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Mini review

Synthesis of functionalized alkenes by transition metal-catalyzed carbostannylations of alkynes and dienes followed by cross-coupling reactions

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Abstract

Transition metal-catalyzed carbostannylation of alkynes and 1,2-dienes provides alkenylstannanes having an alkynyl, alkenyl or acyl group with or without conjugation. The alkenylstannanes are transformed to various unsaturated compounds with diverse functionalized structures through palladium-catalyzed cross-coupling reactions with organic electrophiles. © 2002 Published by Elsevier Science B.V.

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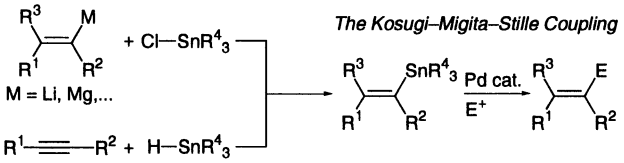
1. Introduction

The cross-coupling reaction of organostannanes with organic electrophiles, called the Kosugi–Migita–Stille coupling, has features of high chemoselectivity and easy handling and has become one of the most straightforward tools for organic synthesis especially in laboratory use [1]. Among organostannanes used in the cross-coupling reaction, alkenylstannanes are very important substrates and usually are prepared by the reaction of alkenylmetals with trialkyltin chlorides or by hydrostannylation of alkynes (Scheme 1). However, these synthetic reactions are very often incompatible with labile functional groups and do not always conserve stereochemistry. In addition, it is difficult to apply the reaction to synthesis of trisubstituted vinylstannanes.



Scheme 1.

We have disclosed that the transition metal-catalyzed carbostannylation of alkynes or 1,2-dienes allows us to conveniently synthesize structurally complicated alkenylstannanes having an alkynyl, alkenyl or acyl group with or without conjugation by properly choosing an organostannane, an unsaturated acceptor and a catalyst (Scheme 2). In this account, we would like to summarize our recent studies on the carbostannylation reactions and transformation of the resulting alkenylstannanes into various conjugated and unconjugated unsaturated compounds through the palladium-catalyzed cross-coupling reaction.

2. Palladium- or nickel-catalyzed alkynylstannylation of alkynes [2,3]

2.1. Carbostannylation

The history of the transition metal-catalyzed carbostannylation of unsaturated compounds began with alkynylstannylation of alkynes catalyzed by a palladium–iminophosphine complex, which was brought about by our observation that an alkynylstannane could

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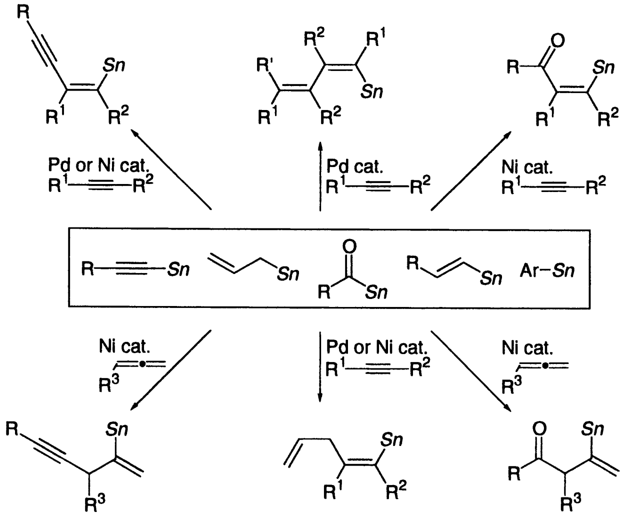
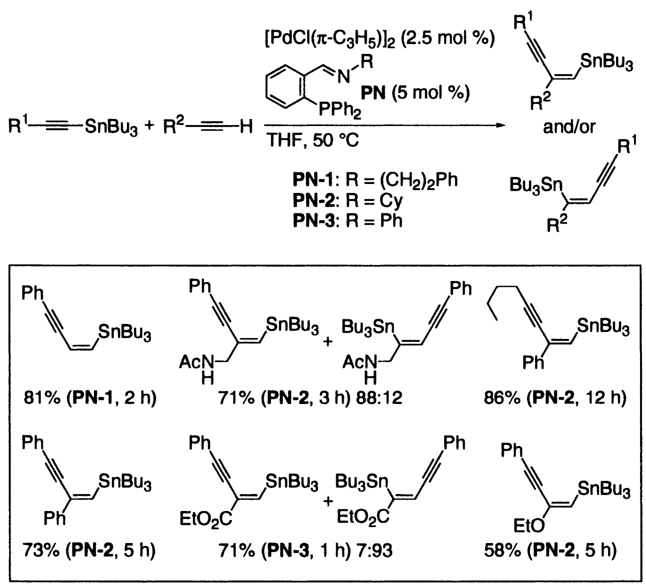


