# Transition Metal-Catalyzed/ Mediated Reaction of Allenes with a Nucleophilic Functionality Connected to the α-Carbon Atom

SHENGMING MA

*State Key Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 354 Fenglin Lu, Shanghai 200032, People's Republic of China*

Received August 19, 2002

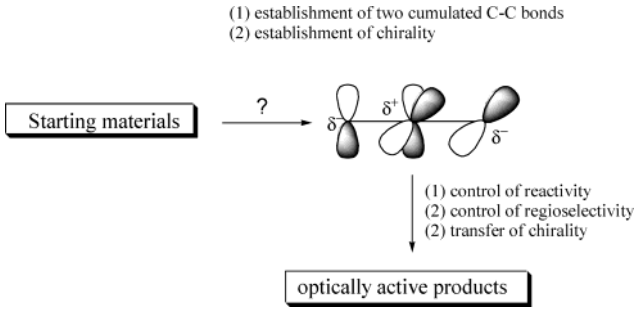
**ABSTRACT**

Allenes with a nucleophilic functionality connected to the α-carbon atom have been shown to be versatile building blocks for the synthesis of γ-butenolides, γ-lactams, γ-iminolactones, vinylic epoxides, 4-amino-2-alkenols, 2-amino-3-alkenols, 2,5-dihydrofurans, furans, vinylic cyclopropanes, and cyclopentenes, depending on the nature of the nucleophilic centers. The reaction may proceed via the carbometalation-nucleophilic attack mechanism or nucleometallation-reductive elimination. The stereochemical outcomes by these two pathways are different.

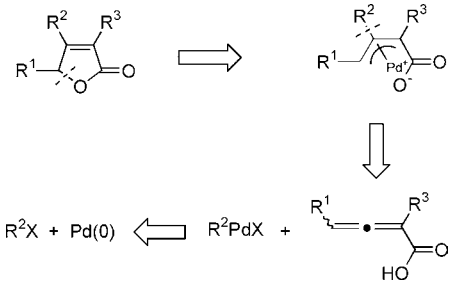
## I. Introduction

The report on the first synthetic allene can be dated back to as early as 1887,[1] and its structure was confirmed in 1954.[2] Allenes can also be found in many natural sources.[3] Due to the notion that these compounds would be thermally unstable, for a long period of time, their chemistry and synthetic routes had not been well established. However, due to the presence of the unique cumulated diene structual unit, allenes are a class of compounds with the following interesting properties:[4] (1) with up to four substituents, methodologies starting from allenes provide synthetic diversity; (2) the electron density and the reactivity of each carbon atom of the allene unit can be tuned by the substituent effect; (3) the inherent axial chirality provides a challenge for the highly stereoselective synthesis of optically active allenes and the transfer of the chirality of the allenes into final products (Scheme 1). Thus, the chemistry of allenes has been catching the attention of chemists[5] and some nice reviews have appeared.[6] In this Account, we will present some of our own recent results involving allenes with a nucleophilic functionality connected to the α-carbon atom.

**Scheme 1**




**Scheme 2**




## II. Cyclization of 2,3-Allenoic Acids

Besides the chirality and substituent-loading capability, the acidity of 2,3-allenoic acids provides the possibility of getting both enantiomers by a simple recrystallization of salts formed by their reaction with optically active bases, which are usually cheap and easily available. Butenolides are a class of compounds with a broad range of interesting biological activities, which have attracted much attention.[7] However, in all the procedures published, there are three problems remaining to be tackled (1) Lengthy procedure; (2) Transition metal does not participate in the formation of the chiral center; (3) Diversity (the possibility of facile solid-phase synthesis). Thus, cyclization reactions starting from 2,3-allenoic acids would address some of these issues leading to a library of butenolides[7] of high enantiopurities with diverse structures.

**A. Pd-Catalyzed Coupling Cyclization of Organic Halides with 2,3-Allenoic Acids.** On the basis of the carbopalladation of the allene moiety[8] of 2,3-allenoic acids followed by intramolecular trapping to construct a C−O bond, butenolides may be constructed by a one-pot reaction of $R^2X$ with 2,3-allenoic acids with the possible introduction of chirality in the prospective enantioselective C−O bond formation step (Scheme 2).

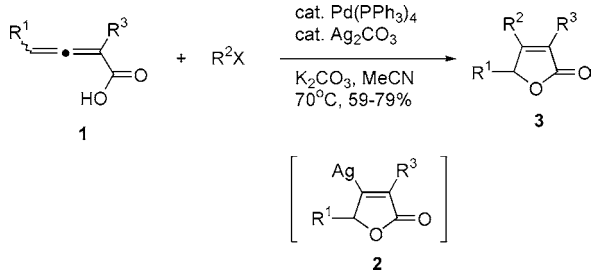
On the basis of this concept, a Pd(0)/$Ag^+$-cocatalyzed coupling−cyclization of organic halides and 2,3-allenoic acids was developed.[7,9] Here the addition of a catalytic amount of $Ag^+$ is the key, which may be responsible for the formation of a cyclic silver intermediate **2** (Scheme 3).[10]

Recently, much attention has been paid to the combinatorial synthesis of libraries of compounds with interesting properties.[11] We have succeeded in attaching an organic halide to a polymeric chain; upon its treatment

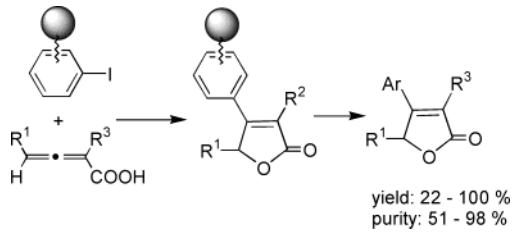
Shengming Ma is originally from Zhejiang Province, China. He received his B.S. degree in Chemistry from Hangzhou University (1986) and M.S. degree (1998) and a Ph.D. degree (1990) from Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences. After the postdoctoral research experience at ETH of Switzerland and Purdue University, he joined the faculty of Shanghai Institute of Organic Chemistry (1997), where currently he is Professor of Chemistry and the Director of State Key Laboratory of Organomeatllic Chemistry.

