New Strategies for the Synthesis of Carbocycles Based on Transition Metal Catalyzed Cyclization Reactions of Organostannanes and Organosilanes

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Intramolecular reactions between organosilanes or organostannanes and (η^3-allyl)palladium complexes give rise to a variety of functionalized carbocycles. Conceptually related cyclizations catalyzed by Pd^{II} (or a related electrophilic metal) proceed by coordination of a 1,3-diene or alkyne with the electrophilic metal, followed by nucleophilic attack by the allylsilane or allylstannane.

Introduction

Nucleophilic attack on unsaturated organic functional groups under catalytic conditions is one of the most attractive transformations based on the organometallic chemistry of the transition metals.[1] From the synthetic chemist's point of view, nucleophilic attack onto alkenes, alkynes, dienes, and arenes is particularly attractive, since it allows for the inversion of the normal reactivity of these functional groups and offers new opportunities for the construction of complex molecules by novel pathways.

The objective of this review is to summarize the formation of carbocycles by intramolecular reaction of stannanes and silanes with allyl derivatives, dienes, and alkynes (Scheme 1). The carbocyclizations covered here comprise conceptually related processes, in which, formally, the nucleophile attacks an electrophilic ligand coordinated to the transition metal.[2] In terms of the catalyst, however, it may be convenient to differentiate two classes of processes. Thus, the intramolecular palladium-catalyzed coupling of alkenyl and allyl nucleophiles **I** and **II** to give cycles **III** and **IV** (reactions 1 and 2) are based on a Pd^0 catalyst and proceed by intramolecular attack of the soft nucleophilic reagent onto an intermediate (η^3-allyl)palladium complex. Cyclizations of **V** and **VI** to carbocycles **VII** and **III** (reactions 3 and 4), on the other hand, are catalyzed by Pd^{II} or a related electrophilic metal. In these cases, coordination of the 1,3-diene or alkyne functions with the electrophilic metal triggers the nucleophilic attack by the allyl nucleophile. Intermolecular couplings of allyl electrophiles with organostan-

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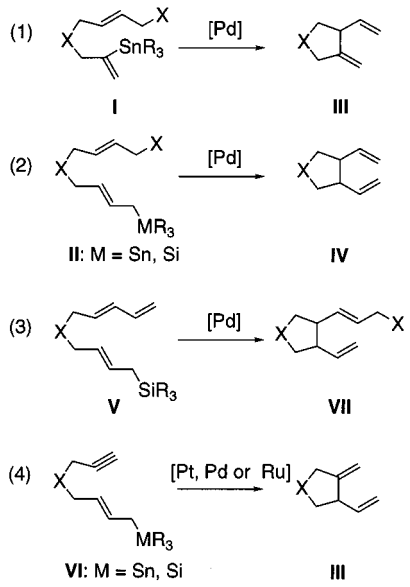
nanes via (η^3-allyl)palladium complexes, which are key for the development of processes 1 and 2 in Scheme 1, are also discussed. The intramolecular reactions of aryl iodides with allylsilanes, however, are not covered in this review,[3,4] since these processes do not proceed through nucleophilic attack onto an unsaturated ligand. Mechanistically, these reactions are based on the insertion of an (aryl)Pd^{II} complex into the alkene (Heck reaction).[5]



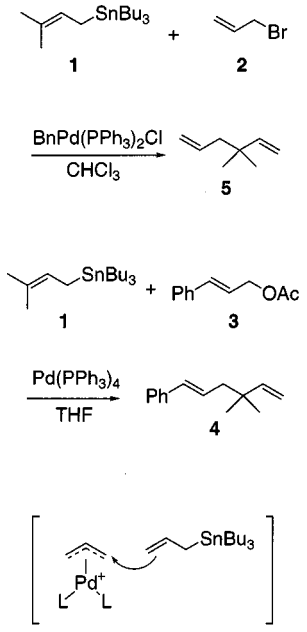
Scheme 1

Reactions of Allyl Carboxylates and Related Electrophiles with Stannanes and Silanes

Intermolecular Coupling of Allyl Carboxylates with Organostannanes

Among the synthetic methods based on the chemistry of transition metals, the Pd^0-catalyzed alkylation of allyl electrophiles is one of the most thoroughly studied transformations.[6,7] Recent theoretical studies of the reactivity of the intermediate (η^3-allyl)palladium complexes have addressed the issue of regioselectivity,[8−10] while most of the mechanistic work has been directed towards the development of enantioselective transformations through the use of a variety of chiral bidentate ligands.[11,12] In most of these studies, the allyl electrophiles were alkylated by malonate-type nucleophiles.[13]

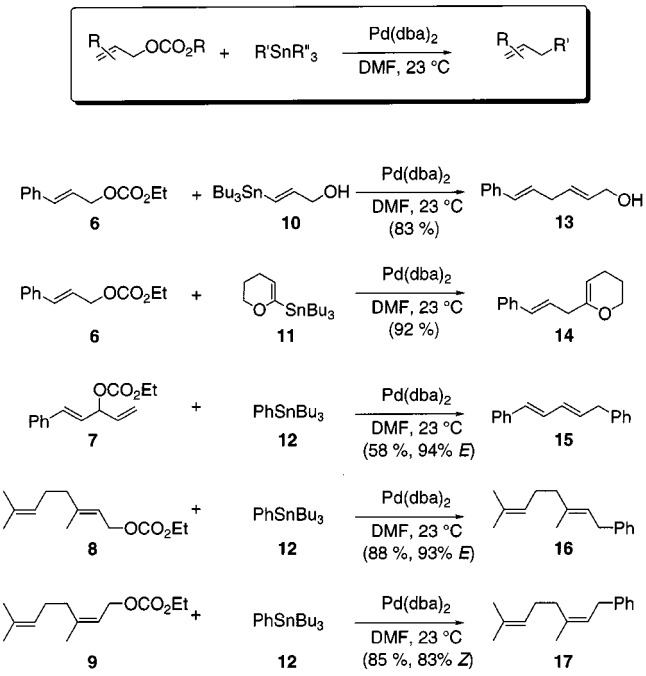
The Pd^0-catalyzed reaction of organostannanes proceeds with a variety of allylic electrophiles.[14] The first reported examples of this reaction used highly reactive allyl halides, which coupled with aryl- and alkenylstannanes under mild conditions through the less substituted terminus of the allyl electrophile.[15,16] The related reaction of allylstannanes such as **1** resulted in the attack of its more substituted terminus on the allyl bromide (**2**)[17] or the allyl acetate (**3**)[18,19] (Scheme 2). Because of this clean allylic inversion on the nucleophilic partner, a direct attack of the stannane on the intermediate (η^3-allyl)palladium complex was proposed as a likely reaction pathway. However, no mechanistic studies of this allyl coupling reaction have been carried out.[20−24]



Scheme 2

More recently, the palladium-catalyzed coupling of allyl acetates with alkenyl and aryl stannanes has been described.[25] Interestingly, the coupling reaction was in this case accomplished with $Pd_2(dba)_3$·dba[26,27] as the catalyst, in DMF in the presence of excess LiCl.[28] Of broader scope is the coupling of allylic carbonates[29,30] with organostannanes (Scheme 3).[31] The allylic carbonates couple under milder conditions and with shorter reaction times than the corresponding acetates, giving rise to the formation of C−C bonds in higher yields. Interestingly, this palladium-catalyzed coupling reaction can even be carried out in water at ambient temperature.