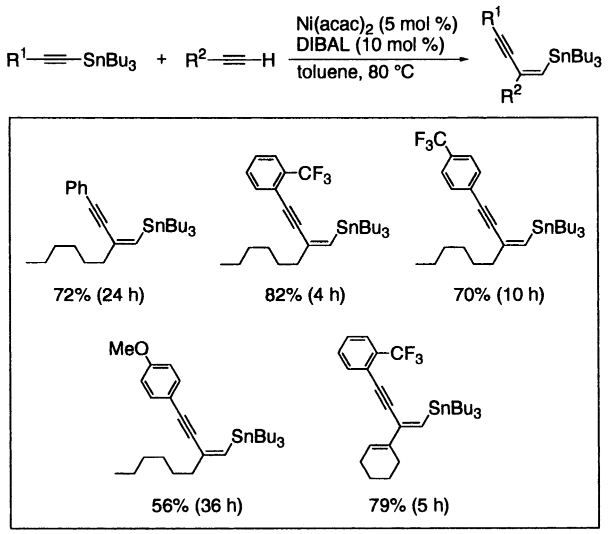
Scheme 2.

undergo oxidative addition to a palladium(0)–iminophosphine complex [4]. Thus, we thought that this oxidative adduct, which we had found to be involved as an intermediate in the palladium-catalyzed cross-coupling reaction of alkynylstannanes with aryl iodides [5], should react with alkynes to give alkynylstannylation products of alkynes. This hypothesis turned out to be the case.

Alkynylstannanes add to a carbon–carbon triple bond of various arylacetylenes, conjugated ynoates, and propargyl amines and ethers in the presence of a catalytic amount of a palladium–iminophosphine complex (Scheme 3). Main products have the stannyl group at a less hindered carbon, though the reaction of ynoates and ynones shows opposite regioselectivity. Compared with other conventional phosphine ligands such as triphenylphosphine and 1,3-bis(diphenylphosphino)propane (**DPPP**), iminophosphine ligands are by far more effective. The substituent on the nitrogen atom of iminophosphines largely affects the regioselectivity on alkynes: a cyclohexyl group for R is suitable for the reaction of arylacetylenes and propargyl amines and ethers, whereas conjugated ynoates and ynones prefer the iminophosphine with R = Ph.



Scheme 3.



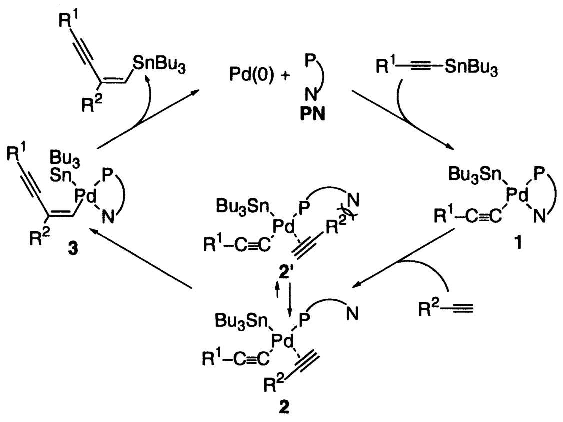
Scheme 4.

A nickel complex also catalyzes the alkynylstannylation of alkynes (Scheme 4). It is noteworthy that the regioselectivity is perfect in contrast to the palladium-catalyzed alkynylstannylation that often gives mixtures of regioisomers. Internal alkynes cannot give products as is the case with the palladium catalyst. Although electron-deficient terminal alkynes are not suitable for the nickel catalyst, the palladium catalyst can complement the reaction of such substrates.