10.1021/ar020133k CCC: $25.00 
Published on Web 06/20/2003

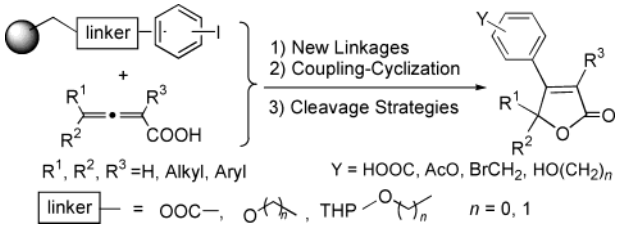
**Scheme 3**




**Scheme 4**




**Scheme 5**



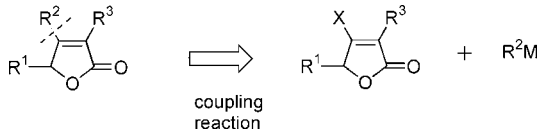

with an excess amount of 2,3-allenoic acids, the reaction afforded the polymer-supported butenolides.

The cleavage was troublesome at the beginning due to the relative stability of the C−O bond of the lactone ring as compared to that in the linkage.[12] With subtle adjustments, three protocols were developed for the removal of the polymer chain (Scheme 5):[13] (1) the carboxyl linkage was cleaved with $AlCl_3$; (2) the ether linkage was cleaved with a combination of $ZnBr_2$ and $CH_3COBr$, and with the benzylic ether linkerage, the final product can be a butenolide with a benzylic bromide moiety, which is suitable for further elaboration; (3) the THP linkage was cleaved with TFA and MeOH.

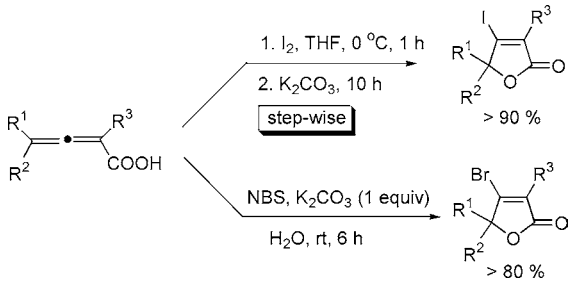
**B. $CuX_2$-Promoted Halolactonization of 2,3-Allenoic Acids.** Cross-coupling reactions, such as Kumada, Suzuki, Stille, Negishi couplings, have been proven to be a very powerful tool for the construction of C−C bonds and C−X bonds.[14] Due to the intrinsic problem of oxidative addition reaction of $sp^3$ C−X bond and the failure experienced with acetylenic halides, we started to consider the coupling reaction of organometallic reagents with $\beta$-halobutenolides as a complementary method for the synthesis of $\beta$-alkyl- or $\beta$-alkynyl-substituted butenolides (Scheme 6).

We have developed iodo- and bromo-lactonization reactions using $I_2$ and NBS, respectively (Scheme 7).[15] For the iodolactonization reaction, the stepwise addition of $I_2$ and $K_2CO_3$ is important to ensure a high yield of the product due to the possible conversion of 2,3-allenoic acids to 2,4-alkadienoic acids under the basic conditions.