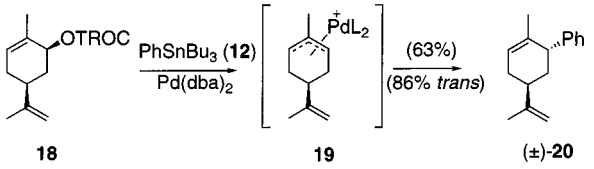
The reaction of allylic carbonates **6**−**9** with alkenyl and aryl stannanes **10**−**12** takes place smoothly in DMF at room temperature with $Pd_2(dba)_3$·dba as the catalyst. Importantly, the use of phosphane-based catalysts failed to give coupled products. The reaction also proceeded well with stannane **10**, bearing an allylic alcohol, to yield a new allylic substrate **13**, which could be elongated further by using the same technique. In most cases the addition of 2−3 equiv. of water proved beneficial in terms of reaction times and/or yields, although this addition of water was not essential. Thus, readily hydrolyzed (dihydropyranyl)stannane **11** was efficiently coupled with carbonate **6** in anhydrous DMF to furnish **14** in excellent yield. Coupling of carbonate **7** with stannane **12** proceeded at the less substituted terminal position, to give conjugated butadiene **15**.[32] The transmetallation of the stannane proceeds at a rate slightly higher than that of the *syn-anti* isomerization of the intermediate (η^3-allyl)palladium complexes. Thus, geranyl carbonate **8** gave (*E*)-**16**, while neryl carbonate **9** preferentially furnished **17**. In these cases, addition of LiCl, which had



Scheme 3

been shown to have a beneficial effect in other coupling reactions,[14] resulted in slower reactions.

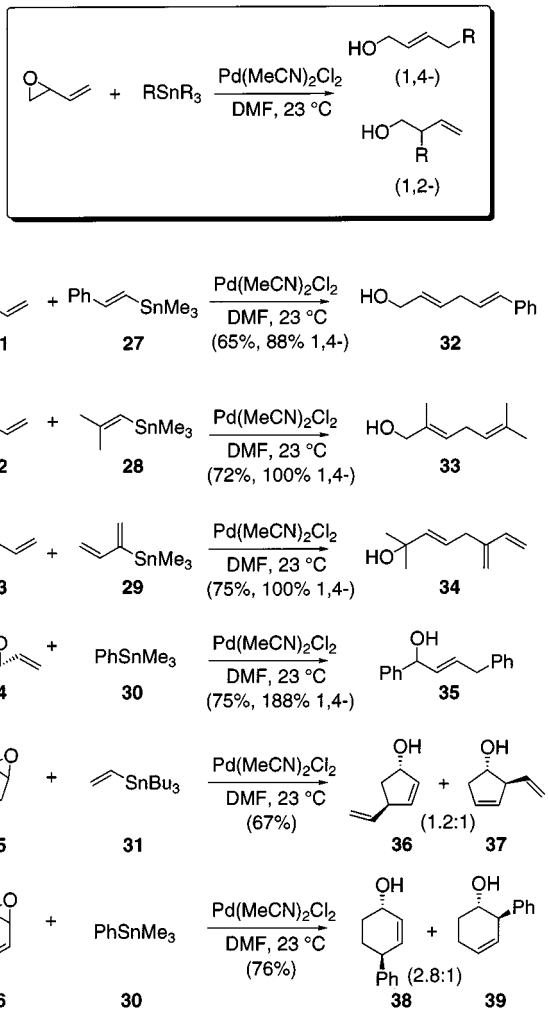
The coupling reaction between the trichloroethyl carbonate of *cis*-carveol (**18**) and stannane **12** afforded *rac-trans*-**20**, as is to be expected for a transmetallation reaction proceeding through a *meso*-(η^3-allyl)palladium intermediate **19** (Scheme 4).[32]



Scheme 4

Coupling of Vinyl Epoxides with Organostannanes

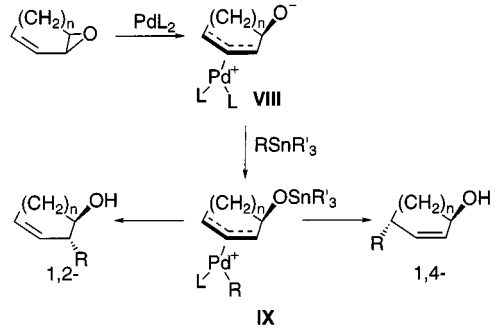
Vinyl epoxides are highly reactive substrates for a variety of palladium-catalyzed transformations. Among the nucleophiles examined, the more general results have been obtained with stabilized enolates.[33−36] In this case, capture of the intermediate (η^3-allyl)palladium complex by the nucleophile should be faster than the competitive rearrangement of this intermediate to form the corresponding ketone.[37] The (η^3-allyl)palladium complexes resulting from ring-opening of the epoxides transmetallate with organostannanes, producing 1,4- and 1,2-addition products (Scheme 5).[28,38] As in the cases of allyl acetates and carbonates, the best catalysts for this coupling were palladium complexes without strongly coordinating ligands. Thus, $Pd(MeCN)Cl_2$ and $Pd_2(dba)_3$·dba gave the best results. The former Pd^{II} complex is undoubtedly reduced by the stannane to form the reactive, "ligandless" Pd^0 species. This



Scheme 5

coupling reaction was also best performed in DMF containing up to 20 equiv. of H_2O.

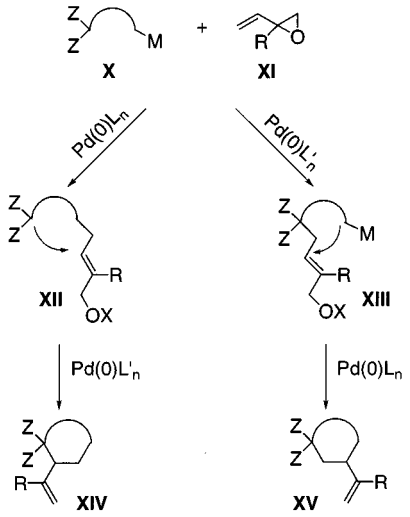
In most cases 1,4-addition products predominate, as a result of the formal attack of the stannane onto the less substituted terminus of the double bond of epoxides **21**−**24**, giving functionalized allyl alcohols **32**−**35** with good yields and regioselectivities (Scheme 5). The coupling of the cyclic epoxides **25** and **26** with stannanes allowed the stereochemistry of the process to be determined. Although mixtures of 1,4- and 1,2-addition products were obtained, the products **36**−**39** were *trans*-configured. This result is consistent with an oxidative addition of the cyclic vinyl epoxide to Pd^0 to form an (η^3-allyl)palladium complex **VIII**, with the oxygen from the epoxide on the ring face opposite to palladium (Scheme 6). Subsequent transmetallation with the organostannane would then furnish complex **IX**, which could reductively eliminate to form 1,4- and 1,2-addition derivatives. Alternatively, the (alkyl)(η^3-allyl)palladium complex **IX** might rearrange to form the regioisomeric (alkyl)(η^1-allyl)palladium complexes prior to reductive elimination.



