Direct vinylation reaction of phenols

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Abstract: Treatment of silyl enol ethers with 1-alkynes in the presence of SnCl$_4$-Bu$_3$N gave conjugated enones with (*E*)-configuration. This new C-C bond formation reaction between an enolate derivative and an unactivated acetylene involves a carbostannylation at the carbon-carbon triple bond. When phenols were subjected to the reaction in place of silyl enol ethers, *ortho*-alkenylation proceeded. Notably, *ortho*-vinylphenol was obtained by treating phenol with ethyne. The transformation described here convertes aromatic C-H bonds directly to C-CH=CH$_2$ bonds.

1. Introduction

In 1908, pure *ortho*-vinylphenol was obtained for the first time by decarboxylation of *ortho*-hydroxycinnamic acid (Scheme 1).[1] Since then, a number of methods appeared for the synthesis of vinylphenols which employed stepwise transformations.[2,3] For example, *para*-vinylphenol was synthesized from phenol by acylation, reduction, and dehydration; this sequence was employed in the industrial production by Maruzen Petrochemical Co., Ltd., in Japan. In the laboratory, vinylation of aromatic halides with organometallic reagents and the Wittig reaction of aromatic aldehydes are convenient methods.
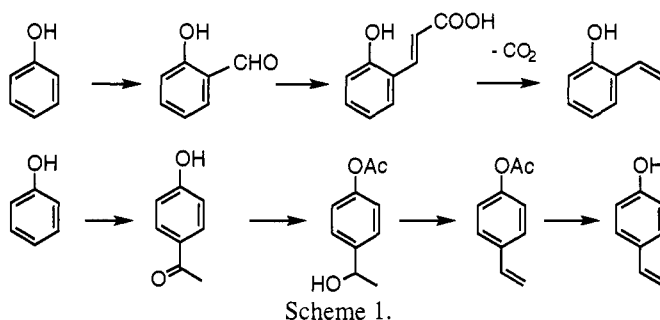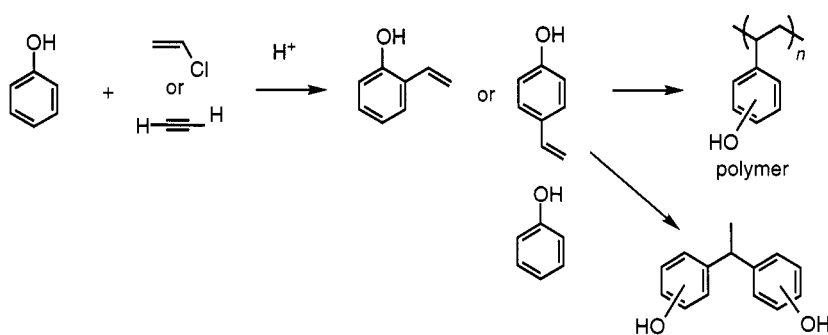

Scheme 1.

The direct vinylation of phenol is apparently the most straightforward method to prepare vinylphenols (Scheme 2). The attempts of the Friedel-Crafts vinylation using oxirane, vinyl acetate, ethyne, vinyl halides, *etc.*, however, failed. Although some claimed formation of vinylphenols,[4] many of them could not be reproduced.[5] Various undesired products such as poly(vinylphenol) and 1,1-diarylethane formed (Scheme 3). This is due to the instability of the vinylated products under the reaction conditions. Low efficiency in generating the electrophilic species may be another reason that the vinylation failed. Previously, we reported that vinylphenols can be directly synthesized from phenol and ethyne using a reagent consisting of SnCl$_4$-Bu$_3$N.[6] This reaction probably achieved the direct vinylation of phenols for the first time. Use of inexpensive ethyne as the vinylating reagent is another advantage. Described here is how we discovered this new reaction.
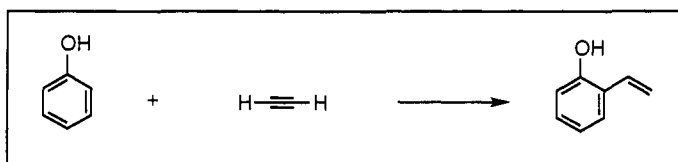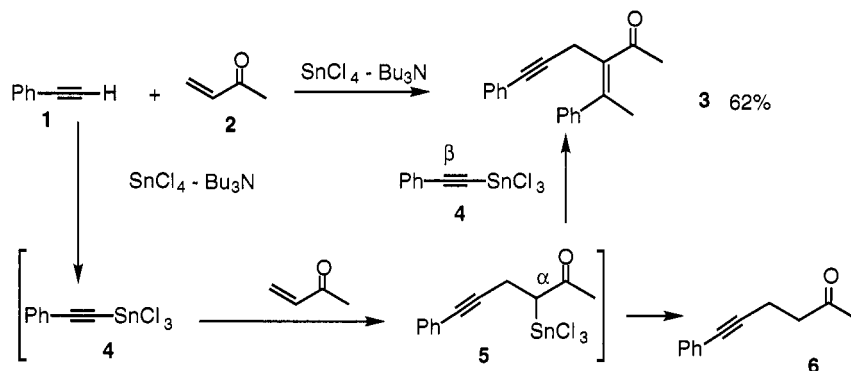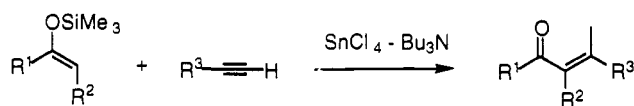

