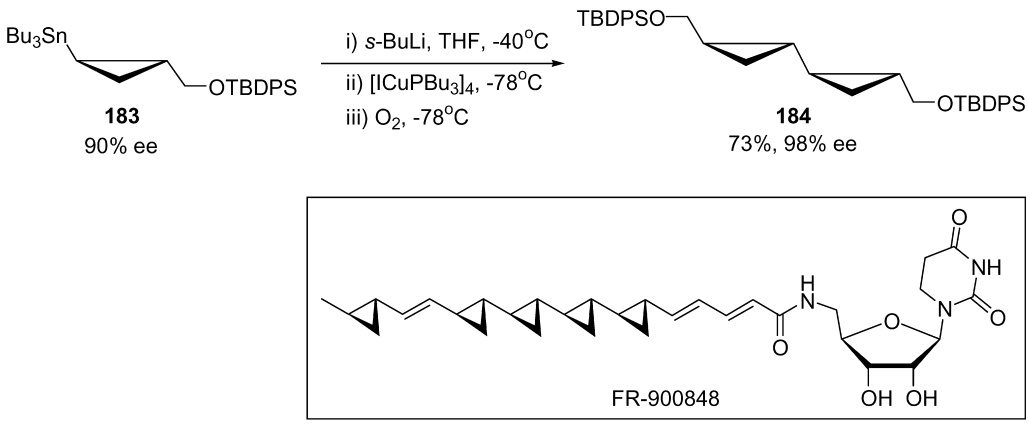


Scheme 59.

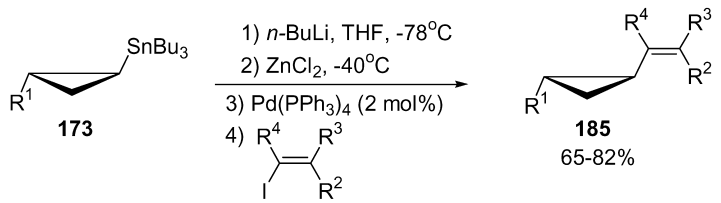
treated with *n*-butyllithium followed by trapping with MeI and desilylation to provide **181a** in 73% yield. Alternatively, lithiodestannylation of cyclopropane **182** produced lithium derivative, which upon alkylation with chloromethylbenzyl ether and deprotection with TBAF afforded **181b** in 48% overall yield (Scheme 59).

Tin–lithium exchange followed by oxidative homo-coupling of two cyclopropyllithium species was employed by Falck as an efficient protocol in the assembly of polycyclopropane framework of antibiotic FR-900848 (Scheme 60).[50] Tin group of silylated cyclopropylmethanol **183** was transmetalated with *sec*-BuLi and the resulting lithium anion was treated with $[ICuPBu_3]_4$ and then subjected to an oxygen-induced dimerization at low temperature to give *syn-trans*-bis-cyclopropane **184**. The observed enrichment in enantiomeric excess is a result of a statistical distribution of products and represents a variant of the Horeau amplification principle.[90]

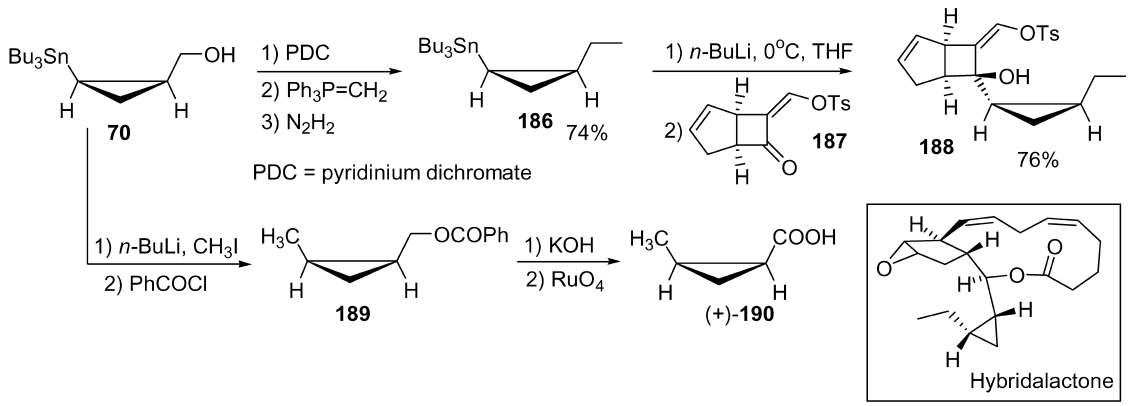
In synthetic studies toward sesquiterpenoids (±)-prezizanol and (±)-prezizaene, Piers demonstrated that cyclopropylstannanes **173** can efficiently be employed as remote precursors for Negishi cross-coupling reactions with various



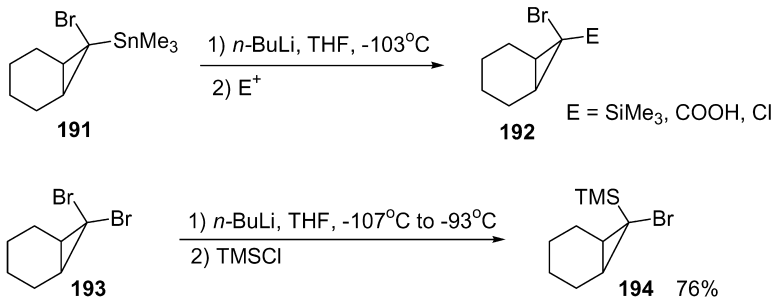
Scheme 60.



Scheme 61.



Scheme 62.

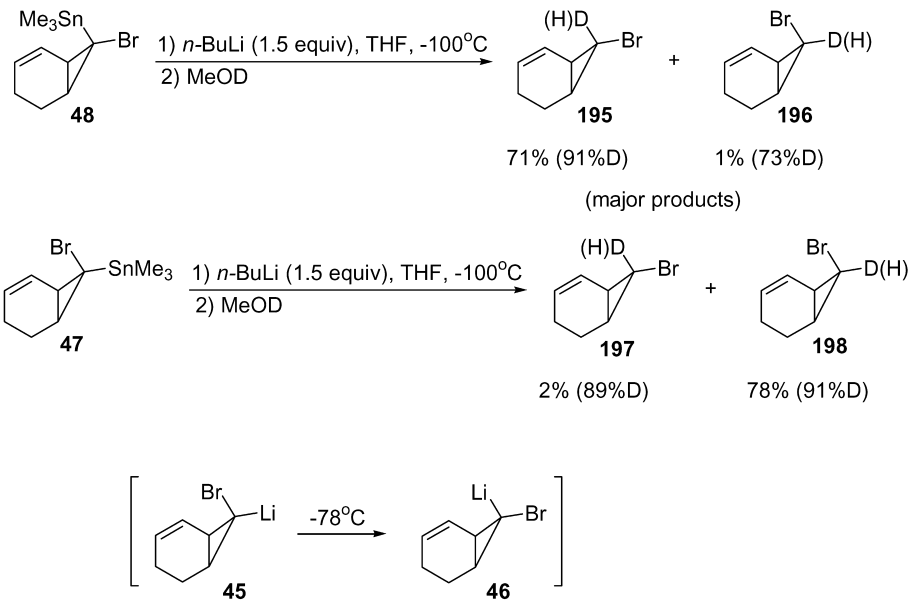


Scheme 63.