Scheme 6

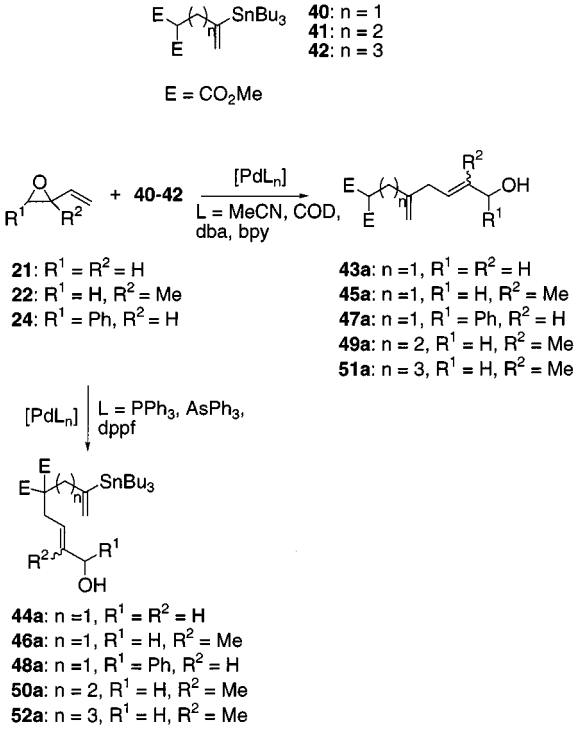
Carbocyclization by Treatment of Vinyl Epoxides with Palladium-Switchable Bis(nucleophiles)

Since reactions between stabilized enolates and vinyl epoxides are carried out in the presence of palladium complexes with phosphane ligands,[33,34] bis(nucleophiles) of type **X** bearing a malonate (Z = CO_2R) or a related C−H-activating group and an organostannane (M = SnR_3) might react with vinyl epoxides **XI** in the absence of phosphane ligands to give **XII** (X = H) (Scheme 7). Alternatively, alkylation of an (η^3-allyl)(phosphane)palladium complex derived from the vinyl epoxide **XI** would form the allylic alcohol **XIII** (X = H). The desired chemoselective activation of the palladium-switchable bis(nucleophiles) **VIII** was therefore expected to be achievable through use of palladium catalysts with the appropriate ligands. Allylic alcohols **XII** and **XIII** could be activated by acylation (X = COR or CO_2R) and then subjected to a second palladium-catalyzed alkylation or transmetallation (Scheme 7).[39]



Scheme 7

Crucial for the success of the strategy outlined in Scheme 7 was the question of the chemoselective reaction of the intermediate (η^3-allyl)palladium complex with bis(nucleophiles) such as **40**−**42**, bearing malonate and alkenylstannane functions. In analogy with the situation found for the palladium-catalyzed coupling of allyl carbonates with stannanes,[31] palladium complexes without strongly coordinating ligands such as MeCN, COD, or dba favored Pd/Sn transmetallation products of type **XII** (Scheme 7). The optimum conditions were obtained by using $Pd(MeCN)_2Cl_2$ as the catalyst, which furnished coupled products in good yields (Scheme 8 and Table 1, odd-numbered Entries). On the other hand, when $Pd_2(dba)_3$·dba and 2 equiv. of PPh_3 was used as the catalyst, alkylated products were obtained (Table 1, even-numbered Entries). The reaction proceeded with complete chemoselectivity in all cases.



Scheme 8

Table 1. Reactions between stannanes **40**−**42** and diene epoxides **21**, **22**, and **24** (Scheme 8)

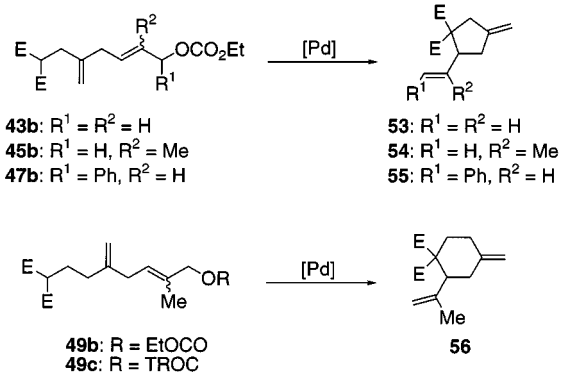
Entry[a]	Bis(nucleophile)	Epoxide	Catalyst[b]	Product	Yield [%]
1	**40**	**21**	A	**43a**	69
2	**40**	**21**	B	**44a**	60
3	**40**	**22**	A	**45a**	93
4	**40**	**22**	B	**46a**	92
3	**40**	**24**	A	**47a**	75
4	**40**	**24**	B	**48a**	64
5	**41**	**22**	A	**49a**	71
6	**41**	**22**	B	**50a**	66
7	**42**	**22**	A	**51a**	72
8	**42**	**22**	B	**52a**	81

[a] The reactions were run in DMF at 23 °C in the presence of 10−20 mol equiv. of H_2O at ca. 0.1 M in substrate. − [b] Method A: $Pd(MeCN)_2Cl_2$ (5 mol %), Method B: $Pd(dba)_3$·dba (2.5mol %)/PPh_3 (10 mol %).

From these results it is clear that phosphane ligands do not promote Pd^{II}/Sn transmetallation, presumably because

they reduce the electrophilicity of the (η^3-allyl)palladium complexes, thus favoring the nucleophilic attack of the malonate-type anion. On the other hand, MeCN, DMF, COD, and dba give intermediate (η^3-allyl)palladium complexes that are highly electrophilic and undergo clean transmetallation with the organostannane to yield coupled products.[40] While addition of water (10−20 mol equiv.) gave improved results, its role in the mechanism of the nucleophilic attack of the malonate and the transmetallation of the organostannane is not clear, although it might facilitate the transmetallation process.[40]

Allyl carbonates have commonly been used as reactive substrates in palladium-catalyzed allylic alkylations by malonate-type nucleophiles.[29,30] These reactions can be carried out under neutral conditions, since the leaving group decarboxylates to generate the alkoxide in situ, and this acts as the base to form the desired enolate from the malonate-type substrate.[29,30] Therefore, for the synthesis of carbocycles **XIV** (Scheme 7), substrates **XII** were first activated by formation of the corresponding ethyl or trichloroethyl (TROC) carbonates. Cyclization of ethyl carbonates **43b**, **45b**, and **47b** was best carried out by using the catalyst $Pd(dba)(PPh_3)_2$, prepared in situ at room temperature in DMF containing 2 equiv. of water, to give carbocycles **53**−**55** in satisfactory yields (Scheme 9 and Table 2). Cyclization of ethyl carbonate **49b**, however, failed to proceed under the standard conditions. Use of TROC derivative **49c** allowed for the preparation of the six-membered ring carbocycle **56** (Table 2, Entry 4). However, neither ethyl nor TROC carbonates of allyl alcohol **51a** afforded the expected seven-membered ring carbocycle, giving elimination products instead.[41]