Scheme 2.

Scheme 3.

2. Carbostannylation of Carbon-Carbon Triple Bonds

The discovery of the carbostannylation reaction of carbon-carbon triple bonds provided a clue to the development of the phenol vinylation reaction.[7] Several years ago, we were studying nucleophilic reactions of alkynyltin compounds.[8] The intermediates were generated from 1-alkynes by treatment with the reagent $SnCl_4$-Bu_3N, and were added to aldehydes or acetals. When the organotin **4** generated from phenylacetylene **1** was treated with methyl vinyl ketone **2**, an unusual byproduct **3** was obtained along with the normal Michael adduct **6** (Scheme 4). Spectroscopic studies indicated that **3** consisted of 2 molecules of **1** and one molecule of **2**, and possessed a tetrasubstituted olefin. Chemical methods turned out to be helpful for the structure elucidation. When **3** was treated with ozone followed by dimethyl sulfide, acetophenone was obtained. Reduction with $NaBH_4$ revealed that **3** contained a CH_3CO unit. Such adducts were obtained not only from aromatic acetylenes but also from an aliphatic acetylenes, which indicated a broad applicability of this new C-C bond forming reaction. It should be noted that the tetrasubstituted olefins are (E)-configurated. Since the normal conjugate adduct **6** was obtained along with **3**, it seems reasonable to assume that the C-C bond formation took place at the α-carbon atom of **5** and β-carbon atom of **1**. Involvement of stannylacetylene **4** appeared more likely for the second reaction. *C-C bond formation occurred between an enolate and an unactivated 1-alkyne.*

Scheme 4.

It was known at that time that α-stannyl ketones could be generated by transmetalation of silyl enol ethers with $SnCl_4$, and that the resulting organotin compounds were preferentially formed as α-stannyl ketones rather than as enolates.[9] Thus, silyl enol ethers and 1-alkynes were treated in the presence of $SnCl_4$-Bu_3N under refluxing acetonitrile-dichloroethane (4 : 1) conditions, and the conjugated enones were obtained in high yields (Scheme 5). Since treatment of tributylstannylacetylenes and silyl enol ethers with $SnCl_4$ also gave the enones, participation of stannylacetylene species in the C-C bond formation was confirmed. The reaction always took place at the internal carbon of 1-alkynes. All the trisubstituted and tetrasubstituted enones again possessed (E)-configurated double bonds. By this transformation tetrasubstituted olefins are stereoselectively constructed with concomitant carbon-carbon double bond formation.

R^1 = Et, R^2 = Me, R^3 = Ph: 85%

R^1 = Et, R^2 = Me, R^3 = n-C_5H_{11}: 75%

R^1 = R^2 =$(CH_2)_4$, R^3 = Ph: 63%

R^1 = R^2 = $(CH_2)_5$, R^3 = n-C_5H_{11}: 77%

R^1 = Ph, R^2 = Me, R^3 = n-C_5H_{11}: 72%

R^1 = $PhCH_2CH_2$, R^2 =H, R^3 = n-C_5H_{11}: 70%

Scheme 5.