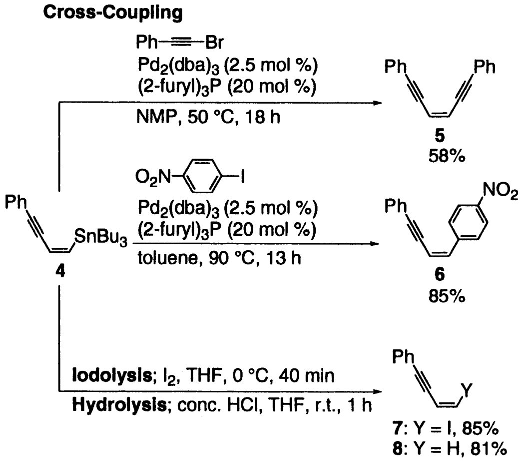
The palladium-catalyzed alkynylstannylation of alkynes is considered to be initiated by oxidative addition of an alkynylstannane to a palladium(0) complex as mentioned above. An arylacetylene or a propargyl amine or ether should insert into the carbon–palladium bond of oxidative adduct **1** to give alkenylpalladium **3** through **2** in a manner that avoids the steric repulsion as illustrated in Scheme 5, which should be followed by reductive elimination. On the other hand, ynoates and ynones should accept the alkynyl group of the oxidative adducts in a Michael fashion. The catalytic cycle of the nickel-catalyzed reaction may follow a similar scheme.

2.2. Cross-coupling reaction of 2-(1-alkynyl)ethenylstannanes

The alkynylstannylation products of alkynes are versatile precursors of highly π-conjugated systems. For example, (*Z*)-2-(phenylethynyl)ethenylstannane **4**



Scheme 5.

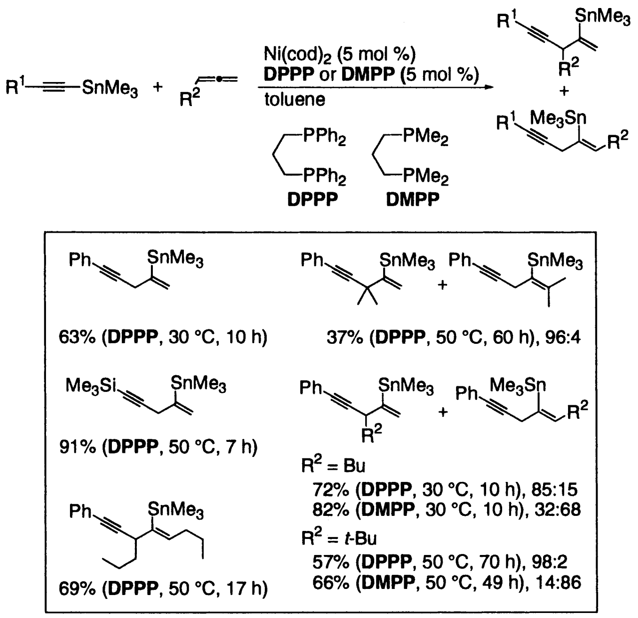


Scheme 6.

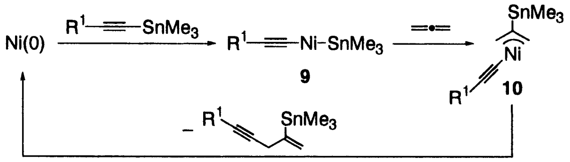
synthesized by the alkynylstannylation of acetylene underwent the palladium-catalyzed cross-coupling reaction with phenylethynyl bromide or p-nitroiodobenzene to give effectively enediyne **5** or arylenyne **6**, using tri(2-furyl)phosphine as a ligand (Scheme 6). Iodolysis of stannylenyne **4** gave iodoenyne **7**, a good substrate of the cross-coupling reactions, whereas hydrolysis by hydrochloric acid afforded terminal enyne **8**.

3. Nickel-catalyzed alkynylstannylation of 1,2-dienes [6]

3.1. Carbostannylation



Scheme 7.



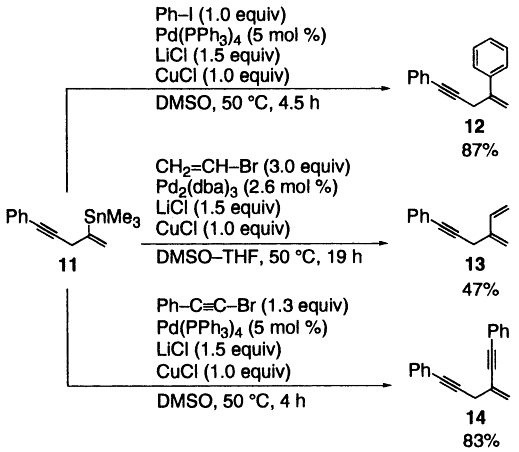
Scheme 8.