Scheme 9

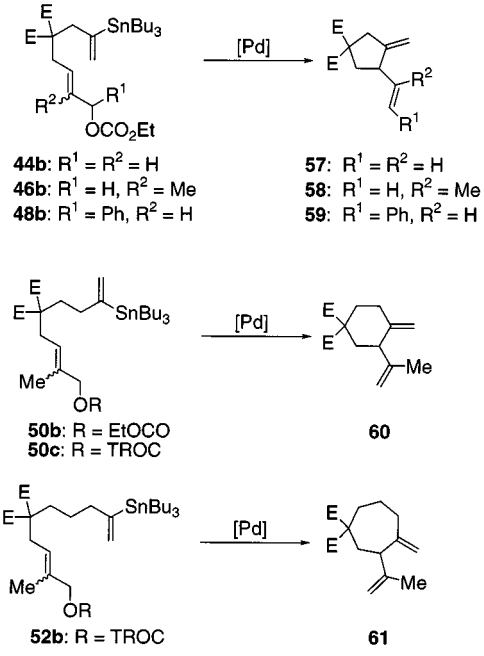
The alternative cyclization of substrates of type **XIII** to carbocycles **XV** (Scheme 7) might be achievable through Stille coupling of the corresponding acetates.[25,42] Thus, when the acetate of **46a** was treated with $Pd(dba)_2$·(dba) as the catalyst and LiCl (3 equiv.) in THF, carbocycle **58** was obtained (40% yield). Best results were obtained by using the intramolecular version of the Stille coupling of allyl carbonates with stannanes.[31] Thus, ethyl carbonates **44b**, **46b**, and **48b** gave five-membered ring carbocycles **57**−**59** in good yields when $Pd(MeCN)_2Cl_2$ was used as the catalyst in DMF at 23 °C (Scheme 10 and Table 3, Entries 1−3).

Table 2. Palladium-catalyzed cyclization of allyl carbonates from Scheme 9

Entry[a]	Substrate	Reaction time [h]	Product	Yield [%]
1	**43b**	20	**53**	62
2	**45b**	24	**54**	63
3	**47b**	24	**55**	65
4	**49c**	14[b]	**56**	54

[a] The reactions were run in DMF at 23 °C in the presence of 2 mol equiv. of H_2O at ca. 0.1 M in substrate. with $Pd(dba)_3$·dba (2.5 mol %)/PPh_3 (10 mol %). − [b] The enolate was preformed by treatment with NaH.

Again, formation of six- and seven-membered ring carbocycles proved a more difficult task. Thus, cyclization of ethyl carbonate **50b** failed to give **60**. The use of TROC derivative **50c** allowed the cyclization to proceed, giving rise to **60** in moderate yield (Table 2, Entry 4). Formation of a seven-membered ring compound proved possible by using palladium-catalyzed cyclization of the TROC derivative **52b**, affording carbocycle **61** (Table 3, Entry 5).



Scheme 10

Table 3. Palladium-catalyzed cyclization of allyl carbonates of Scheme 10

Entry[a]	Substrate	Reaction time [h][b]	Product	Yield [%]
1	**44b**	24	**57**	62
2	**46b**	1.5	**58**	81
3	**48b**	8	**59**	69
4	**50c**	19[c][d]	**60**	58
5	**52b**	17[c] [d]	**61**	55

[a] The reactions were run in DMF at 23 °C in the presence of 2 mol equiv. of H_2O at ca. 0.1 M in substrate with $Pd(MeCN)_2Cl_2$ (5 mol %). − [b] Identical results were obtained with $Pd_2(dba)_3$·dba. − [c] $Pd_2(dba)_3$·dba (2.5 mol %) in anhydrous DMF. − [d] Reaction run at 50 °C in the presence of 1 equiv. of iPr_2NEt.

Beyond the synthetic interest of this carbocyclization methodology, these results demonstrate that stannanes and soft nucleophiles such as malonate enolates can, by using the appropriate palladium complexes as catalysts, be orthogonally activated with complete chemoselectivity in their reactions with allylic electrophiles.

Carbocyclization by Intramolecular Coupling of Allylstannanes and Allylsilanes with Allyl Carboxylates

The synthesis of the lobane diterpenes, such as fuscol (**62**) and lobatriene (**63**), is of interest as this group of marine natural products displays potent anti-inflammatory activity through selective blocking of the synthesis of leucotrienes.[43] Interestingly, lobane diterpenes possess the opposite configurations at the three stereogenic centers of the six-membered ring to those displayed by the elemane sesquiterpenes, such as β-elemene (**64**)[44] and elemol (**65**) (Figure 1). These terpenes possess *trans*-1,2-dialkenyl groups. However, epi-elemol (**66**),[45] a rare member of the elemane family of sesquiterpenes, bears *cis*-1,2-dialkenyl groups.

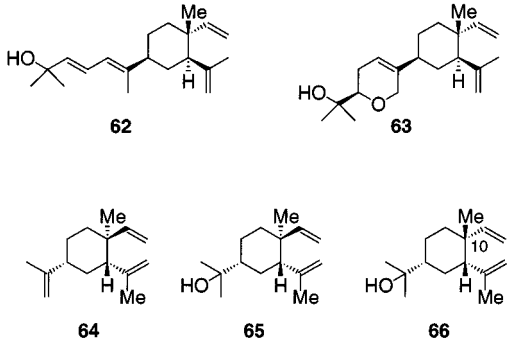
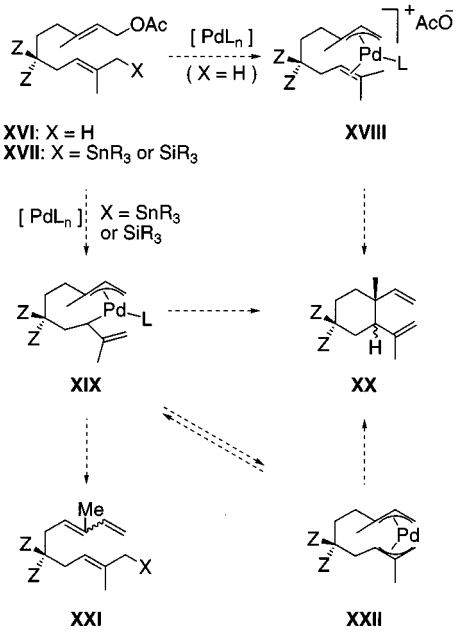


Figure 1. Representative lobanes and elemanes

For the construction of the six-membered rings of the elemanes, we had first tried to apply the Oppolzer carbocyclization of substrates **XVI**,[46] via (η^2-alkenyl)(η^3-allyl)palladium complexes of type **XVIII** (Scheme 11).[47] However, introduction of methyl groups at C-3 of the allyl had retarded the cyclization and resulted in recovery of unchanged starting materials under catalytic conditions.[47a]

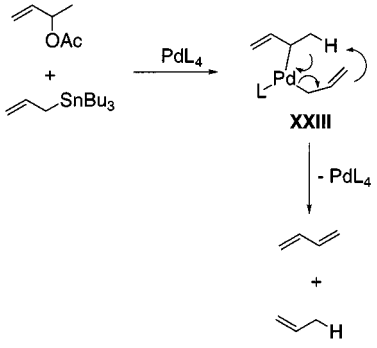
We therefore decided to examine the possibility of effecting the cyclization of substrates **XVII** by means of an intramolecular palladium-catalyzed cross-coupling of an allylstannane with an allyl acetate.[48] This coupling might proceed through complexes of type **XIX** or its regioisomer,[49] which would undergo reductive elimination to give carbocycle **XX**.[50] Alternatively, a bis(η^1-allyl)palladium complex or bis(η^3-allyl)palladium **XXII**[51] might be the precursors of **XX**. This last pathway appears less likely,[50a−50b] since complexes of type **XXII** have recently been prepared by Yamamoto and did not show any tendency to undergo reductive elimination.[52,53]