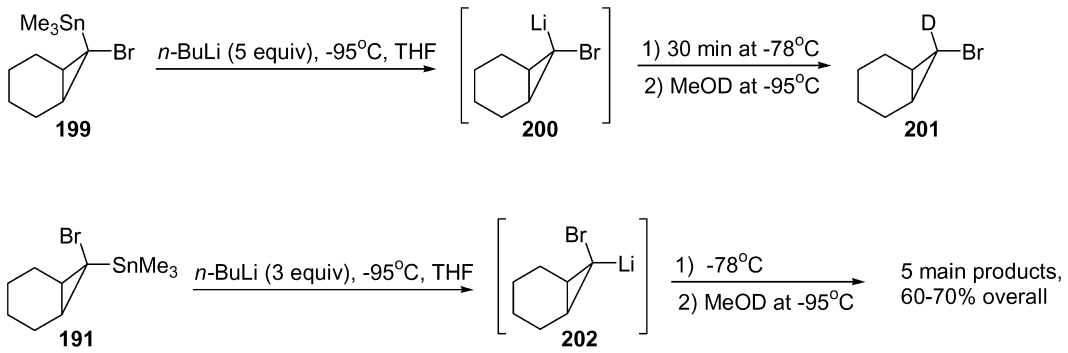
alkenyl iodides (Scheme 61).[91] Tin–lithium exchange followed by Li–Zn transmetalation afforded cyclopropylzinc halide species, which smoothly underwent stereoselective Pd-catalyzed coupling with vinyl iodides to efficiently produce corresponding vinylcyclopropanes **185**.

Corey took advantage of the facile tin–lithium exchange of *cis*-tributylstannylcyclopropane **186** in the total synthesis of Hybridalactone (Scheme 62).[40,41] A coupling reaction between β-tosyloxyenone **187** and cyclopropyllithium generated from **186**, afforded a good yield of one of the key intermediates **188**. To unambiguously establish the absolute configuration of the starting stannylcyclopropane **70**, the sequence involving tin–lithium exchange, electrophile trapping, esterification and oxidation was realized to provide known acid (+)-**190**.

Seyferth demonstrated for the first time the possibility of performing a stereoselective transmetalation of tin in the presence of a geminal bromine substituent (Scheme 63).[11] Thus, transmetalation of *syn*-7-bromo-*anti*-7-trimethylstannylnorcarane **191** followed by trapping with electrophile produced *anti*-TMS-norcarane **192** as a sole



Scheme 64.



Scheme 65.

Scheme 66.

stereoisomer. Alternatively, isomeric *anti*-7-bromo-*syn*-7-TMS-norcarane **194** can stereospecifically be prepared by the metal–halogen exchange of dibromide **193** with *n*-BuLi, followed by treatment with TMSCl.

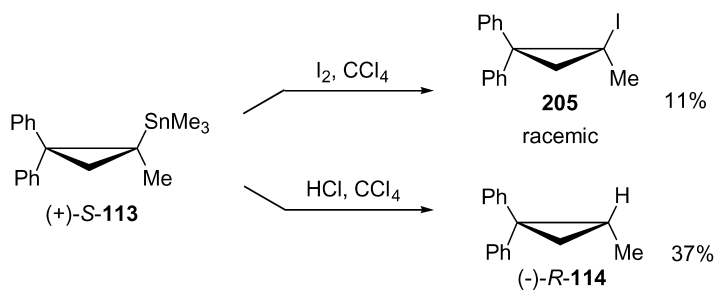
Analogously, Warner demonstrated that treatment of either epimer **48** or **47** with *n*-BuLi at −100 °C followed by MeOD workup provided deuteriodestannylated products with retention of configuration with trace amounts of inverted isomers detected (Scheme 64).[24] However, when lithium derivatives obtained from **48** or **47** were allowed to warm up to −78 °C prior to MeOD quenching, mixtures of several products with variable ratios, depending upon reaction time, were obtained. It was proposed that irreversible isomerization of **45** into **46** takes place at this temperature thereby providing mixtures of *syn*- and *anti*-isomers along with some amounts of dimeric products (Scheme 64).[24]

Likewise, lithium derivatives **200** and **202**, obtained from stannanes **199** and **191**, respectively, displayed different stability when allowed to warm up from −95 to −78 °C (Scheme 65).[92] Under these conditions, **200** provided single product **201**, whereas **202** produced, depending on reaction time, up to five main products. The results of these experiments confirmed that, although being relatively slow, the isomerization **202** to **200** takes place; however, its mechanism is unclear. These results are in accord with those obtained on the unsaturated series (see above).

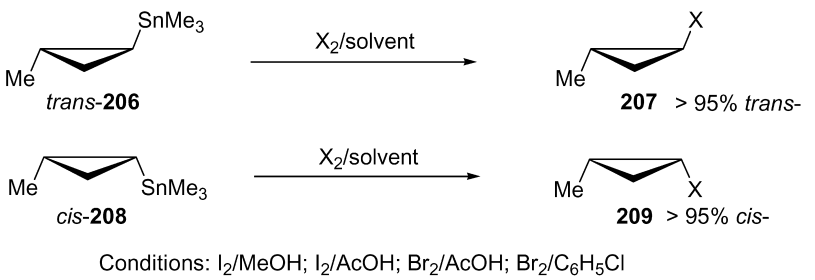
3.1.2. Tin–halogen exchange reactions. While tin–lithium exchange of cyclopropylstannanes proceeded with complete retention of configuration, regardless of the substitution pattern, a dramatic difference was observed in the stereochemical outcome of the tin–halogen exchange reactions. Thus, when α-unsubstituted cyclopropylstannanes provided corresponding halogenated products with complete retention of configuration at the reaction center, the α-substituted analogs normally led to racemic products. It was proposed that these two types of cyclopropylstannanes undergo tin–halogen exchange via different mechanisms. An ionic pathway via a four-centered transition state **203** leading to retention of configuration was proposed for α-unsubstituted substrates (Scheme 66). Formation of tertiary radical species of type **204**, capable to undergo epimerization leading to racemic mixtures, was suggested for reaction involving α-substituted analogs. While the former pathway was supported experimentally, no studies were performed to confirm the latter pathway.