Alkenylstannanes with an unconjugated alkynyl moiety can be obtained from 1,2-dienes by the nickel-catalyzed alkynylstannylation (Scheme 7). Use of a 1,3-bisphosphinopropane is essential. The reaction is applicable to arylethynyl- and silylethynylstannanes, which successfully reacted with unsubstituted, monosubstituted and disubstituted allenes. The ligands play important roles in the selection of an allene double bond. The use of **DPPP** as a ligand gave the addition product of an internal double bond predominantly, whereas the dimethylphosphino derivative (**DMPP**) preferred a terminal double bond.

The catalytic cycle is considered again to include oxidative addition of an alkynylstannane to a nickel(0) complex (Scheme 8). Insertion of a 1,2-diene to the tin–nickel bond of oxidative adduct **9** should afford π-allylnickel complex **10** having a stannyl group at the central carbon of the π-allyl moiety. Following reductive elimination gives an unconjugated stannylenyne.

3.2. Cross-coupling reaction of propargyl-substituted alkenylstannanes

Alkynylstannylation product **11** underwent the palladium-catalyzed cross-coupling reaction with phenyl iodide, vinyl bromide or phenylethynyl bromide to afford conjugated unsaturated compounds **12**–**14** having a propargylic substituent (Scheme 9). The reaction proceeded under mild conditions in the presence of copper(I) chloride and lithium chloride.

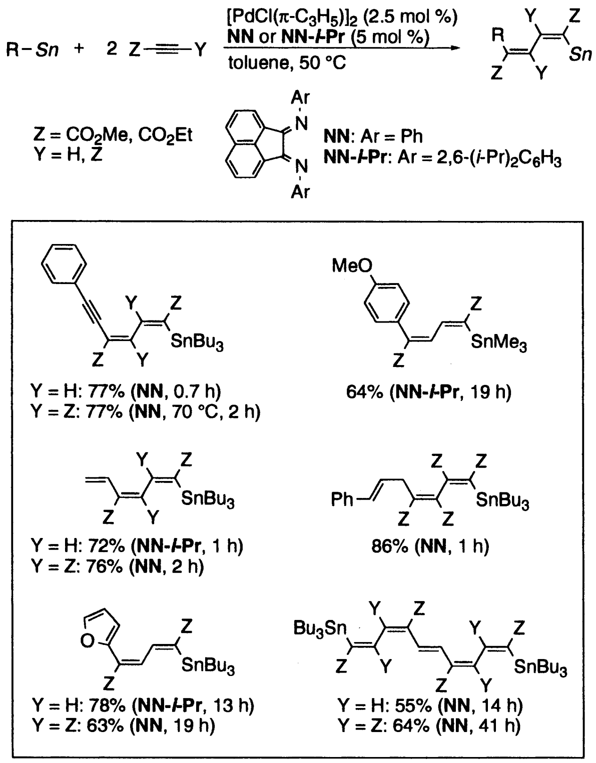


Scheme 9.

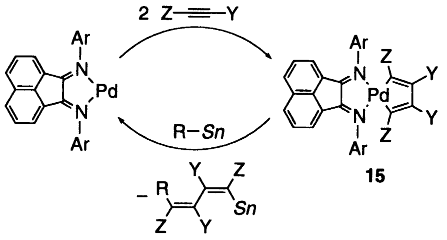
4. Palladium-catalyzed dimerization–carbostannylation of alkynes [7]

4.1. Carbostannylation

As we described in Section 2.1, the addition of alkynylstannanes to ethyl propiolate in the presence of a catalytic amount of a palladium complex coordinated by an iminophosphine ligand takes place to afford 1:1 adducts as a mixture of regioisomers. In contrast, use of bis(phenylimino)acenaphthene (**NN**) instead of iminophosphine drastically changed the reaction course to afford dimerization–alkynylstannylation products of ethyl propiolate (Scheme 10). The reaction is applicable not only to alkynylstannanes but also to alkenyl-, allyl- and arylstannanes, which upon reaction with ethyl propiolate or dimethyl acetylenedicarboxylate gave conjugated alkynyldienylstannanes, trienylstannanes and aryldienylstannanes with high stereoselectivity. Although a mixture of regioisomers is produced in the reaction of ethyl propiolate with other organostannanes than alkynylstannanes, more bulky diimine ligand **NN-*i*-Pr** expels minor isomers completely. The reaction of 1,2-bisstannylethene afforded bisstannylpentaenes, generating six new covalent bonds all in one batch. Palladacyclopentadiene **15** generated by oxidative cyclization between a palladium(0) complex and two molecules of alkynes is shown to be a key intermediate, which reacts with organostannanes to give the dimerization–carbostannylation products exclusively (Scheme 11).