Scheme 6 illustrates a mechanism of the reaction between diethyl ketone silyl enol ether **7** and **1**. It involves carbostannylation of an α-stannyl ketone **8** with an alkynyltin **4** generated *in situ*. Protonation of the resulting γ,γ-distannylated intermediate **9** and double bond shift to an allyl metal species **10** then takes place. Quenching of the reaction with H_2O finally gives β-enone **11**. The intermediate **9** and its conversion to **10** could be followed by NMR. The proton source required in this transformation was ascribed to Bu_3NHCl, which was formed from the reaction of the 1-alkyne and $SnCl_4$-Bu_3N. The formation of the (*E*)-enone **11** was explained by the protonation of the (*Z*)-allyl metal **10**, and its stereochemistry was confirmed by NOE studies. It should also be noted that this mechanism involves a catalytic cycle for the activation of the alkyne **1**. In accordance, the amount of Bu_3N could be reduced to 20 mol% without affecting the yield.
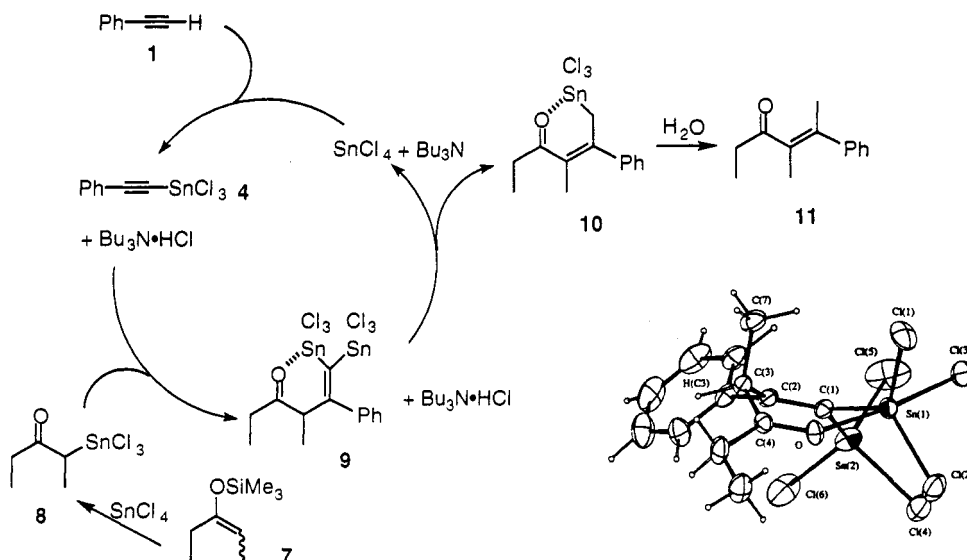
Scheme 6 (ORTEP drawings of **9** was reproduced from *Chem. Lett.*. **1993**, 1881 by permission of the Chemical Society of Japan).

Fortunately, intermediate **9** was obtained as a single crystal. so that a X-ray crystallographic analysis could be conducted.[10] The structure coincided with that obtained by spectroscopic studies. The two tin atoms possess a penta-coordinated trigonal bipyramidal and a tetracoordinated tetrahedral structure, respectively. The six-membered chelate adopts a boat conformation. The structure clearly indicates that carbostannylation took place between the trichlorostannylacetylene and the α-trichlorostannyl ketone. The carbostannylation of unactivated alkynes has not been known before.

It was then considered that if the protonation of the allyltin took place at the α-carbon atom, β-enones could be synthesized. Indeed, such β-enones were obtained selectively, when Me_3SiCl was added before aqueous workup (Scheme 7).[11] The overall transformation allows the alkenylation of enolate derivatives. It was later found that ketones could be used in place of silyl enol ethers. which showed that ketones can be directly stannylated with the $SnCl_4$-Bu_3N reagent.
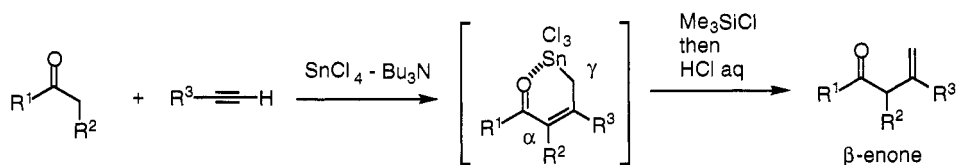
$$R^1 = C_2H_5, R^2 = CH_3, R = n\text{-}C_5H_{11}: 69\%$$
$$R^1 = R^2 = (CH_2)_5, R = n\text{-}C_5H_{11}: 58\%$$
$$R^1 = Ph, R^2 = CH_3, R = n\text{-}C_5H_{11}: 74\%$$

Scheme 7.