First experiments on tin–halogen exchange were performed by Sisido in 1967.[74] The authors observed complete racemization when optically active **113** was subjected to iodine in carbon tetrachloride (Scheme 67). Reaction of **113** with hydrogen chloride, however, resulted in formation of protiodestannylated product **114** with complete retention of configuration. Homolytic cleavage of the tin–carbon bond and formation of configurationally unstable cyclopropyl radical species were proposed to account for racemization observed for the iodination reaction. Protiodestannylation of **113** was believed to proceed via an ionic mechanism.[74]

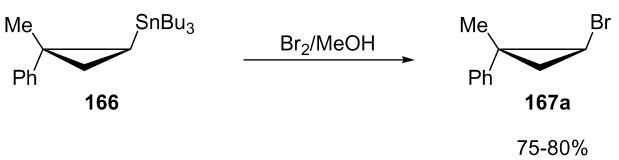
Shortly after Sisido's report, Baekelmans published his results on tin–halogen exchange using geminally unsubstituted *trans*- and *cis*-cyclopropylstannanes **206** and **208** (Scheme 68).[93,94] Both reactions proceeded with retention of configuration regardless of the solvent or



Scheme 67.



Scheme 68.

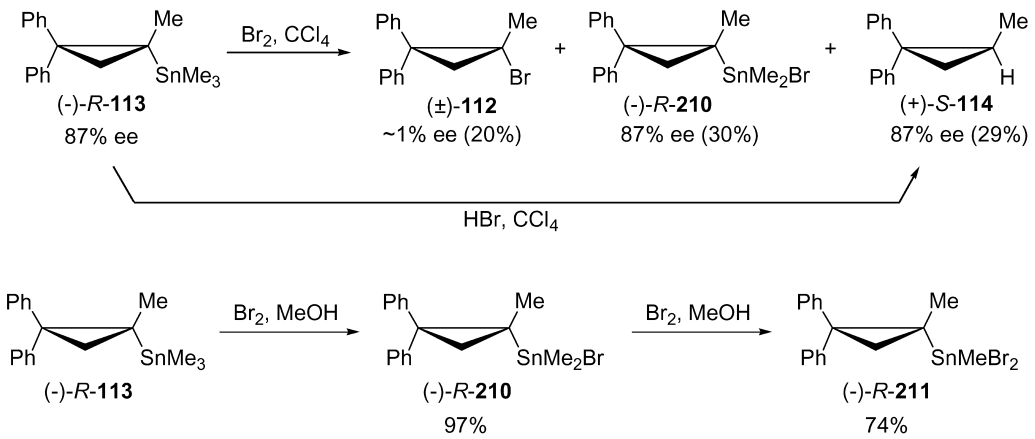


Scheme 69.

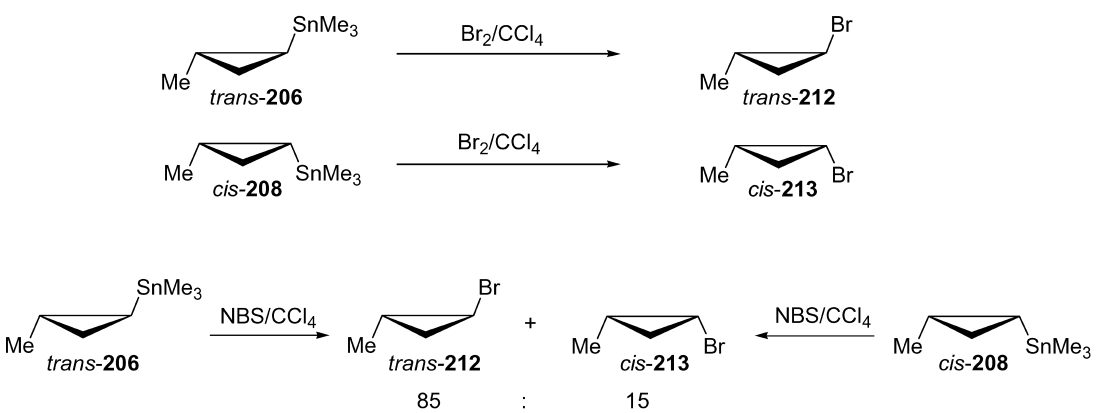
halogen source used. However, a dramatic solvent effect on the rate of halodemetalation was observed; the reaction proceeded very quickly in chlorobenzene, and considerably slower in methanol.

Analogously, the tributyltin group in trisubstituted **166** smoothly underwent tin–bromine exchange upon treatment with bromine in methanol to produce bromocyclopropane **167a** with complete retention of configuration (Scheme 69).[88]

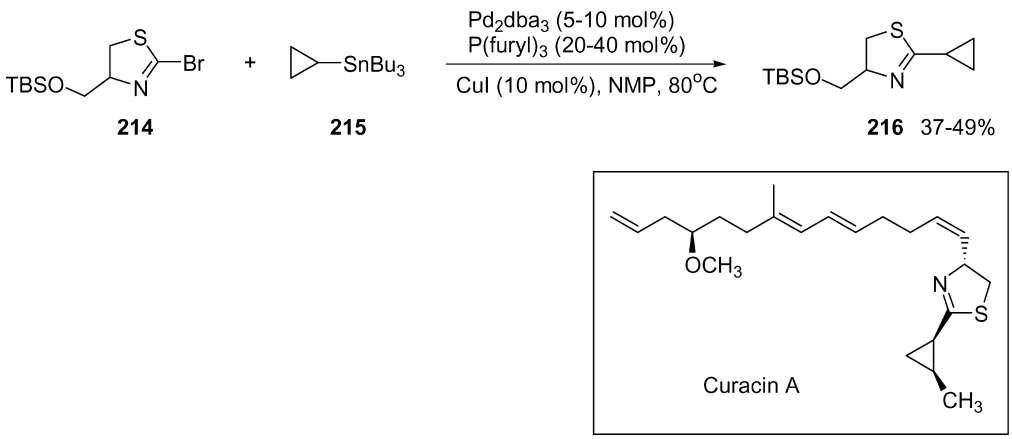
Baekelmans' results prompted Sisido to reinvestigate the halodestannylation reaction of **113** (Scheme 70).[75] Again, treatment of **113** with bromine in carbon tetrachloride resulted in racemic product **112** along with bromodimethylcyclopropylstannane **210** and protiodestannylated product **114**; formation of the latter resulted from the reaction of **113** with HBr, formed in situ. When the reaction of **113** with bromine was carried out in methanol, a selective cleavage of the tin–methyl bond occurred to produce **210** in nearly quantitative yield. Treatment of **113** with two equivalents of bromine resulted in exchange of an additional methyl group with bromine to give **211**. No racemization occurred during these transformations.



Scheme 70.



Scheme 71.