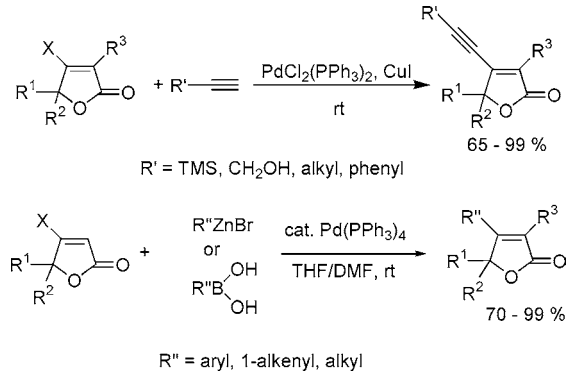
**Scheme 6**



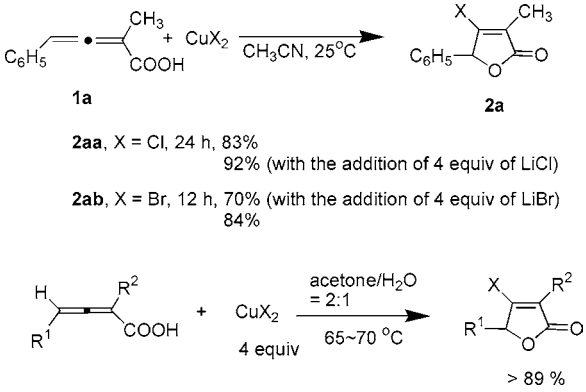

**Scheme 7**




**Scheme 8**




**Scheme 9**



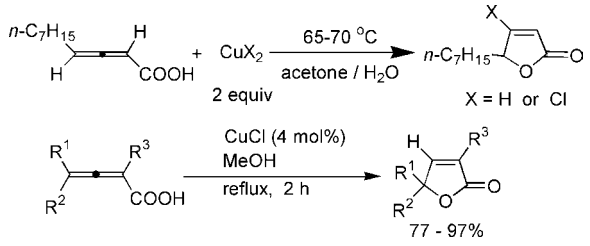




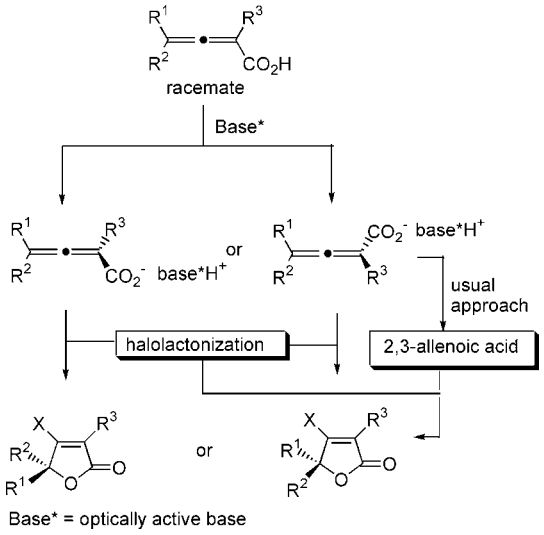
The Pd(0)-catalyzed coupling reaction with terminal alkynes and organic zincs underwent smoothly to afford $\beta$-differently substituted butenolides.[16,17] Using this method, sp-C-, $sp^2$-C-, and $sp^3$-C-centered substituents can be introduced to the $\beta$-position, and a formal synthesis of cis-whisky lactone was realized (Scheme 8).[16]

But for the synthesis of the corresponding chlorides, NCS either does not work well or does not work at all. Thus, the chlorolactonization reaction was established employing the reaction of $CuCl_2$ with 2,3-allenoic acids (Scheme 9). For 4-aryl-substituted 2,3-allenoic acids, the reaction with $CuX_2$ (X = Cl, Br) in MeCN at room temperature afforded the corresponding $\beta$-halobutenolides in good yields. However, the reaction of 4-alkyl-

**Scheme 10**




**Scheme 11**



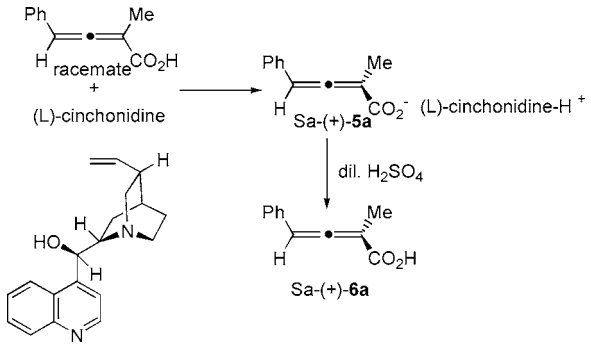

substituted 2,3-allenoic acids did not occur smoothly. Thus, a new set of reaction conditions, i.e., acetone/$H_2O$ (2:1) and 65−70 °C, was established (Scheme 10). This set of aqueous conditions is general for all the substrates. The reaction for bromides is usually faster and higher yielding than that for chlorides.[18]

Four equivalents of $CuX_2$ were required in order to avoid the formation of a cycloisomerization product. Actually when only a catalytic amount of CuCl was applied in MeOH or EtOH, the cycloisomerization product can be formed as the only product in fairly high yields, indicating that the in situ formed Cu(I) is responsible for the formation of the cycloisomerization product (Scheme 10).[10,18,19]

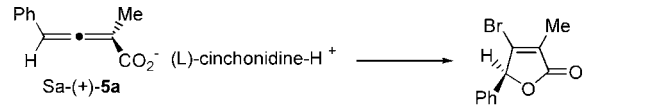
As previously discussed, the reaction of racemic 2,3-allenoic acids with optically active bases would afford optically active 1:1 acid−base salts, which may be easily enriched by recrystallization (Scheme 12).[20,21] Upon treatment with dilute aqueous $H_2SO_4$ solution, 2,3-allenoic acid was released, which may be halolactonized. Another possibility is to use the optically active 1:1 salt directly as the starting point for the halolactonization. However, attention should be paid to the influence of the steric information of the resolving optically active base on the stereochemical outcome of the halolactonization (Scheme 11).

Indeed, the reacion of racemic 2-methyl-4-phenyl-2,3-butadienoic acid with L-(−)-cinchonidine afforded the salt Sa-(+)-**5a**, which upon treatment with dilute $H_2SO_4$ afforded Sa-(+)-2-methyl-4-phenyl-2,3-butadienoic acid Sa-(+)-**6a**. The absolute configuration of the allene moiety

**Scheme 12**




**Scheme 13**




| reagent | reaction time (h) | yield of (S)-(+)-**7a** (ee) |
|---|---|---|
| NBS/$H_2O$/rt | 6 | 21% (94% ee) |
| NBS/$H_2O$/rt | 24 | 50% (64% ee) |
| $CuBr_2$/acetone-$H_2O$(2:1)/60-65°C | 3 | 95% (98% ee) |

was established by an X-ray diffraction study of a single crystal of (+)-**5a**, which contains a water molecule (Scheme 12).