Although the potential of metal-promoted allyl/allyl coupling for the construction of sesquiterpenes had been demonstrated early on by Corey, using $Ni(CO)_4$ in the syntheses of **65**,[54,55] the regioselectivity and stereoselectivity



Scheme 11

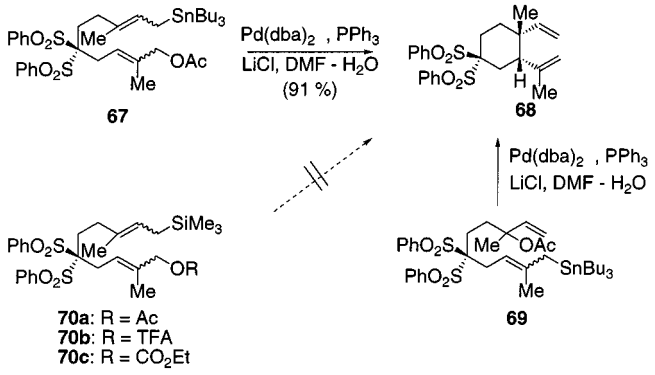
of the coupling was rather low and the reaction required an stoichiometric quantity of the highly toxic metal complex $Ni(CO)_4$. However, precedents for an approach based on an intramolecular allyl/allyl coupling were not particularly encouraging, since this type of Stille reaction is limited to allyl substrates that cannot eliminate to form conjugated dienes **XXI**.[18,48] It has been proposed that this facile β-elimination proceeds through intermediates of type **XXIII** by a concerted pathway, probably via a 6-electron, 6-center transition state (Scheme 12).[41c]



Scheme 12

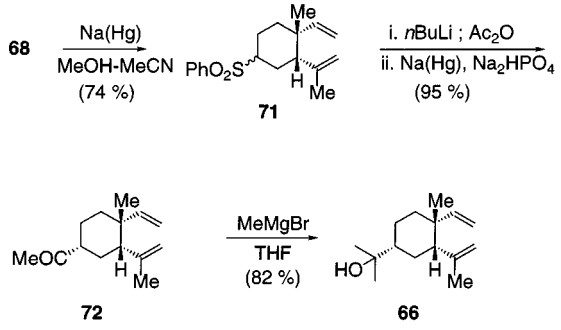
However, it proved possible to carry out the intramolecular coupling efficiently, without any significant elimination, by using a palladium catalyst prepared from $Pd_2(dba)_3$·dba and PPh_3 (2 equiv. per Pd) in the presence of LiCl in 0.5% aqueous DMF at 80 °C. Similar results were obtained by using NMP as the solvent and $Pd(PPh_3)_4$ and $Pd_2(dba)_3$·dba/PCy_3 as the catalysts. Interestingly, the coupling of allylstannane **67** proceeded in a highly stereoselective manner to provide *cis*-1,2-dialkenylcyclohexane **68** in good yield (Scheme 13). The reaction could also be performed in the absence of PPh_3, although a full equivalent of palla-

dium was required. The same carbocycle **68** was obtained from **69**, while the reaction of allylsilanes **70a**−**c** failed to give any cyclization product.[56]



Scheme 13

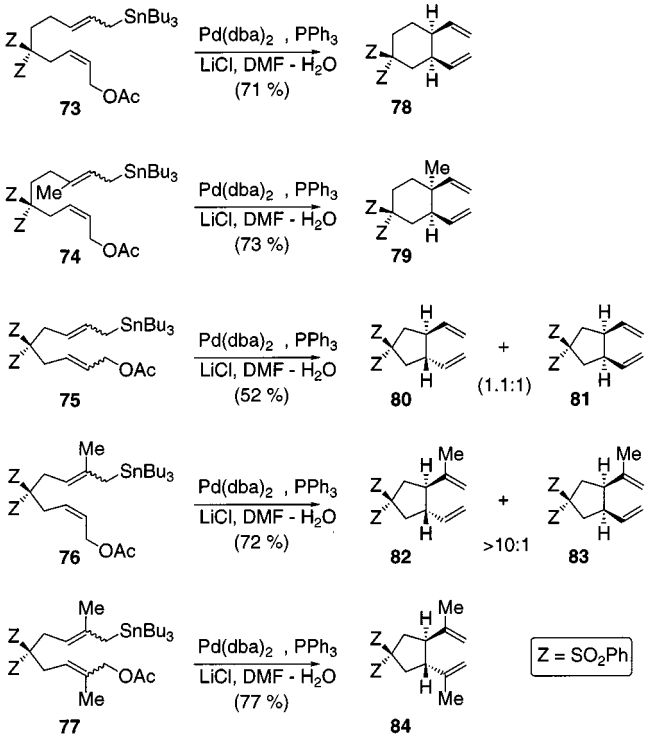
The configuration of **68** was proven by its transformation into naturally occurring 10-epi-elemol (**66**) (Scheme 14). Thus, reductive desulfonation of **68** afforded **71**, the anion of which was acetylated to give, after reductive desulfonation, **72** as a 9:1 mixture of α-ketone epimers. Final treatment of **72** with methylmagnesium bromide afforded racemic **66**.[57]



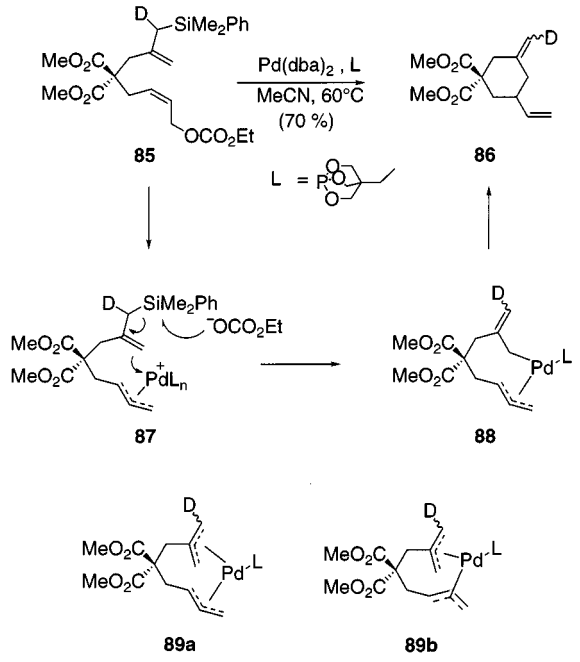
Scheme 14

The cyclization of allylstannanes by treatment with allyl acetates is a general reaction, as shown in Scheme 15. Thus, substrates **73**−**77** cyclize at 80 °C to afford carbocycles **78**−**84**. Interestingly, treatment of **73** and **74** stereoselectively provided **78** and **79**, respectively, with the two *cis*-vinyl groups. Cyclization of **75**, however, gave a 1.1:1 mixture of *trans* and *cis* isomers **80** and **81**. A better selectivity was obtained in the cyclizations of **76** and **77**, which gave *trans* derivatives as the major compounds.[58]

The participation of bis(η^3-allyl)palladium complexes in this carbocyclization is strongly suggested by the fact that **67** (mixture of four stereoisomers), together with its regioisomer **69** (two stereoisomers), both afforded **68** as the exclusive product from the palladium-catalyzed coupling process (Scheme 13). However, it had been demonstrated that the cyclization of (η^3-allyl)palladium complexes with allylsilanes does not proceed through a bis(η^3-allyl)palladium complex.[59] Thus, cyclization of monodeuterated allylsilane/allyl carbonate **85** gave only carbocycle **86**, by the transmetallation of intermediate **87** to give (η^1-allyl)(η^3-allyl)palladium complex **88** (Scheme 16). This intramolecular coupling reaction requires the use of a cyclic phosphite as the ligand for palladium. Alternatively, the allylsilane might directly attack the allyl ligand of **87** to give **86**. In any case, the lack of deuterium scrambling in this experiment ruled out formation of bis(η^3-allyl)palladium complexes **89a** or **89b** as the intermediates.