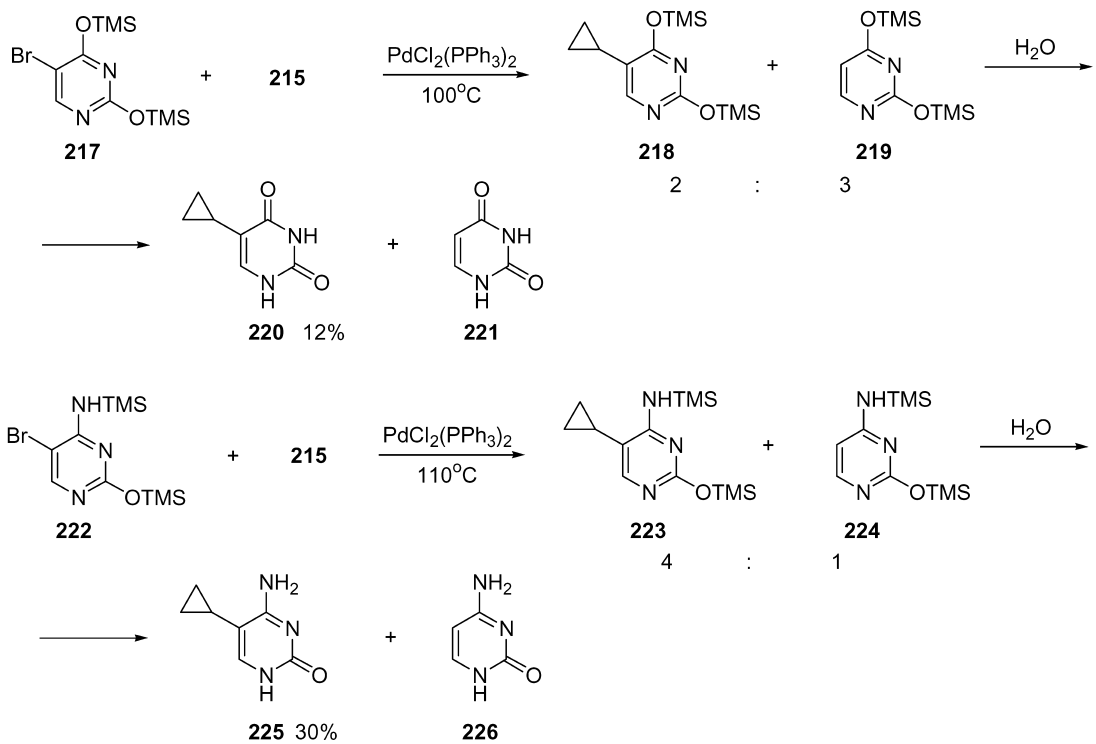


Scheme 72.

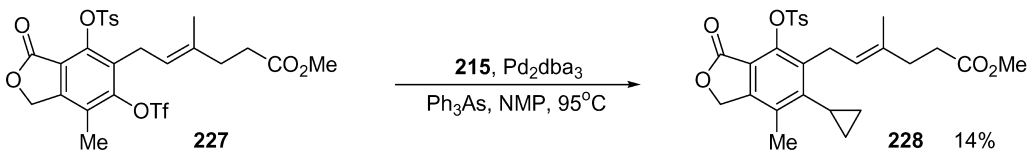
However, in the analogous reaction with geminally unsubstituted cyclopropyl derivatives **206** and **208** under the same reaction conditions, complete retention of configuration was observed (Scheme 71).[95] Sisido speculated that formation of a stable, tertiary cyclopropyl radical in case of **113** favored a radical pathway via intermediate **204**, whereas **206** and **208** reacted via a four-centered transition state **203** (Scheme 66). Under conditions of radical brominolysis (NBS, AIBN), a 85:15 mixture of *trans*-**212** and *cis*-**213** was produced regardless on whether *cis*-**208** or *trans*-**206** were employed (Scheme 71).

3.1.3. Cross-coupling reactions. Introduction of cyclopropyl moiety via the Pd-catalyzed cross-coupling reaction of cyclopropylstannanes with electrophilic counterparts potentially can serve as a very attractive approach to synthesis of complex cyclopropane-containing molecules. Although a number of reports document attempts on Stille cross-coupling reactions of cyclopropylstannanes with different halides and triflates, unfortunately, most of the known examples provide unsatisfactory low yields of the coupling products. In contrast to cyclopropylboronate analogs, which are well-known to readily undergo Suzuki cross-coupling reaction,[96] cyclopropylstannanes display very poor reactivity primarily as a result of sluggish transmetalation of a weakly nucleophilic cyclopropyltin moiety.

Thus, in studies toward Curacin A, Romo investigated the possibility of installing a cyclopropyl moiety in thiazoline ring using Stille cross-coupling reaction (Scheme 72).[97] Under standard Stille coupling conditions 2-cyclopropylthiazoline **216** was obtained as an inseparable mixture with pyrroline (~4:1) in low yield. Addition of copper iodide allowed for increasing yields of reactions and



Scheme 73.



Scheme 74.

improving selectivity providing **216** in moderate yields (Scheme 72).

Cyclopropyluracil **220** and cyclopropylcytosine **225** were prepared by Stille coupling of pyrimidine **217** and trimethylcytosine **222** with tributylstannylcyclopropane **215** (Scheme 73). Both reactions provided low yields of desired cyclopropane derivatives **220** (12%) and **225** (30%), and were accompanied by formation of substantial amounts of dehalogenated by-products **221** and **226**, respectively.[98]

The coupling of triflate **227** with tributylstannylcyclopropane provided poor results despite the use of a labile triphenylarsine ligand (Scheme 74). Apart from slow transmetalation at cyclopropyltin, the significant steric bulk created by two *ortho*-substituents at the aryl ring may also impede the oxidative addition step in this reaction, thus additionally accounting for the very low yield of coupling product **228**.[99]

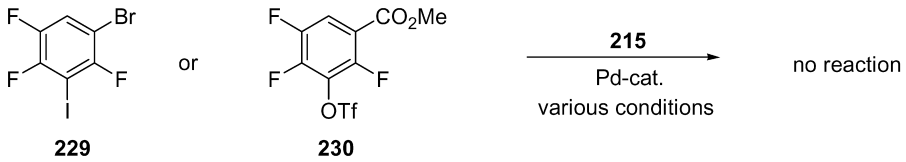
Cross-coupling of neat tributylstannylcyclopropane with very electron poor aryl iodide **229** under various conditions was unsuccessful (Scheme 75).[100] Reaction of **229** with tetracyclopropylstannane **39** was also unsuccessful with a series of different solvents and palladium catalysts. Attempted cross-coupling with triflate **230** led to the triflate cleavage to form the corresponding phenol only.

Cross-coupling reaction of triflate **231** with **215** also proved inefficient; harsh reaction conditions as well as a complicated isolation procedure allowed for synthesis of coupling product **232** in trace amounts only (Scheme 76).[101]

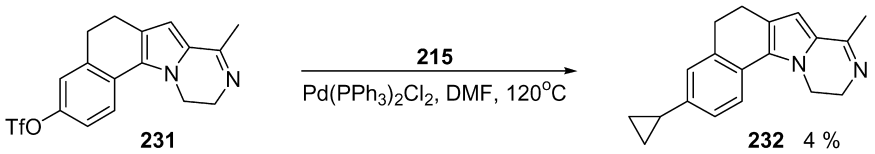
While Stille cross-coupling reaction on cyclopropylstannanes normally provides poor yields or no product at all, the oxidative homocoupling of two cyclopropyltin derivatives appeared to be a much more efficient method, as demonstrated by Itoh.[37] Conditions, originally reported by Liebeskind for the palladium-catalyzed oxidative dimerization of stannylquinones,[102] were successfully applied for coupling of **233** furnishing the corresponding bis-cyclopropane **234** in 66% yield (Scheme 77).