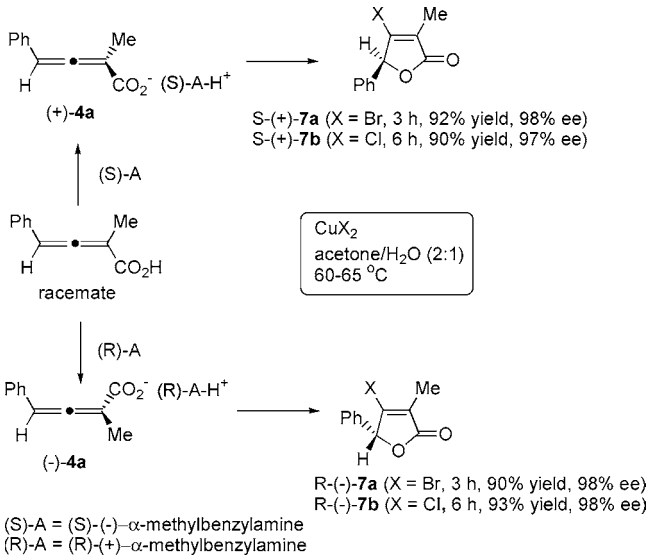
Its reaction with $CuX_2$ led to the synthesis of optically active $\beta$-halobutenolides **7** in high yields and ees.[21] Furthermore, it is interesting to note that the direct reaction of the salt Sa-(+)-**5a** with NBS in $H_2O$ afforded 21% of (*S*)-(+)-**7a** with 94% ee within 6 h. With prolonged reaction, the yield was improved to 50%. However, the enantiopurity of the $\beta$-bromobutenolide dropped to 64% ee (Scheme 13).

Luckily, when Sa-(+)-**5a** was treated with $CuBr_2$ in an aqueous solution of acetone, the reaction went smoothly to afford the product (*S*)-(+)-**7a** in 95% yield and 98% ee (Scheme 13). From this reaction, we can concluded that (1) the efficiency of chirality transfer is high and (2) the steric information in cinchonidine has no influence on the stereochemistry of this halolactonization.[21]

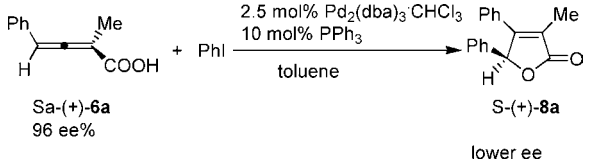
Since the steric information of the optically active base has no influence on the stereochemical outcome of the halolactonization reaction, we applied α-methylbenzylamine as the resolving agent. Two advantages for this compound are that (1) both *R* and *S* isomers are easily and cheaply available and (2) its molecular weight is low, which makes the reaction more atom economic. For the synthesis of (*S*)-$\beta$-halobutenolides, (*R*)-α-methylbenzylamine should be applied, while with (*S*)-α-methylbenzylamine, (*R*)-$\beta$-halobutenolides can be prepared (Scheme 14).

However, when we ran the corresponding coupling reaction of optically active $\beta$-halobutenolides with organometallic reagents,[15−17] the $\beta$-substituted butenolides were formed in good yields but with obvious loss of the enantiopurity. Therefore, for the propose of getting optically active $\beta$-aryl butenolides directly, the Pd(0)-catalyzed reaction of Sa-(+)-2-methyl-4-phenyl-2,3-butadienoic acid Sa-(+)-**6a** with PhI was studied. The results were rather disappointing with a highest ee of 60% (Scheme 15). [22]

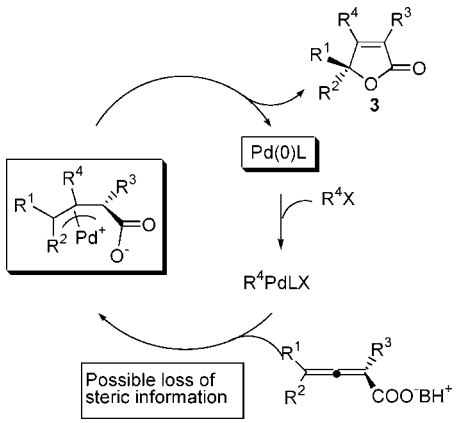
**Scheme 14**




**Scheme 15**




**Scheme 16**

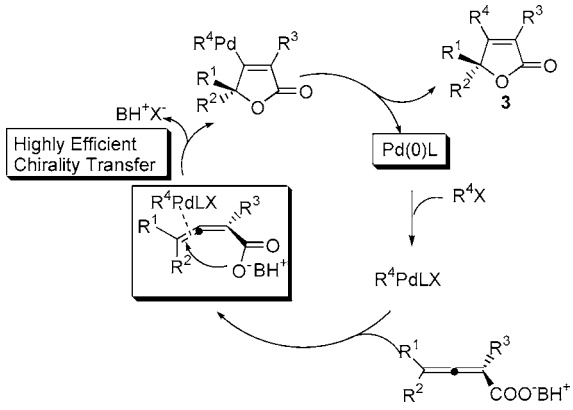



The chirality may be lost in formation of the $\pi$-allyl palladium intermediate by the carbopalladation reaction (Scheme 16).

This prompted us to try a different mechanistic pathway which involves a $R^4$ PdX-coordination-directed oxypalladation-reductive elimination process, through which the chirality may be reasonably kept (Schme 17).[22]

Thus, the 1:1 salt of Sa-(+)-2-methyl-4-phenyl-2,3-butadienoic acid and *i*-$Pr_2$NEt Sa-(+)-**9a** was prepared from their reaction in ethyl acetate at room temperature. Its corresponding Pd(0)-catalyzed reaction with PhI afforded (*S*)-(+)-**8a** in 91% ee, a dramatic improvement (Scheme 18).[22] With the cinchonidine salt Sa-(+)-**5a**, the reaction should be carried out in the presence of TBAB as the phase transfer catalyst.[22] The preformed $COO^-$ in the salt may speed up the oxypalladation process.