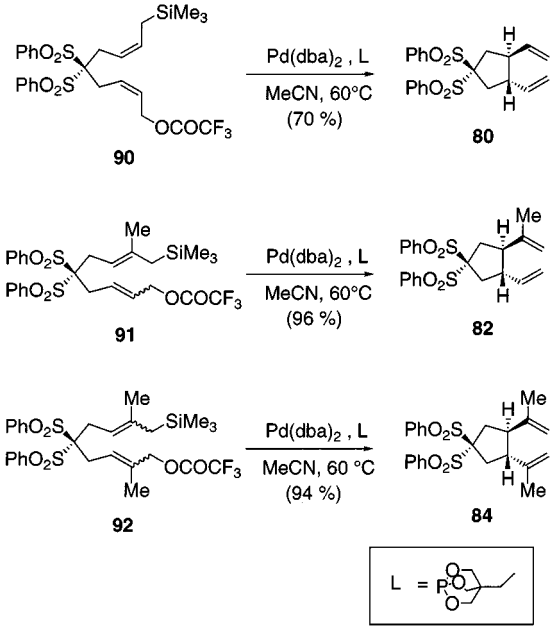


Scheme 15



Scheme 16

The cyclization of allylsilanes/allyl trifluoracetates **90**−**92** under the above conditions afforded carbocycles **80**, **82**, and **84**, respectively, as the exclusive products (Scheme 17). The highly selective formation of *trans*-**80** from the allylsilane **90** contrasts with the formation of a mixture of stereoisomeric carbocycles from allylstannane **75**, which suggests that two different pathways might be competing in this last cyclization. It is important to stress that, in contrast with a suggestion previously put forward by Oppolzer,[46] no equilibration of *cis* and *trans* isomers occurs in the presence of the palladium catalyst under the reaction conditions used for these cyclizations.[60][61]

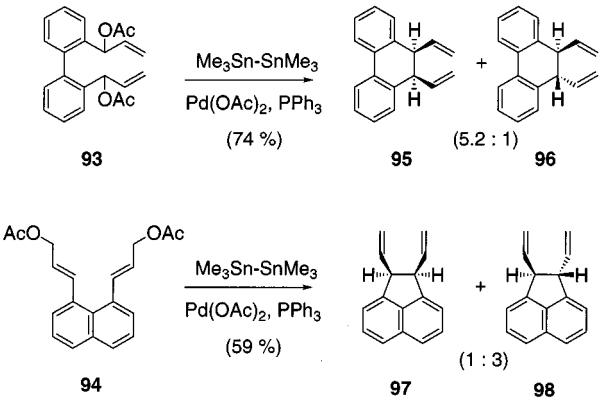


Scheme 17

Although bis(η^3-allyl)palladium complexes may be formed as intermediates in the cyclization reactions, this does not mean that the final C−C bond formation takes place from these intermediates. With regard to the stereoselectivity of the cyclization, it appears that a strong bias exists towards the formation of *cis* six-membered rings and *trans* five-membered rings. Indeed, Trost found the same stereoselectivity in the cyclization of diacetates **93** and **94** with $(Me_3Sn)_2$, which proceeds by the formation of an allylstannane in situ (Scheme 18).[48b] Thus, **93** furnished a 5.2:1 mixture of *cis*- and *trans*-dehydrophenanthrene derivatives **95** and **96**, while **94** gave acenaphthenes **97** and **98** as a 1:3 *cis*/*trans* mixture. However, no clear rationale for the stereoselectivity in these carbocyclizations is at hand and must await further experimental and theoretical work.

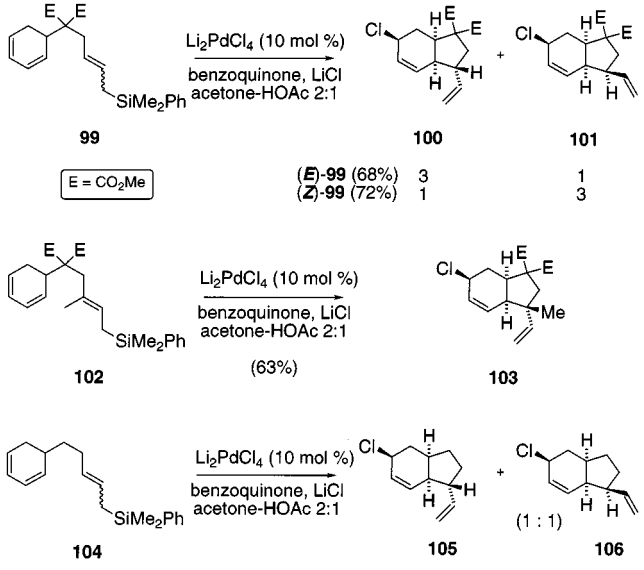
Reactions of Dienes with Allylsilanes

The intramolecular palladium-catalyzed cyclization of allylsilanes with 1,3-dienes has been described by Bäckvall.[62] The reaction is a formal 1,4-oxidation of conjugated dienes to give carbocycles containing an allyl chloride functionality. The cyclizations proceed with Li_2PdCl_4 as the



Scheme 18

catalyst in the presence of excess LiCl and require the addition of *p*-benzoquinone or $CuCl_2$ as the oxidant for Pd^0 to regenerate the active Pd^{II} catalyst (Scheme 19). The analogous allylstannanes were not suitable as substrates for the cyclization, since these compounds suffered direct transmetallation with the Pd^{II} complex to form dimeric (η^3-allyl-)palladium chloride complexes, which failed to insert into the conjugated diene.

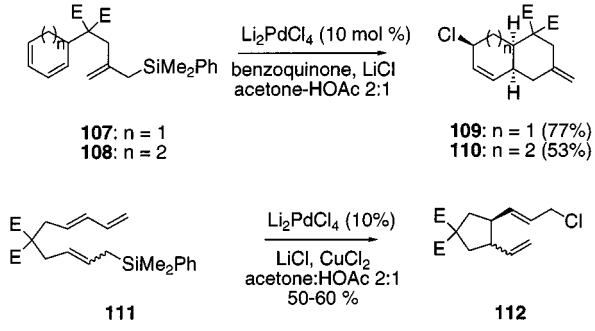


Scheme 19

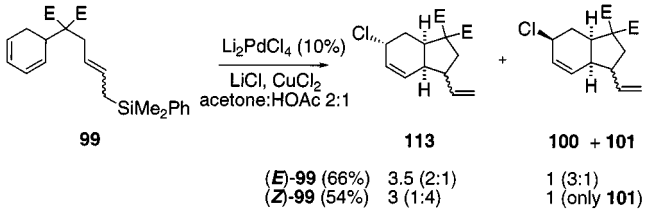
In this reaction, 1,4-addition of the allyl moiety and the chloride across the diene was observed. In addition, the reaction was shown to be highly stereoselective, resulting mainly in 1,4-*syn* addition products regardless of the stereochemistry of the starting silane. However, formation of 1,4-*anti* isomers as minor products was occasionally observed. In those cases, it was proved that isomerization of the 1,4-*syn* to the 1,4-*anti* derivatives occurred under the reaction conditions. This process could be minimized by slow addition of LiCl to the reaction mixture. In contrast, the relative stereochemistry of the vinyl substituent was highly dependent on the configuration and substitution of the allylsilane. Thus, unsubstituted (*E*)-allylsilane **99** gave carbocycles **100** and **101** as a 3:1 mixture of isomers, whereas (*Z*)-**99**, under