3.1.4. Miscellaneous. Addition of dihalocarbenes to 2-trimethylstannyl methylenecyclopropane **12** occurs stereospecifically from the less hindered site to form *anti*-**235** as a single product (Scheme 78).[6] However, addition of dichlorocarbene to methylenecyclopropane **237** bearing bulky cyclopropyl substituents at the double bond produces a mixture of *syn*- and *anti*-products **238** and **239**, respectively, with the *anti*-isomer being a major component.[103] Interestingly, with other substituents in place of the trimethyltin group in **237** (i.e., TMS, Br, alkyl) the reaction was completely stereospecific, affording the corresponding *anti*-product only. These results are explained by the greater length of the C–Sn bond, which makes the steric effect of this substituent less pronounced.

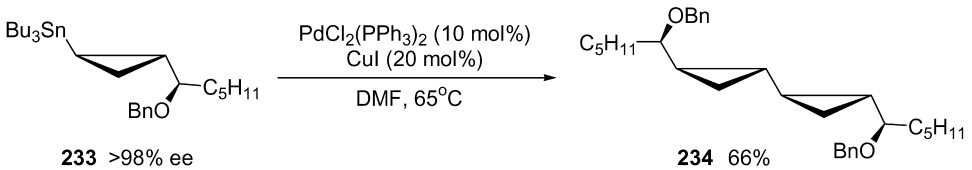
In the [2+2] cycloaddition reaction of dichloroketene with **240**, formation of more hindered isomer **242** was observed



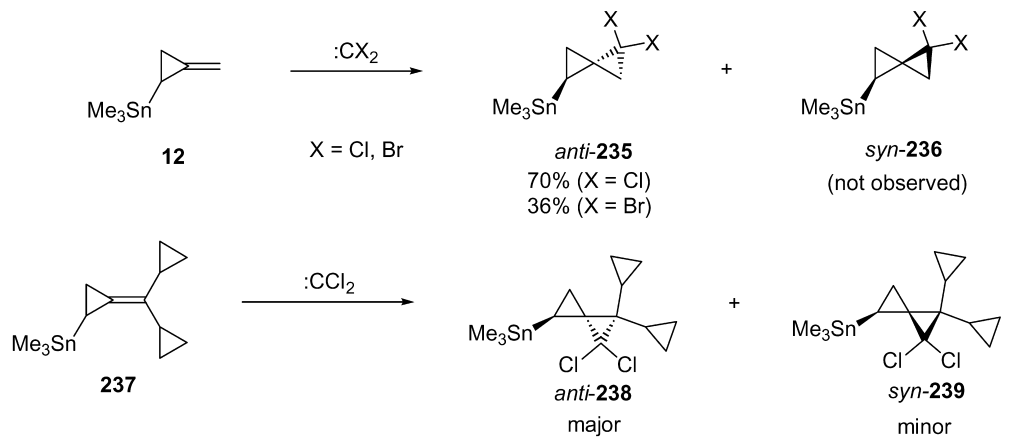
Scheme 75.



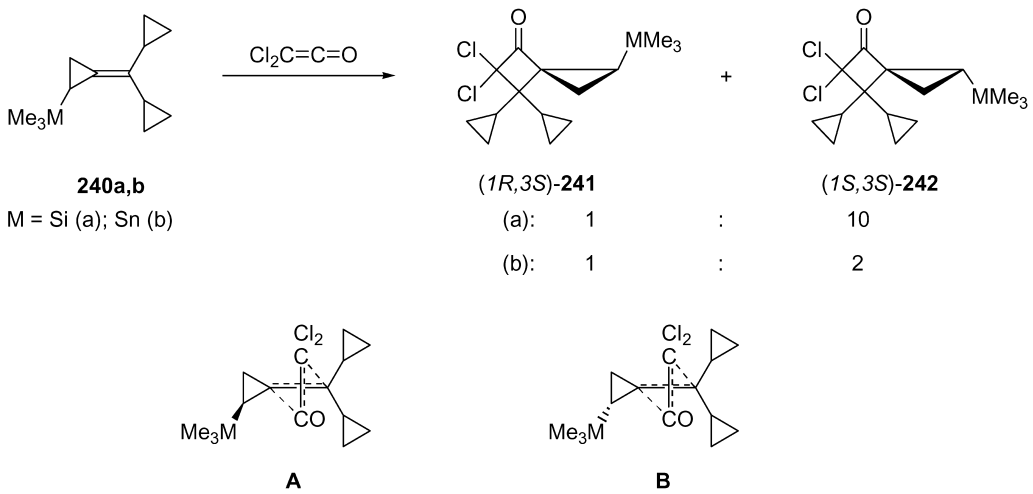
Scheme 76.



Scheme 77.



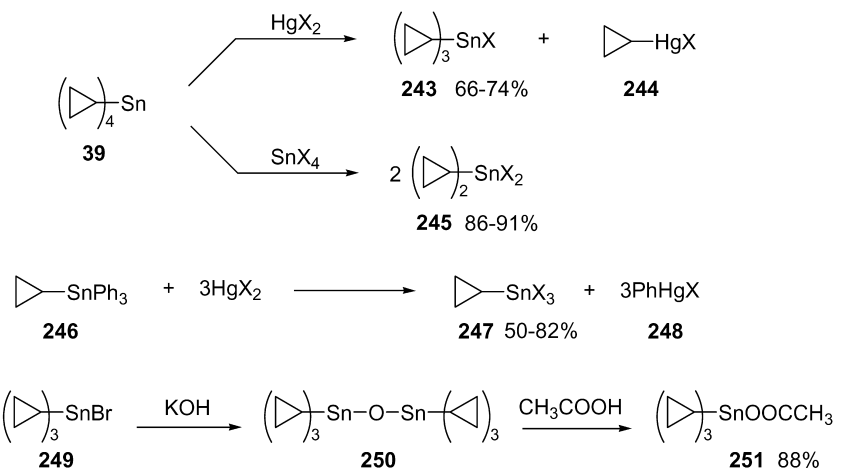
Scheme 78.