**Scheme 17**




The stereochemistry of this reaction was established by the X-ray diffraction study of Sa-2-(*n*-propyl)-4-(*p*-bromophenyl)-2,3-butadienoic acid and (*S*)-(+)-**8f** and the related study of (*S*)-(+)-**8g**, which provides further evidence for the plausible mechanism shown in Scheme 17 (Scheme 19).[22]

## III. $CuX_2$-Promoted Cyclization of 2,3-Allenoates

Usually 2,3-allenoic acids were prepared by the hydrolysis of 2,3-allenoates. In some cases, a mixture of 2,3-allenoic acids and 3-alkynoic acids can be obtained. Furthermore, it is more convenient to synthesize the optically active 2,3-allenoates. Thus, it is desirable to develop methodologies starting from 2,3-allenoates (Scheme 20).

As a first try, the direct reaction of 2,3-allenoates with $CuBr_2$ at 80−85 °C in equeous ethanol was developed, indicating that the carbonyl oxygen atom is nucleophilic enough to paticipate the cyclization reaction (Scheme 21).[23]

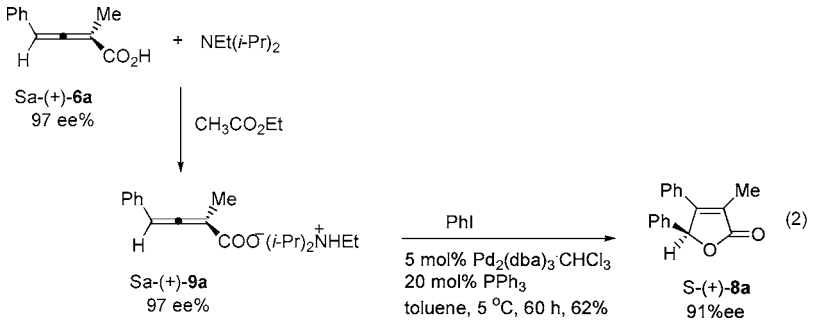
In some difficult cases, the benzyl ester is a better choice (Scheme 22).[23]

## IV. Cyclization of 2,3-Allenamides-Synthesis of $\gamma$-Lactams or $\gamma$-Iminolactones

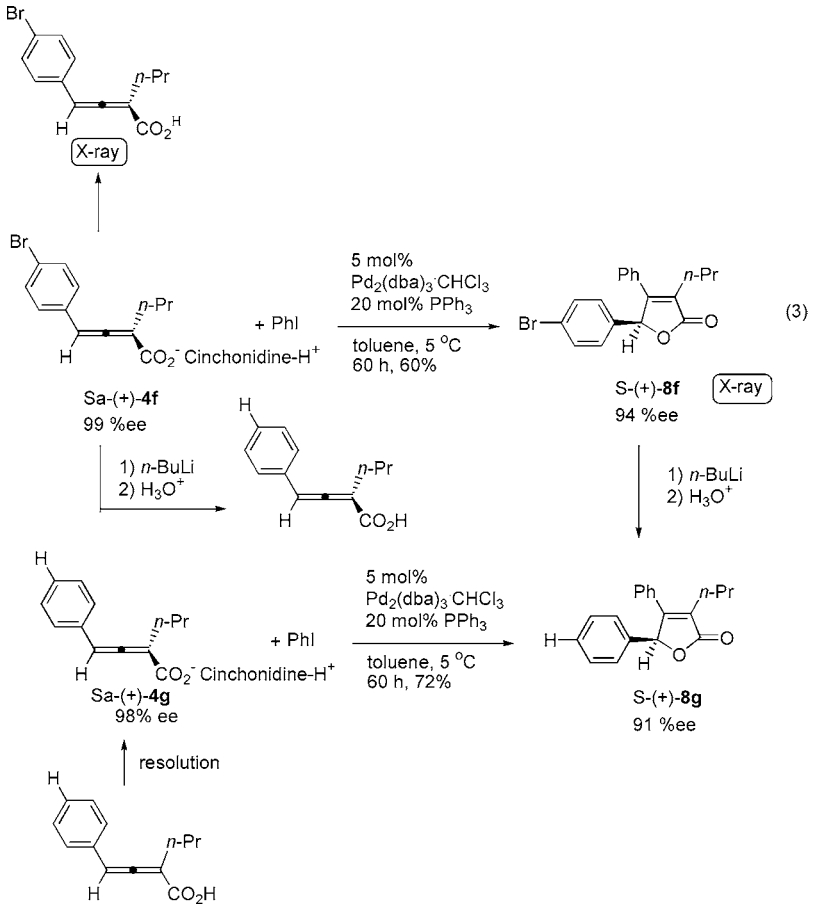
$Ag^+$-catalyzed cycloisomerization of 2,3-allenylamines and Pd(0)-catalyzed coupling cyclization of 2,3-allenylamines with organic halides have been studied by Claesson[24] and Ibuka,[25] respectively. No reports had been disclosed for the cyclization of 2,3-allenamides. On the other hand, 5-hydroxypyrrol-2(5H)-ones exhibit interesting biological activities.[26] Typical examples are **10**, **11**, and **12** (Scheme 23). Compared to other known methodologies,[27] due to the easy availability of starting materials, the methods described here are efficient, and the products were formed in high yields with high stereoselectivity and diversity.