the same reaction conditions, afforded a 1:3 mixture of the carbocycles. Substitution on the double bond of the silane **102** increased the stereoselectivity of the reaction, almost exclusively yielding carbocycle **103**. The relative configuration of the vinyl substituent was also dependent on the presence or absence of geminal esters substituents on the substrates, as shown by the cyclization of substrate **104** (> 95% (*E*)], which gave a 1:1 mixture of isomers **105** and **106** (Scheme 19).

Allylsilanes **107** and **108** underwent palladium-catalyzed 6-*endo* cyclizations with good yields and stereoselectivities (Scheme 20). On the other hand, acyclic allylsilane/diene **111** [(*E*)and (*Z*)] was best cyclized using $CuCl_2$ as the oxidant, to give **112** as a 1.3:1 mixture of isomers. Surprisingly, when the cyclization of silane **99** was performed in the presence of $CuCl_2$ instead of *p*-benzoquinone, the stereoselectivity of the 1,4-addition was reversed to give the 1,4-*anti* carbocycles **113** (mixture of epimers) preferentially (Scheme 21).[62]

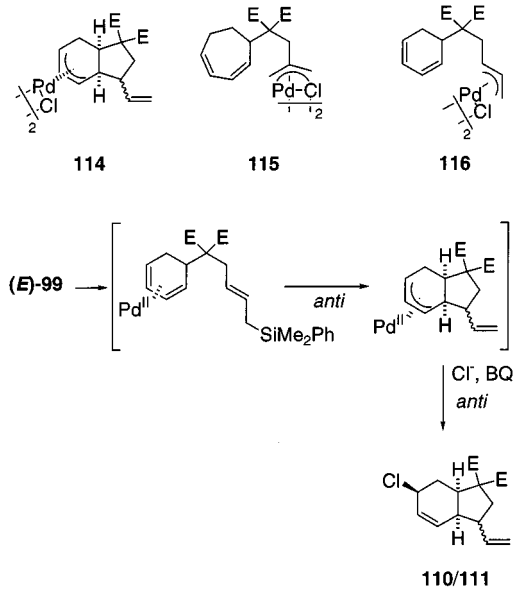


Scheme 20



Scheme 21

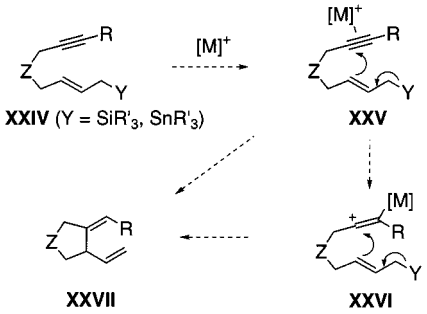
Mechanistic information was obtained by investigation of the reactions of isolated (η^3-allyl)palladium complexes **114** (α and β epimers), which gave rise to the corresponding carbocycles **110** and **111** (Scheme 22). In addition, (η^3-allyl-)palladium complexes **115** and **116** were not productive intermediates in the carbocyclization process. Accordingly, it was proposed that an external *anti* attack of the allylsilane onto the 1,3-diene, activated by coordination to Pd^{II}, could generate the intermediate (η^3-allyl)palladium complex, which would then undergo external *p*-benzoquinone-induced *anti* attack by chloride anion (Scheme 22).[63] The different stereochemical outcome observed with $CuCl_2$ as the oxidant may be explained as a result of an oxidative Pd−C cleavage involving a carbocationic intermediate.[64]



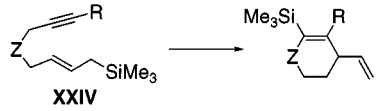
Scheme 22

Transition Metal-Catalyzed Reactions of Alkynes with Stannanes and Silanes

A great variety of methods for the cyclization of enynes have recently been developed.[65−67] In particular, great attention has been given to the development of their cycloisomerization to afford cyclic dienes.[65,68] However, transition metal catalyzed carbocyclizations involving intramolecular attack of mild nucleophilic reagents such as allylsilanes or allylstannanes (**XXIV**: M = SiR_3, SnR_3) onto alkynes to form dienes **XXVII** was unknown (Scheme 23), although a stoichiometric process using $HgCl_2$ as an electrophile in the presence of a base had been developed by Forsyth.[69,70] Use of several electrophilic Pt^{II}, Pd^{II}, Ru^{II}, and Ag^{I} metal salts as catalysts allows allylsilanes and allylstannanes to cyclize with alkynes.[71] This cyclization process was expected to proceed through intermediates **XXV**, in which the metal coordinates the alkyne in an η^2-fashion, or through metal-stabilized vinyl cations **XXIV**.[72] Interestingly, strong Lewis acids such as $HfCl_4$ promote the alternative *endo-dig* cyclization of allylsilanes **XXIV** (M = SiR_3) (Scheme 24).[73]



Scheme 23

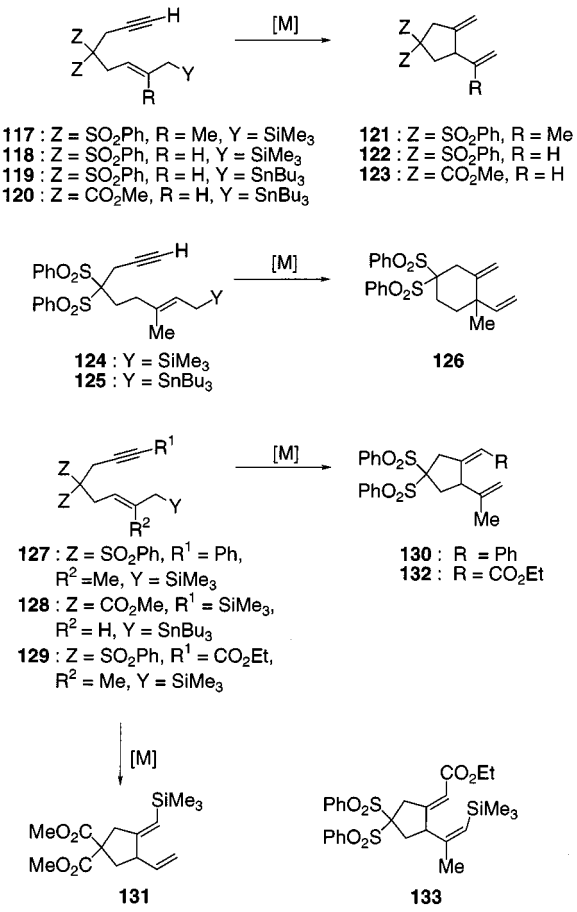


Scheme 24

Heating of a solution of allylsilanes **117**−**118** and allylstannanes **119**−**120** with Ru^{II}, Pd^{II}, Pt^{II}, and Ag^{I} as the catalysts gave rise to five-membered ring carbocycles **121**−**123** (Scheme 25 and Table 4, Entries 1−15). More general results were obtained by using $PtCl_2$ as the catalyst, with MeOH or acetone as the solvent. Additionally, metal-catalyzed cyclization of allylsilane **124** or allylstannane **125** provided six-membered ring carbocycle **126** by formation of a quaternary carbon center (Table 4, Entries 16−19).