2. Phenol Alkenylation Reaction

The new C-C bond formation methodology was then extended to the coupling reaction of phenols and alkynes. It was expected that phenoxytin and alkynyltin would react *via* carbostannylation to give alkenylphenols. Since we were working on the chemistry of polyketides,[12] behaviors of ketone and phenol appeared to be somewhat similar.
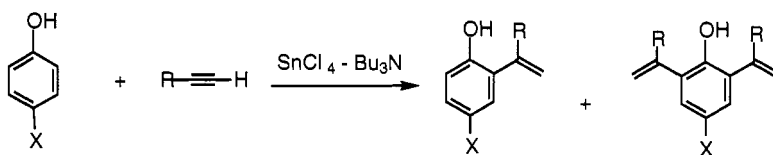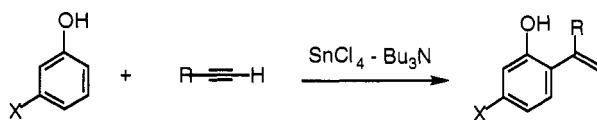

X = H, R = PhCH$_2$CH$_2$: 65 % (10 %)
X = Me, R = PhCH$_2$CH$_2$: 62 % (8 %)
X = MeO, R = n-C$_5$H$_{11}$: 74 %
X = NHCOt-Bu, R = t-BuPh$_2$SiO(CH$_2$)$_2$: 65 %
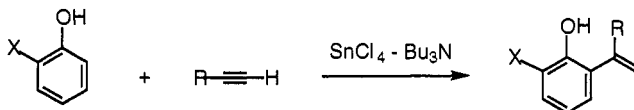X = COOEt, R = n-C$_5$H$_{11}$: 45 %

Shown in parentheses are yields of
dialkenylated product.

X = Me, R = PhCH$_2$CH$_2$: 68 %
X = MeO, R = n-C$_5$H$_{11}$: 69 %
X = NMe$_2$, R = n-C$_5$H$_{11}$: 73%


X = Me, R = PhCH$_2$CH$_2$: 68 %
X = Me, R = m-MeOPh: 69 %

Scheme 8.

Reaction of 1-alkyne, phenol, SnCl$_4$, and Bu$_3$N in refluxing acetonitrile followed by aqueous workup gave *ortho*-alkenylphenols (Scheme 8). Both aliphatic and aromatic 1-alkynes reacted at the internal carbon atom giving *exo*-olefins. The C-C bond formation occurred at the *ortho*-position of the phenolic hydroxy group. *Meta*-substituted phenols were alkenylated at the less hindered *ortho*-site.

Phenols possessing electron-donating groups reacted faster than those with electron-withdrawing groups. Functionalities such as ester, *sec*-amide, dimethylamino, and *t*-butyldiphenylsilyloxy were not affected.

The mechanistic studies indicated that the alkenylation again took place *via* carbostannylation. The regioselective *exo*-olefin formation *via* a 1,1-bis(stannyl)alkene rather than a 1,2-bis(stannyl)alkene could be explained based on the electrophilic properties of alkynyltrichlorotins, taking into account the higher reactivities of electron-rich phenols (Scheme 9). *Ab initio* calculations of $HC\equiv CSnF_3$ showed that the β-carbon atom is less negatively charged than the α-carbon atom. In addition, the coefficients of the π^* orbitals of C-C triple bond are larger at the β-carbon atom. We regard the carbostannylation reaction as a nucleophilic reaction of phenoxytin with alkynyltin at the electron-deficient β-carbon atom.
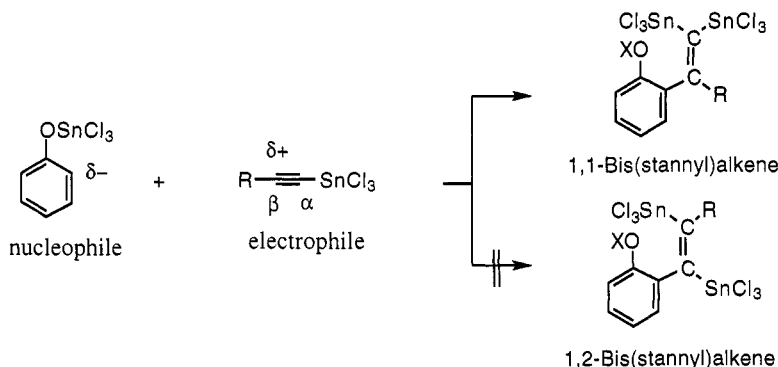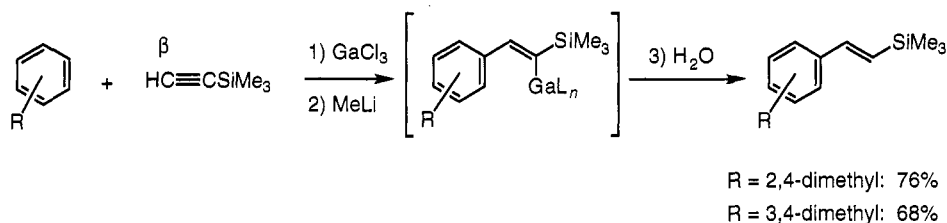