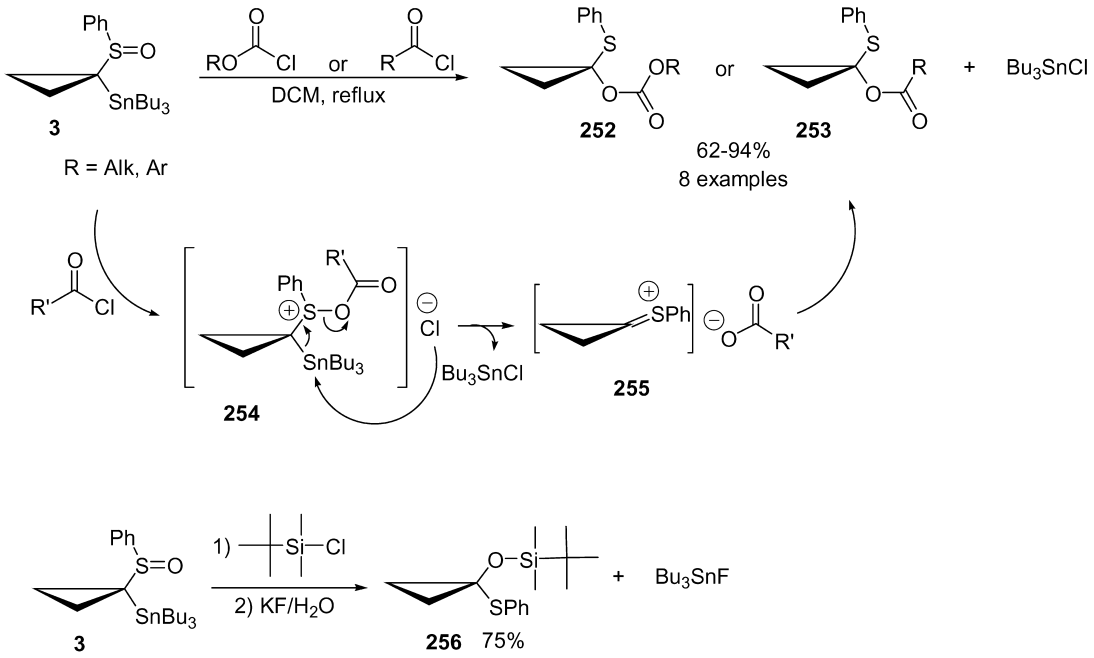
Scheme 79.

in case of both trimethylsilyl and trimethylstannyl substituents (Scheme 79). As expected,[104] such stereoselectivity is a result of a more favorable transition state **B**, in which dichloroketene is approaching from the face opposite to that occupied by a bulky substituent. Relatively strong steric control observed for **240a** deteriorated in the case of tin analog **240b**, which again is attributed to the greater length of the carbon–tin bond as compared to that for the carbon–silicon bond.[105]

Seyferth demonstrated that tetracyclopropyltin **39** can undergo disproportionation reactions with mercury or tin halides to produce corresponding cyclopropylmercuric **244** and -tin chlorides **243** and **245**, respectively (Scheme 80).[106]



Scheme 80.



Scheme 81.

The reaction with **246** confirms that phenyl group is cleaved from tin much more readily than is the cyclopropyl group. Tricyclopropyltin acetate **251** was obtained in 88% yield by the reaction of **249** with potassium hydroxide followed by treatment with glacial acetic acid (Scheme 80).

Pohmakotr reported the destannylative Pummerer-type rearrangement of 1-phenylsulfinyl-1-tributylstannylcyclopropane **3** (Scheme 81).[29,107] The reaction proceeds analogously to the previously reported rearrangement of α-silyl substituted cyclopropylsulfoxides[108] and allows for good to high yields of acyl derivatives **252** or **253**. The mechanism of this reaction involves acylation of α-stannyl sulfoxide to form acylsulfoxonium species **254** followed by the attack of chloride ion at the tin moiety, providing thionium salt **255**. The recombination of the thionium ion with the carboxylate gives products **252** or **253**. Following essentially the same pathway, α-siloxycyclopropane **256** was obtained from **3** in the presence of TBDMS-Cl in 75% yield (Scheme 81).

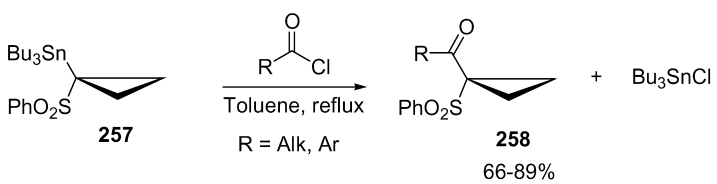
Acyldestannylation of α-stannylsulfone **257** proceeded smoothly in refluxing toluene affording 1-acyl-1-sulfonylcyclopropanes **258** (Scheme 82).[4] While acyl chlorides provided good yields of the corresponding products, the less reactive chloroformates did not undergo this transformation at all.

3.2. Reactions involving opening of the cyclopropyl ring

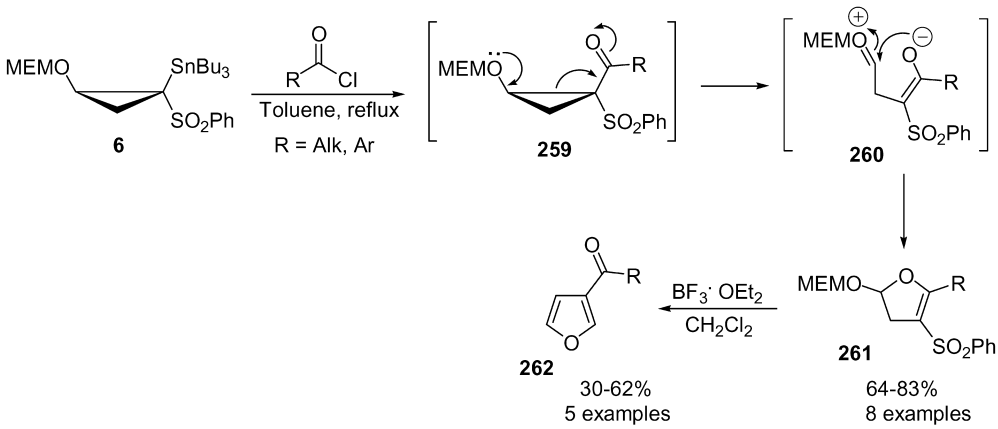
3.2.1. Ring opening reactions involving ionic intermediates. Destannylative acylation of MEM-protected cyclopropanol **6** followed by a facile ring opening of the resulting 1,2-donor–acceptor substituted cyclopropane **259** and subsequent cyclization of zwitterionic intermediate **260**, provided good yields of dihydrofurans **261** (Scheme 83).[3] Treatment of the latter with BF_3–OEt_2 resulted in the formation of furans **262** in moderate yields.

In the synthesis of series of stannylated troponoids, Banwell applied a modified Swern oxidation protocol (with trifluoroacetic anhydride, TFAA) to dihydroxynorcaranes **263** and **267** (Scheme 84).[18] Under these conditions, significant amounts of bicyclic hydroxyenones **265** and **268** were obtained. However, prolonged reaction times or excess of oxidant effected ring expansion/dehydrobromination of the intermediate hydroxyenones leading to troponoids **264** and **269**, respectively. Alternatively, methylation of **265** with dimethylsulfate followed by treatment with 1,8-diazabicyclo[5.4.0]undec-5-ene (DBU) afforded tropolone **266** in good yield (Scheme 84).