Scheme 10.



Scheme 11.

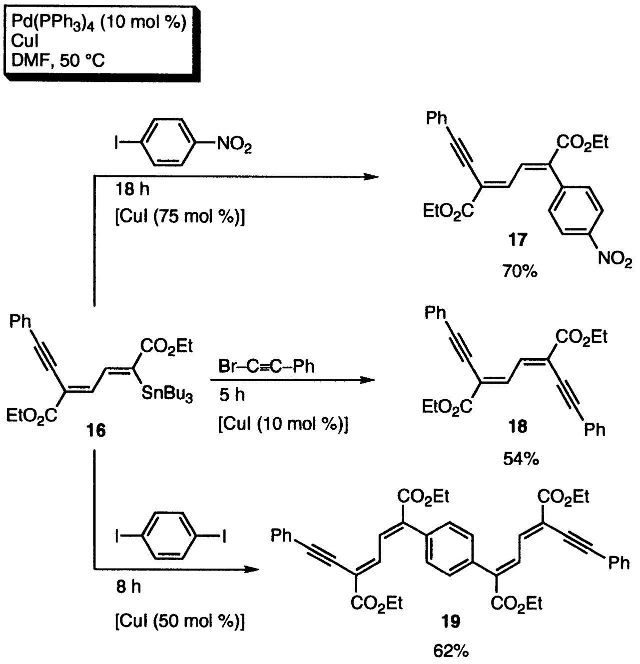
4.2. Cross-coupling reaction of 1,3-alkadienylstannanes

Although the dimerization–carbostannylation products have a highly conjugated framework, the π-conjugation can be further extended through the palladium-catalyzed cross-coupling reactions. Alkynyldienylstannane **16** shown in Scheme 12 underwent the cross-coupling reaction with 4-nitrophenyl iodide, phenylethynyl bromide or phenylene diiodide, giving more conjugated products **17**–**19**.

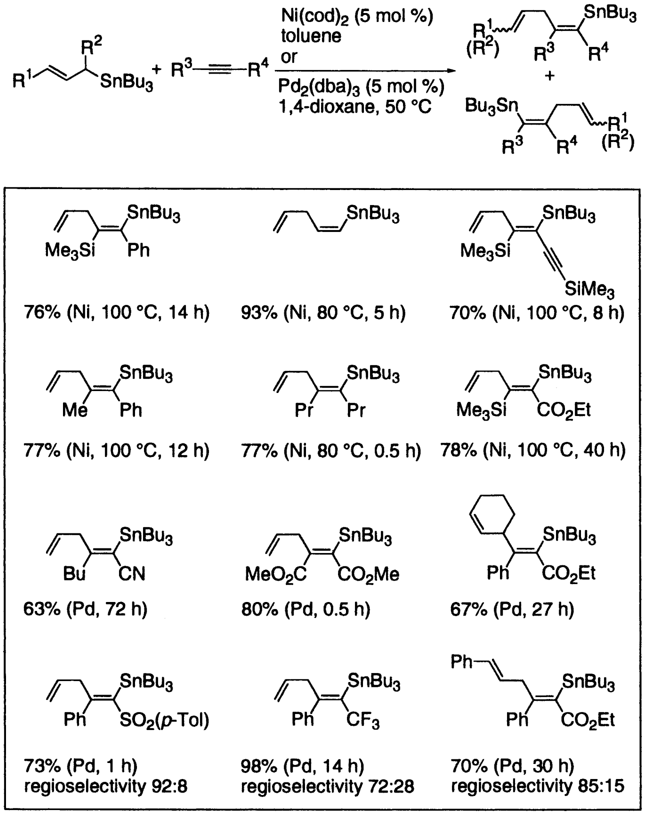
5. Nickel- or palladium-catalyzed allylstannylation of alkynes [3,8]