Scheme 9.

3. Phenol Vinylation Reaction

Trimethylsilylacetylene reacted with phenols in the presence of the $SnCl_4$-Bu_3N reagent to give β-silylvinyl derivatives (Scheme 10). 1,2-Dichloroethane was a favorable solvent for this reaction. In contrast to the alkenylation reactions, the silylvinylation took place at the external carbon atom of the substituted alkyne.
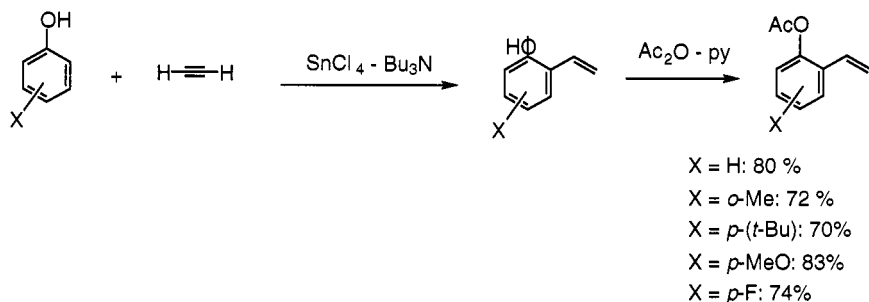

X = *o*-Me: 62 %
X = *p*-(*t*-Bu): 51%
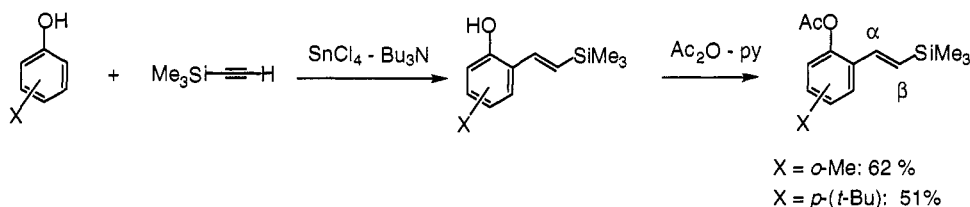
Scheme 10.

Recently, the β-silylvinylation reaction was applied to aromatic hydrocarbons, where $GaCl_3$ turned out to be effective promoter (Scheme 11).[13] A vinylgallium species was detected as an intermediate, and this C-C bond formation turned out to proceed *via* a carbogallation reaction of the carbon-carbon triple bond. These findings led us to study novel organogallium chemistry. Since the silyl group could be removed by acid treatment, the β-silylvinylation reaction is an equivalent of the direct aromatic C_2-olefination.

R = 2,4-dimethyl: 76%
R = 3,4-dimethyl: 68%

Scheme 11.

To our delight, the vinyl group can be introduced to phenols with gaseous ethyne in the presence of $SnCl_4$-Bu_3N (Scheme 12). The reaction can be carried out on a 10 g-scale, and is applicable to phenols

with both electron-donating groups and electron-withdrawing groups. The vinylphenols were relatively unstable, and were isolated as acetates. The reactive olefins of the vinylphenols may be protected from oligomerization and polymerization by bisstannylation in the reaction mixture. Fundamental C-C bond formation reactions of phenols are known, such as the Reimer-Tieman reaction, the Kolbe-Schmidt reaction, *etc.* We were able to add the vinylation reaction to this family. We believe that new vinylarenes now obtained by the direct vinylation of phenols can be useful intermediates in organic chemistry and polymer chemistry.

X = H: 80 %
X = *o*-Me: 72 %
X = *p*-(*t*-Bu): 70%
X = *p*-MeO: 83%
X = *p*-F: 74%

Scheme 12.

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