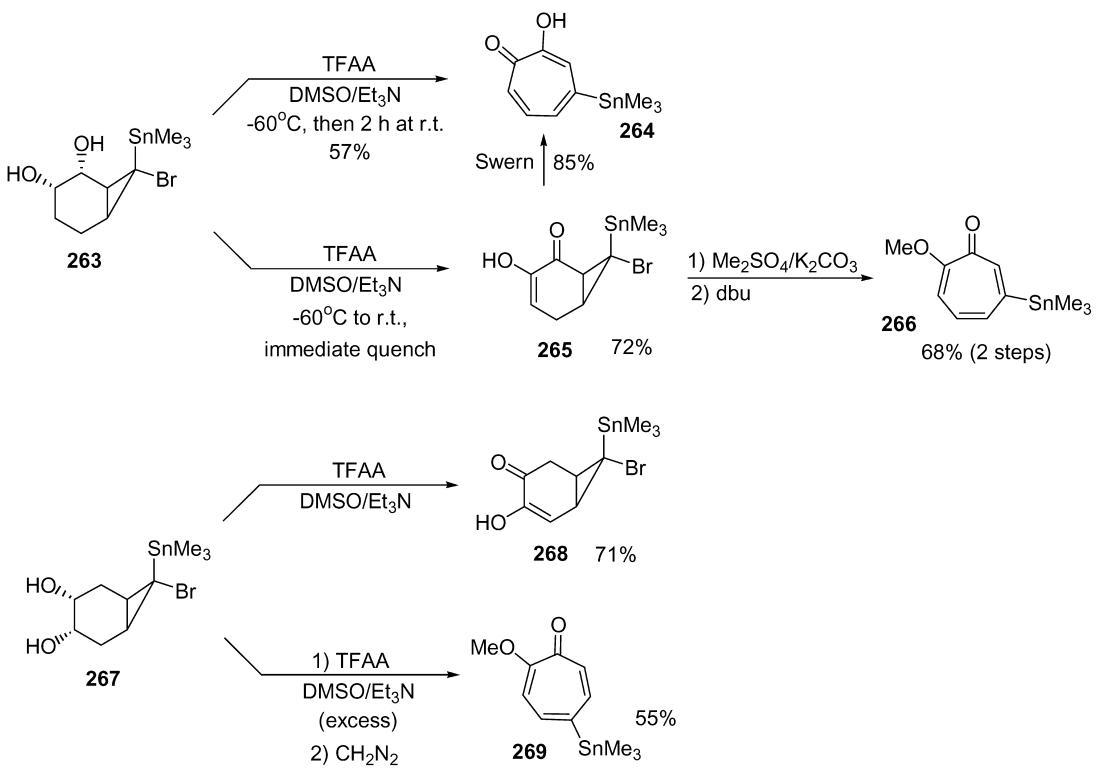
Synthesis of 3-stannyltropolone **273** was achieved by subjecting **270** to allylic oxidation conditions with chromium trioxide–3,5-dimethylpyrazole (3,5-dmp) complex, which provided enone **271** accompanied with trace



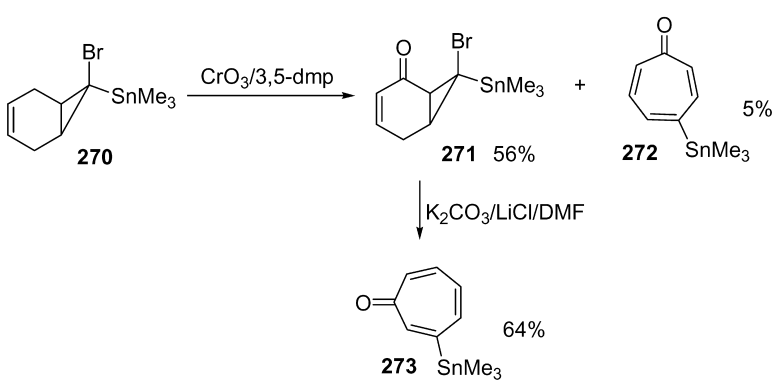
Scheme 82.



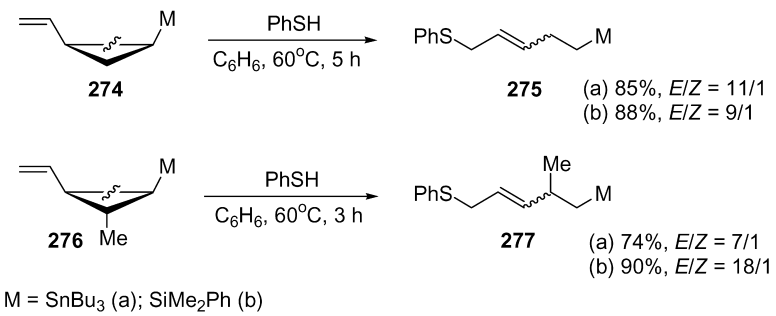
Scheme 83.



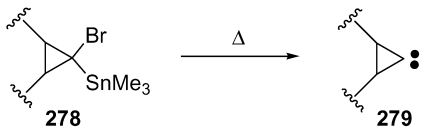
Scheme 84.



Scheme 85.



Scheme 86.



Scheme 87.

amount of tropolone **272** (Scheme 85). While treatment of **271** with DBU failed to provide any isolable products, reaction of this substrate with potassium carbonate and lithium chloride in DMF resulted in dehydrobrominative ring expansion to give **273** in 64% yield. It was pointed out that the use of either isomer (with *syn* or *anti* orientation of bromine) did not affect the reaction course. The resulting stannylated tropolones were successfully employed in further transformations including Stille cross-coupling reactions with aryl halides and in electrophilic substitution reactions.[18]

3.2.2. Radical-initiated ring opening. Radical-induced ring opening reactions of trialkylsilyl- and tributylstannyl-cyclopropanes **274** and **276** were investigated by Oshima and Utimoto (Scheme 86).[39] Both silicon and tin analogs provided homoallylic silanes or stannanes, respectively. A selective cleavage of the proximal bond occurred in this reaction, regardless of the metal and substitution pattern at cyclopropanes, which can be explained by a formation of the more stable α-stannyl or α-silyl radicals. In all cases predominant formation of the thermodynamically more favorable *E*-olefin was observed.

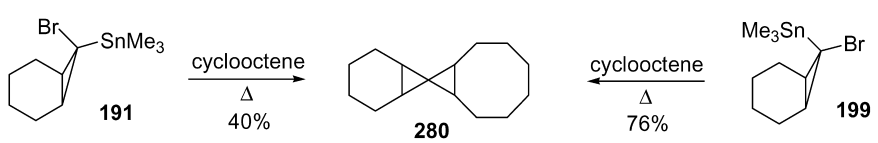
3.2.3. Ring opening via α-elimination. Seyferth and Lambert first proposed that α-halocyclopropylstannanes **278** can undergo thermolysis, potentially, via formation of cyclopropylidene **279** (Scheme 87).[109] Although most α-halocyclopropylstannanes tested underwent ring-opening reactions providing allenes, norcaranes **191** and **199** produced insertion products of putative carbene species of type **279**.

Thus, the reaction with pure *syn*-isomer **199** in refluxing cyclooctene afforded after 6 h tetracyclic product **280** in 76% yield, while 40% of **280** only was produced from the *anti*-isomer **191** after 23 h (Scheme 88).