5.1. Carbostannylation

Various 1,4-dienylstannanes can be prepared by the nickel- or palladium-catalyzed allylstannylation of alkynes (Scheme 13). The two catalysts again complement each other with regard to electronic nature of alkynes. $Ni(cod)_2$ is sensitive to electronic character of a substituent on a carbon≡carbon triple bond, and favors regioselective attack of a stannyl group to an alkyne carbon having a more electron-withdrawing substituent. $Pd_2(dba)_3$ catalyzes the reaction without any phosphine or imine ligand in sharp contrast to the alkynylstannyla-

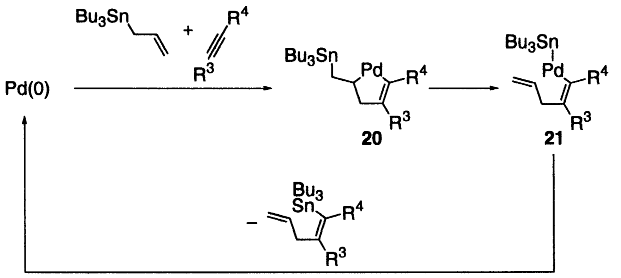


Scheme 12.



Scheme 13.

tion (Section 2.1) and dimerization–carbostannylation (Section 4.1), which, respectively, requires an iminophosphine or diimine ligand.



Scheme 14.

The palladium-catalyzed allylstannylation of alkynes is considered to proceed through palladacyclopentene complex **20**, which would undergo β-tin elimination to give **21** followed by reductive elimination (Scheme 14). In contrast, the nickel-catalyzed reaction should proceed through oxidative addition of an allylstannane to a nickel(0) complex, insertion of an alkyne and reductive elimination in a manner similar to the alkynylstannylation in Section 2.1.

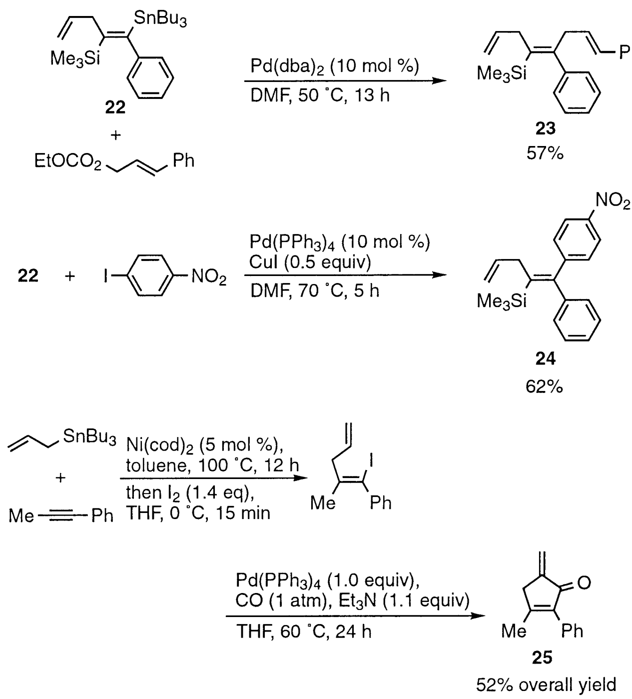
5.2. *Cross-coupling reaction of 1,4-alkadienylstannanes*

Trisubstituted vinylstannane **22** derived from allyl(tributyl)tin and 1-phenyl-2-trimethylsilylethyne (Scheme 15) coupled with an allyl carbonate or an aryl iodide in the presence of a palladium catalyst to give tetrasubstituted ethene **23** or **24**, respectively. Exclusive *syn*-selectivity and high regioselectivity of the nickel-catalyzed allylstannylation readily allow us to synthesize tetrasubstituted ethenes without troublesome separation of isomers. For example, the allylstannylation of 1-phenylpropyne followed by iodolysis and the palladium-mediated carbonylative cyclization gave *exo*-methylenecyclopentenone **25**.