It is interesting to observe that the $CuX_2$-promoted cyclization reaction of 2,3-allenamides afforded 5-hydroxypyrrol-2(5H)-ones directly in high yields. Here, the 4-halopyrrol-2(5H)-one formed during the reaction was oxidized by the oxygen in air. This process may also be mediated by Cu(II) (Scheme 24).[27]

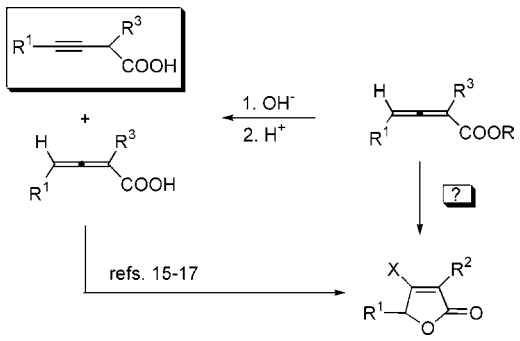
**Scheme 18**




**Scheme 19**

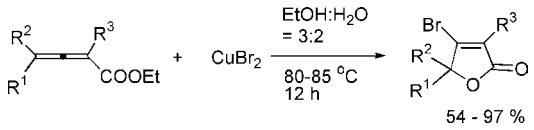



**Scheme 20**




The Pd(0)-catalyzed reaction of organic halides with 2,3-allenamides afforded 5-hydroxypyrrol-2(5H)-ones or iminolactones, depending on the steric effect of the substitutent(s) at the 4-position of 2,3-allenamides: with 4-monosubstituted 2,3-allenamides, the N-atom attacks the carbon terminal connected with $R^1$ group, while with 4,4-disubstituted 2,3-allenamides, the less hindered carbonyl oxygen acts as the nucleophile leading to iminolactones.[28]

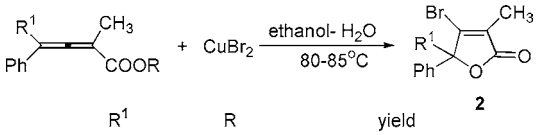
**Scheme 21**




## V. Pd-Catalyzed Reaction of 2,3-Allenols with Organic Halides

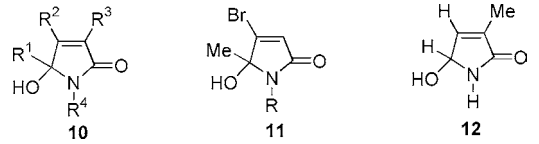
$Ag^+$-catalyzed cycloisomerizations of 2,3-allenols were reported by Claesson[29] and Marshall (Scheme 26).[30]

**Scheme 22**

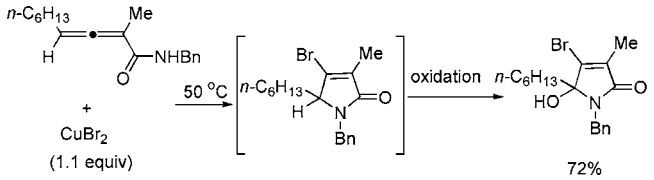


| $R^1$ | R | yield |
|---|---|---|
| H | $C_2H_5$ | 40% |
| H | $CH_2C_6H_5$ | 67% |
| $C_2H_5$ | $CH_2C_6H_5$ | 66% |

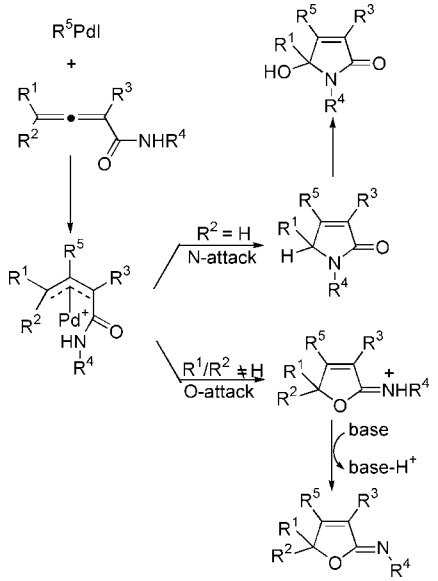
**Scheme 23**



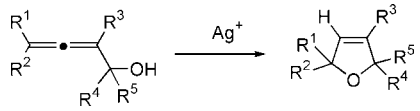
**Scheme 24**



**Scheme 25**

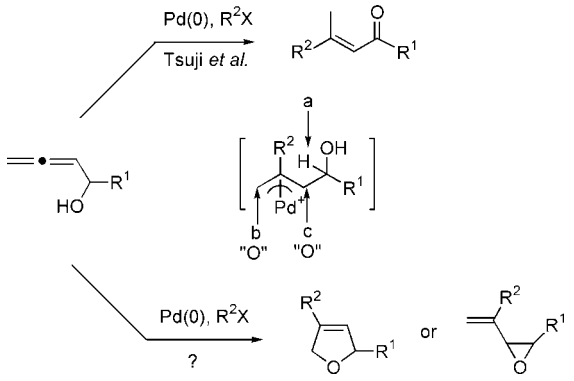


**Scheme 26**

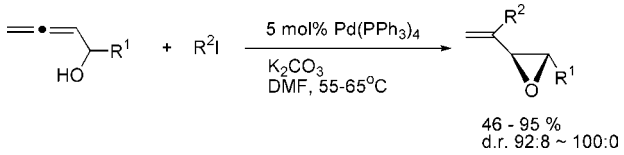


The Pd(0)-catalyzed reaction of organic halides with 2,3-allenols was first studied by Tsuji et al. in Japan,[31] in which, due to the involvement of $\beta$-H elimination, $\alpha,\beta$-unsaturated enone was formed (Scheme 29). Although it is well-known that there should be a big difference in terms of reactivity between 2,3-allenoic acids and 2,3-allenols, we utilized the same reaction conditions for the corresponding coupling-cyclization reaction of 2,3-allenoic acid with organic halide[7] to see the possibity of forming either 4-substituted-2,5-dihydrofurans or vinylic epoxides from 2,3-allenols (Scheme 27).