Substituted alkynes also react with electrophilic metal catalysts to give the corresponding carbocycles. Thus, substrates **127**−**129** gave carbocycles **130**−**132** (Table 4, Entries 20−22). In the last example, cycloisomerized product **133** was obtained stereoselectively.

The reaction of allylsilane **117** with Pt^{II} was expected to take place through a vinylplatinum intermediate **134a** (Scheme 26). Accordingly, when the reaction was performed in [D_4]methanol as the solvent, [D_1]-**121** was obtained. The isolation of (*Z*)-configured carbocycles **130** and **132** is also consistent with an *anti* attack of the allyl nucleophile onto the η^2-coordinated complex **XXV** or a metal-stabilized vinyl cation **XXVI**. On the other hand, the formation of vinylplatinum **131**, with the (*E*) configuration, in the cyclization of **128** can be explained by an attack of the allylstannane *anti* to the sterically more hindered trimethylsilyl substitu-



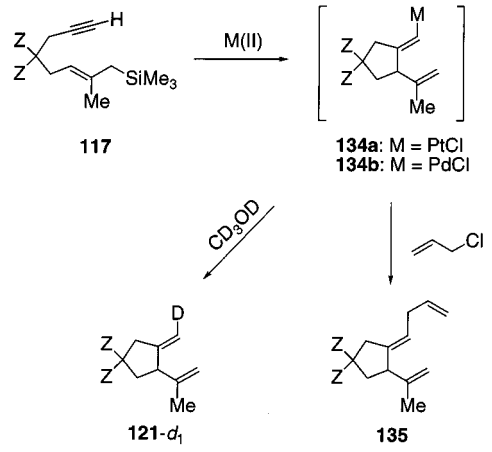
Scheme 25

Table 4. Metal-catalyzed cyclization of enynes (Scheme 24)

Entry[a]	Enyne	Catalyst (mol %)	Solvent	Product	Yield [%]
1	**117**	$CpRuCl(PPh_3)_2$ (5)[b]	MeOH	**121**	92
2	**117**	$RuCl_3$ (5)	MeOH	**121**	53
3	**117**	$PdCl_2$ (5)	MeOH	**121**	47
4	**117**	$Pd(MeCN)_2Cl_2$ (5)	MeOH	**121**	65
5	**117**	$Pd(MeCN)_4(BF_4)_2$ (5)	MeOH	**121**	82
6	**117**	$PtCl_2$ (5)	acetone	**121**	94
7	**117**	$PtCl_2$ (5)	acetone[c]	**121**	83
8	**117**	$Pt(MeCN)_2Cl_2$ (5)	MeOH	**121**	95
9	**117**	AgOTf (5)	dioxane	**121**	54
10	**118**	$CpRuCl(PPh_3)_2$ (20)[b]	MeOH	**122**	50
11	**118**	$PtCl_2$ (5)	MeOH	**122**	82
12	**118**	$PtCl_2$ (5)	acetone[c]	**122**	81
13	**119**	$PtCl_2$ (5)	MeOH	**122**	62
14	**120**	$CpRuCl(PPh_3)_2$ (20)[b]	MeOH	**123**	81
15	**120**	$PtCl_2$ (5)	MeOH[d]	**123**	43
16	**124**	$PtCl_2$ (2)	MeOH	**126**	48
17	**125**	$PtCl_2$ (2)	MeOH	**126**	79
18	**125**	AgOTf (28)	dioxane	**126**	32
19	**125**	$Pd(MeCN)_4(BF_4)_2$ (20)	dioxane	**126**	31
20	**127**	$PtCl_2$ (5)	MeOH	**130**	87
21	**128**	$CpRuCl(PPh_3)_2$ (50)	MeOH	**131**	79
22	**129**	$PtCl_2$ (5)	MeOH	**132** (+ **133**)	50 (+ 43)

[a] Unless otherwise stated, all reactions were carried out under reflux for 17 h. − [b] 2 equiv. (based on Ru) of $NaPF_6$ were also added. − [c] Reaction temperature 23 °C. − [d] Reaction time 48 h.

ent of the vinyl cation, in agreement with that proposed for a similar cyclization mediated by $HgCl_2$.[69]

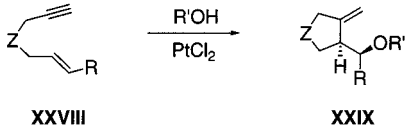


Scheme 26

Trapping of the intermediate vinylmetal intermediate could result in the formation of an additional C−C bond. Thus, insertion of allyl chloride into the alkenyl−Pd bond of **134b**, formed in the reaction between **117** and $Pd(MeCN)_2Cl_2$, followed by elimination of $PdCl_2$,[74] gave the allylated derivative **135** in 43% yield.

The cyclization of allylsilanes and allylstannanes with alkynes is a quite general reaction[75] that proceeds catalytically in the presence of a variety of electrophilic metal salts. The regioselectivity of this reaction is complementary to that promoted by Lewis acids.[73] Metathesis-type products, which are the major products in the cyclization of enynes with electrophilic metal salts,[65,66,75] are not formed in this new metal-catalyzed cyclization. Since allylsilanes and allylstannanes are readily available from allyl carboxylates, this new carbocyclization offers a synthetically useful alternative to the cyclization-carbonylation of allyl halides or carboxylates with alkynes catalyzed by nickel or palladium.[46,76]

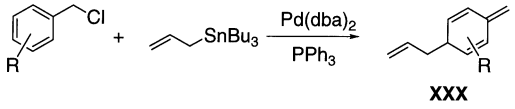
Recently, we have found that even simple enynes **XXVIII** react with $PtCl_2$ as the catalyst in the presence of nucleophilic solvents. In this new reaction, cyclized products **XXIX** are obtained stereospecifically (Scheme 27).[77,78]



Scheme 27

Summary and Outlook

The cyclization of readily available alkenylstannanes,[79] allylsilanes,[80,81] and allylstannanes[82,83] result in regioselective carbocyclization with allyl carboxylates (or carbonates), 1,3-dienes, and alkynes. The use of these soft nucleophiles has allowed in most cases for the highly chemoselective formation of the functionalized carbocycles. New metal-catalyzed transformations using soft nucleophiles will undoubtedly be discovered in the future. In this context, the unprecedented Pd^0-catalyzed allylative dearomatization of benzyl chlorides to give derivatives **XXX**, discovered very recently by Yamamoto, is noteworthy (Scheme 28).[84]



Scheme 28

Development of new selective methods for the introduction of silyl and stannyl functions into organic molecules[85][86] should allow for the application of these carbocyclization methods for the construction of complex molecules. In particular, the use of allylsilanes or allylstannanes as terminators for cascade polycyclizations[87] based on the concept outlined in Scheme 23 is actively under research in our group.

Acknowledgments

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