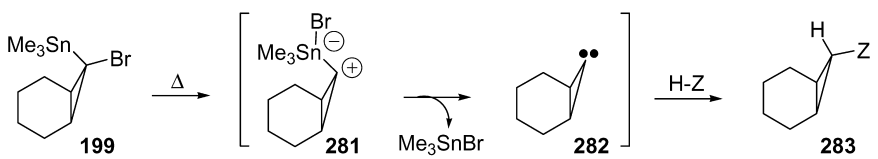
Having obtained some data supporting formation of cyclopropylidene **279**, the authors, however, stated that the exact mechanism of α-elimination was unclear, as there remained a number of uncertainties, such as different reactivity of *syn*- and *anti*-isomers and irreversible decomposition of only one, less reactive *anti*-isomer **191**.[109]

Mechanistic studies on the thermolysis of **191** and **199**, performed later by Warner,[20] suggested that the more reactive **199** decomposes via initial C–Br heterolysis to give an ylide **281**, which upon loss of Me_3SnBr produces norcaranylidene **282**, which then undergoes addition/insertion reactions (Scheme 89). In contrast, thermolysis of less reactive **191** proceeds primarily or solely via an ionic, non-carbenic process, similar to that shown for unsaturated analog **47** (see below).

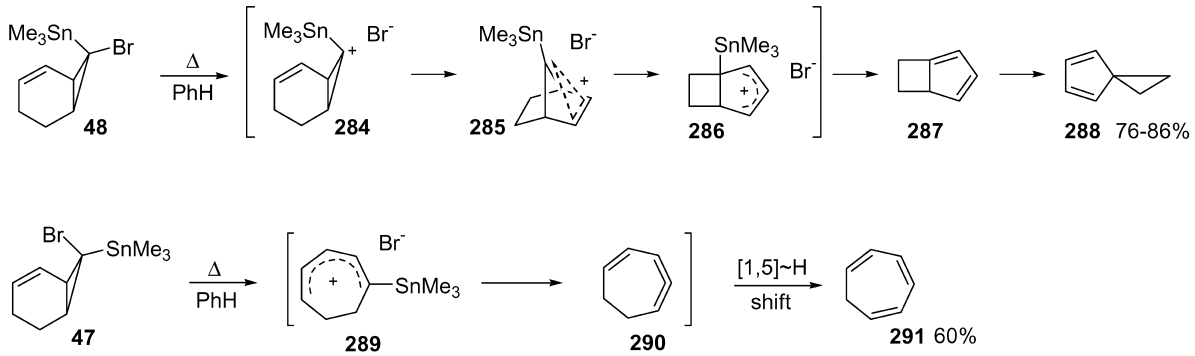
Warner further demonstrated that both isomeric norcarenes **48** and **47** undergo α-elimination, most likely, via ionization rather than via the formation of cyclopropylidene species.[110] He found that pyrolysis of norcarene **48**, carried out at temperatures of 100–160 °C, produced good yields of spirodiene **288**, presumably, via a Scattebol-type



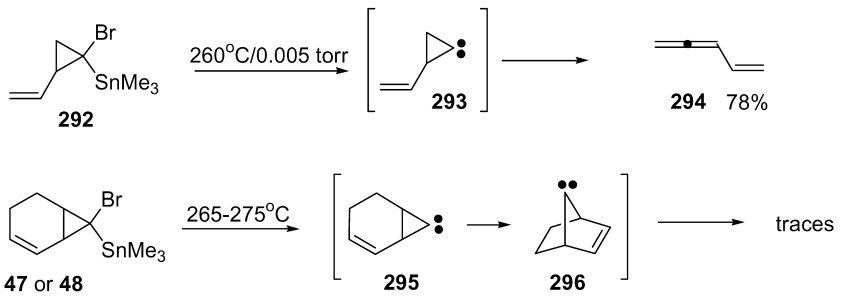
Scheme 88.



Scheme 89.



Scheme 90.



Scheme 91.

rearrangement.[111] Similar treatment of **47** afforded, via facile ionization of *syn*-oriented halogen and subsequent ring-opening, cycloheptatriene **291** accompanied by dimers and trimers of cyclic allene **290** (Scheme 90).[110]

Brinker employed flash vacuum pyrolysis to generate carbene species from α-bromocyclopropylstannane **292** and a norcarene of unknown configuration (**47** or **48**) (Scheme 91).[21] It was found that thermal decomposition of vinylcyclopropane **292**, carried out at 260 °C, afforded vinyl allene **294** in 78% yield, accompanied by traces of isomeric enynes. In contrast, pyrolysis of the parent norcarene (**47** or **48**) proved unsuccessful. The high temperatures required for the decomposition of the latter appeared to be a major problem of this reaction (Scheme 91).[21]

4. Conclusion

Cyclopropylstannanes, versatile building blocks, have found numerous applications in synthetic organic chemistry. Being convenient, rather reactive yet stable synthons, cyclopropylstannanes allow for easy incorporation of a three-membered unit into more complex molecules via tin–lithium exchange combined with a variety of coupling protocols. Furthermore, as discussed above, the tin moiety in cyclopropylstannanes can be readily replaced with a broad range of functional groups with preservation of configuration. Cyclopropylstannanes are also suitable substrates for a number of transformations involving ring expansions. Not surprisingly, development of synthetic methods towards cyclopropylstannanes has attracted a great deal of attention from the synthetic community. Numerous approaches including well-established cyclopropanation procedures as well as functional group transformations at cyclopropyl precursors have been successfully employed for the preparation of cyclopropylstannanes. With new methods being developed, the chemistry of cyclopropylstannanes will continue to fuel future synthetic applications and will open new opportunities for synthetic organic chemistry.

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Biographical sketch

Marina Rubina was born in Syktyvkar, Russia in 1974. She received her BSc from Syktyvkar State University in 1996. She spent 4 years (1995–1999) at The Moscow State University first as an undergraduate researcher and then as a graduate student. Marina is currently a graduate student in Professor Gevorgyan's group at The University of Illinois at Chicago. She is a recipient of the University of Illinois Graduate Fellowship (AY 2002–2003). Her graduate research is focused on the development of new catalytic transformations involving cyclopropenes and investigation of the Pd-catalyzed benzannulation reaction.

Vladimir Gevorgyan was born in Krasnodar, Russia in 1956. He received his BSc from Kuban State University in 1978 and his PhD from the Latvian Institute of Organic Synthesis in 1984, where he was promoted to Group Leader in 1986. He spent 2 years (1992–1994) in Tohoku University in Sendai, Japan, first as a JSPS Postdoctoral Fellow and then as a Ciba-Geigy International Postdoctoral Fellow. In the following year (1995), he worked as a Visiting Professor at CNR, Bologna, Italy. He returned to Tohoku University in 1996 as an Assistant Professor and was promoted to Associate Professor in 1997. In 1999, he moved to The University of Illinois at Chicago as an Associate Professor. He was promoted to the rank of Full Professor in 2003. Professor Gevorgyan's current research interests cover four main areas. The first is concerned with development of highly selective Pd-catalyzed benzannulation reactions. The second area of interest focuses on development of novel transition metal-catalyzed methods for the synthesis of heterocyclic and naturally occurring compounds. The third area of interest covers the development of selective Lewis acid-catalyzed bond formation and cleavage reactions. The fourth deals with the chemistry of strained ring systems.