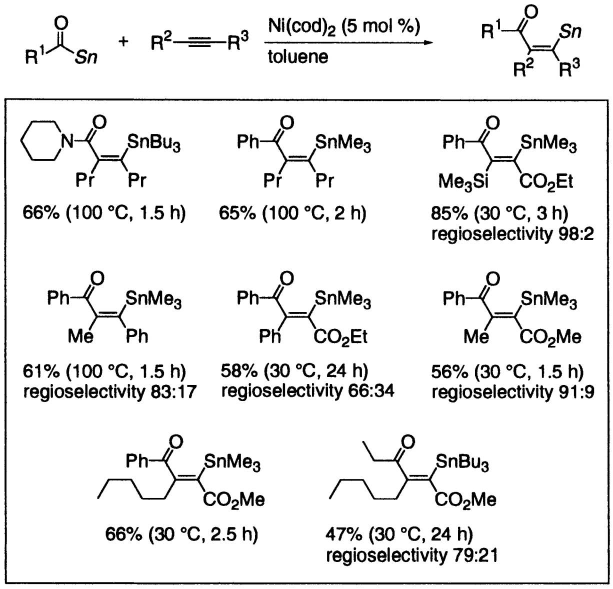
6. Nickel-catalyzed acylstannylation of alkynes [3,9]

6.1. *Carbostannylation*

For the addition of acylstannanes to alkynes, Ni(cod)$_2$ is an excellent catalyst (Scheme 16). The reaction is applicable to aromatic and aliphatic acylstannanes in addition to aminocarbonylstannanes, which react with both electron-rich and -deficient alkynes. The stannyl group of acylstannanes attacks mainly an alkyne carbon having a more electron-withdrawing group. The catalytic cycle should consist of oxidative addition of an acylstannane to a nickel(0) complex, insertion of an alkyne and reductive elimination.



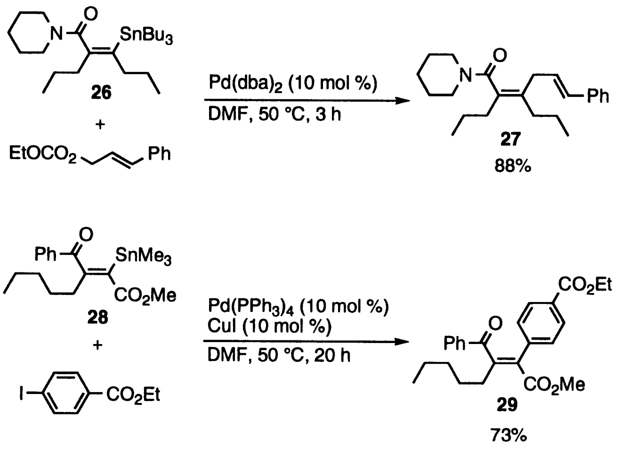
Scheme 15.



Scheme 16.

6.2. *Cross-coupling reaction of 3-keto-1-alkenylstannanes*

Cross-coupling reaction of β-stannyl-α,β-unsaturated amide **26** with an allyl carbonate is catalyzed by a palladium complex to afford trisubstituted acryl amide **27** (Scheme 17). For the cross-coupling reaction of α-stannyl-γ-keto-α,β-unsaturated ester **28**, use of copper iodide as a co-catalyst was effective to give coupling product **29** with retention of configuration.



Scheme 17.

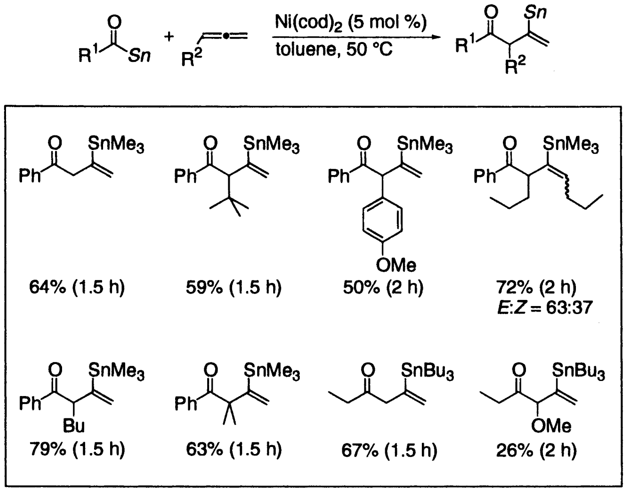
7. Nickel-catalyzed acylstannylation of 1,2-dienes [10]