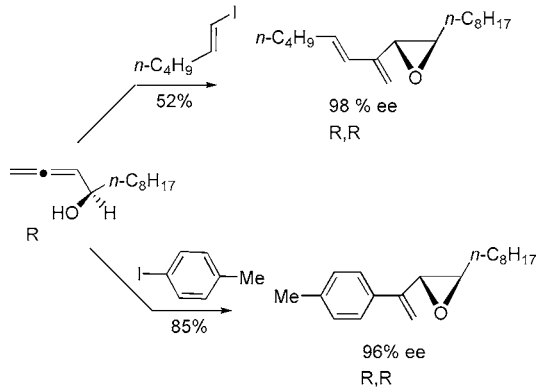
**Scheme 27**



**Scheme 28**



**Scheme 29**



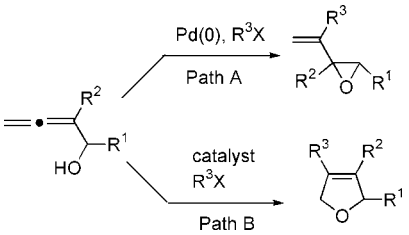
In this reaction,[32,33] we found that $Ag_2CO_3$ is not required, the best solvent is DMF, and the reaction afforded trans-three-membered vinylic epoxides exclusively and highly stereoselectively (Scheme 28).

Under these conditions, optically active trans-vinylic epoxides can be prepared by starting from the optically active 2,3-allenols. The absolute configuration of the chiral center adjacent to the $sp^2C$ center was controlled by the steric information of the chiral center of 2,3-allenol[34] due to the high diastereoselectivity of this reaction (Scheme 29).

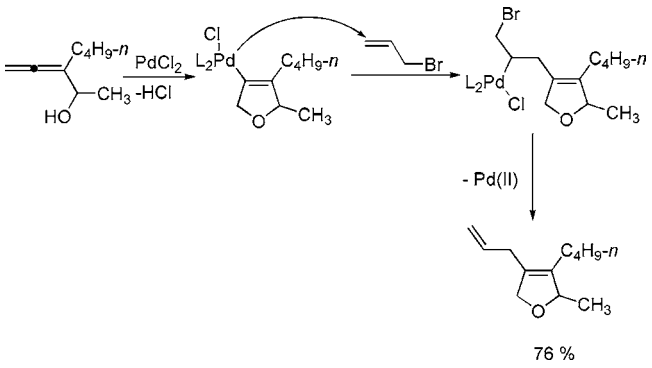
Furthermore, it is interesting to note that even with the increased hindrance by the introduction of $R^2$ group, the reaction still afforded three-membered products exclusively (Scheme 30).[34]

Pursuing the chemistry for the formation of five-membered 2,5-dihydrofunans from 2,3-allenols, a Pd(II)-catalyzed reaction was designed, in which a dehalopalladation reaction was used to regenerate the catalytically active Pd(II) species (Scheme 33). Indeed, a $PdCl_2$-catalyzed coupling reaction of allylic bromide with 2,3-allenols leading to the formation of 2,5-dihydrofurans in DMA occurred smoothly.[35] The reaction is efficient for primary, secondary, and tertiary alcohols.