7.1. *Carbostannylation*

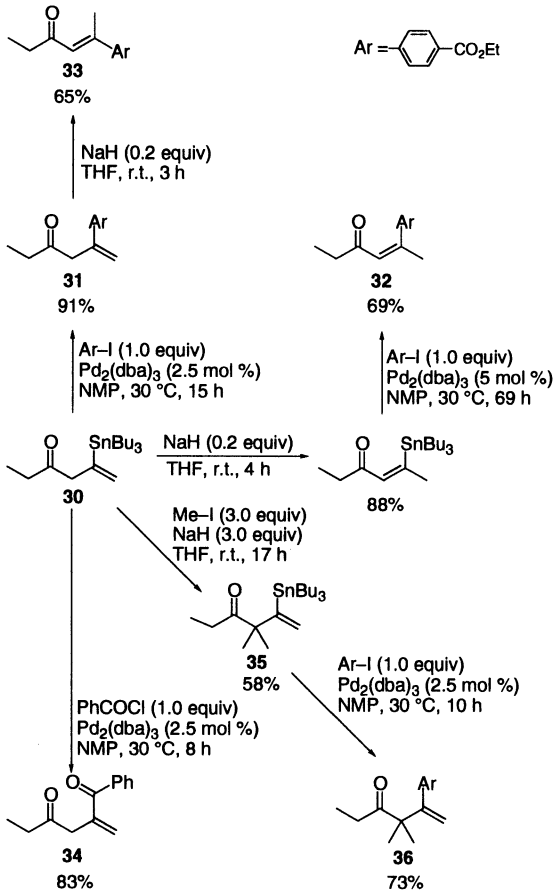
The oxidative adduct of an acylstannane to a nickel(0) complex, which should be an intermediate of the acylstannylation of alkynes in the preceding section, also reacts with 1,2-dienes, giving β-stannyl-β,γ-unsaturated ketones (Scheme 18). Various mono- and disubstituted allenes in addition to parent allene can participate in the reaction. Acylstannanes added mainly at an internal double bond of 1,2-dienes. The mechanism of the reaction should include a π-allylnickel intermediate and resemble the alkynylstannylation of 1,2-dienes discussed in Section 3.1.

7.2. *Cross-coupling reaction of β-stannyl-β,γ-unsaturated ketones*

Synthetic versatility of the acylstannylation products is demonstrated by the transformation of β-stannyl-β,γ-



Scheme 18.

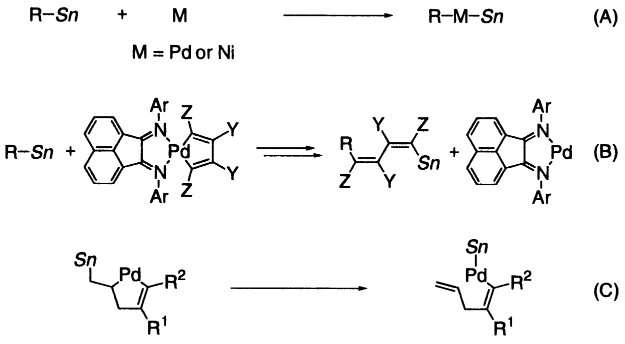


Scheme 19.

unsaturated ketone **30** to a wide variety of conjugated and unconjugated enones (Scheme 19). Palladium-catalyzed coupling reaction with ethyl *p*-iodobenzoate gave coupling product **31**. Conjugated (*Z*)-β-arylenone **32** was obtained by the cross-coupling reaction with the aryl iodide after base-catalyzed isomerization, whereas the corresponding (*E*)-isomer **33** was obtained by isomerization of unconjugated enone **31**. The cross-coupling reaction with benzoyl chloride gave enedione **34**, and **30** reacted with iodomethane in the presence of sodium hydride, giving dimethylated product **35**, which was subjected to the cross-coupling reaction with the aryl iodide to afford aryl-substituted β,γ-enone **36**.

8. Conclusion and prospect

The transition metal-catalyzed carbostannylation reaction disclosed here, in addition to the carbostannylation of 1,3-dienes [11] and arynes [12], is based on a variety of activation methods of a carbon–tin bond of organostannanes by transition metals, (1) oxidative addition of a carbon–tin bonds to a palladium(0) or nickel(0) complex (Scheme 20, A), (2) the reaction of a palladacyclopentadiene with an organostannane in Section 4.1 (Scheme 20, B), (3) β-tin elimination from a 5-(stannylmethyl)palladacyclopent-2-ene in Section 5.1. (Scheme 20, C).



Scheme 20.

These activation methods will provide us with clues to further investigation concerning not only new carbostannylation reactions of carbon–carbon unsaturated bonds using other organostannanes but also tandem carbostannylation involving two different unsaturated compounds and carbometalation using other organometallic compounds.

Acknowledgements

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