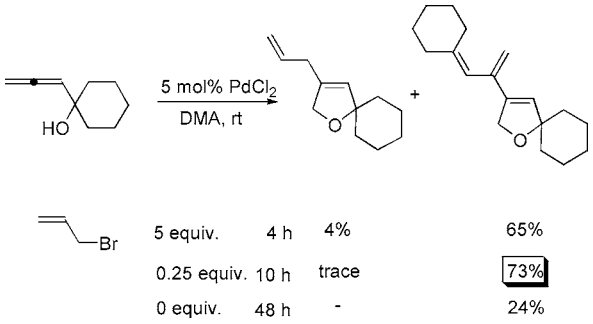
**Scheme 30**



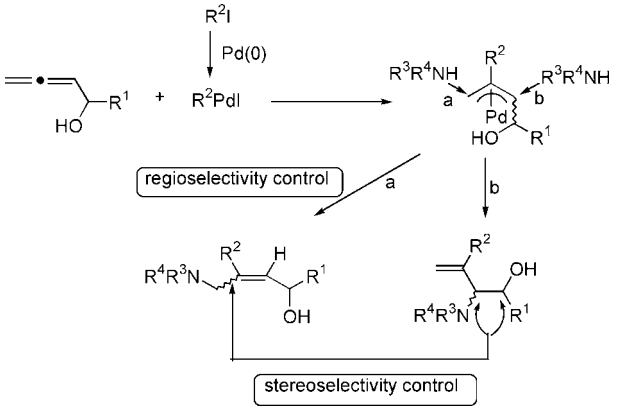

**Scheme 31**




**Scheme 32**



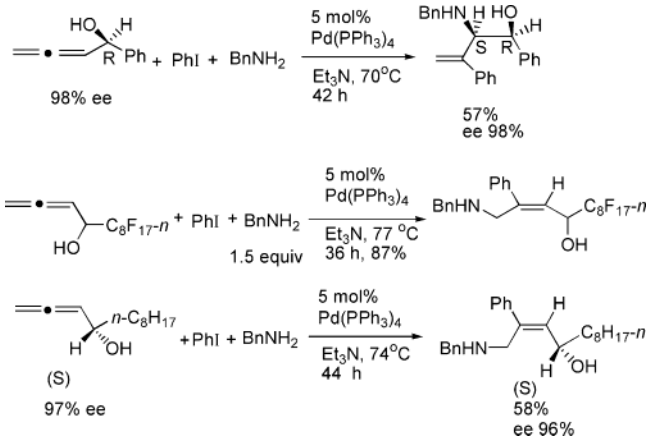

**Scheme 33**



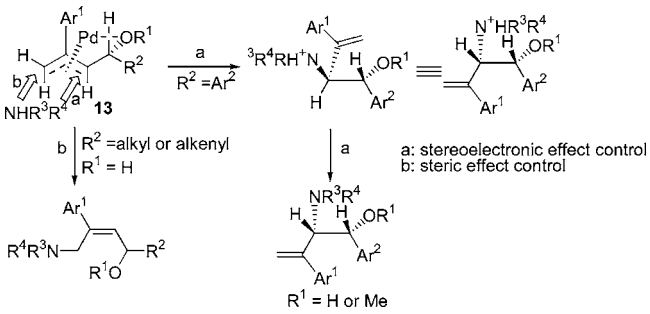

The substituent(s) of the allene moiety was found to play a very important role in this reaction. With unsubstituted allenols, dimerization was observed even in the presence of allyl bromide. This can be rationalized by the relatively higher reactivity of unsubstituted allene moiety, as compared to that of the C−C double bond in allyl bromide (Scheme 32).[36]

In the presence of an external nucleophile, i.e., amine, the three-component reaction with 2,3-allenols and organic halides would provide a convenient entry to amino alcohols, providing that the issues of regio- and stereoselectivity can be addressed (Scheme 33).

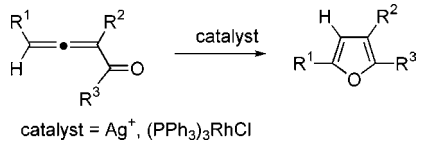
**Scheme 34**



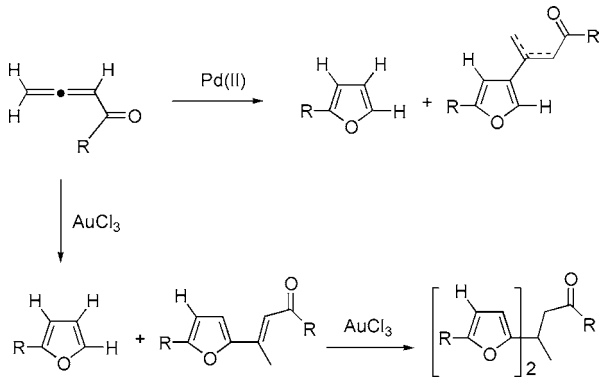

**Scheme 35**




**Scheme 36**

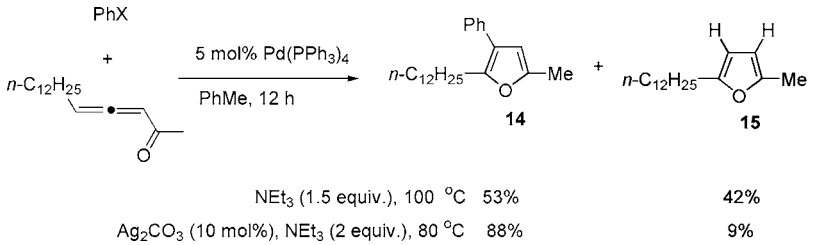



**Scheme 37**

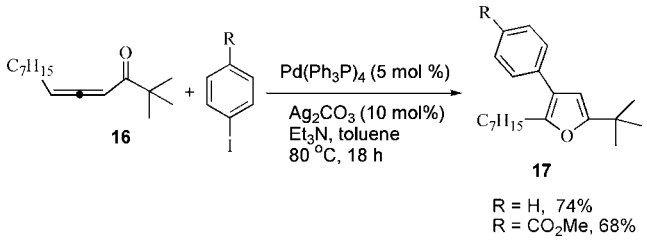



Through trial and error, it was observed that both issues can be controlled by the substituent adjacent to the hydroxyl group: with $R^1$ being the aryl group, the reaction afforded α-amino homoallyl alcohol; with $R^1$ being alkyl, alkenyl, and prefluoroalkyl groups, the reaction produced γ-amino allylic alcohols with a *Z*-selectivity for the C=C bond (Scheme 34).[37] $Et_3N$ is the best solvent for this reaction.

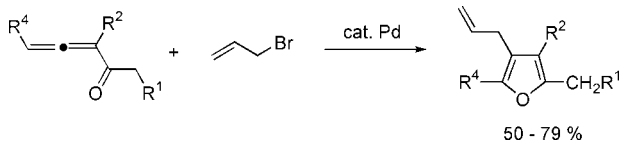
**Scheme 38**



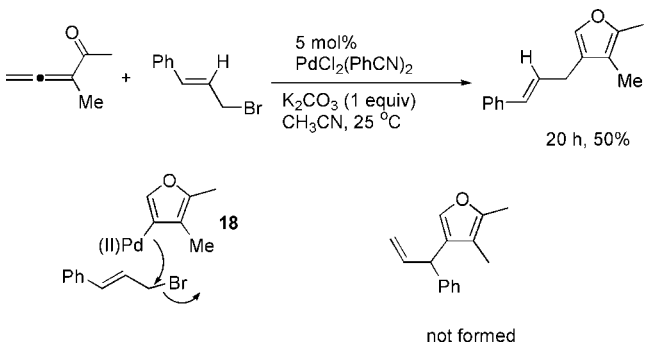

**Scheme 39**



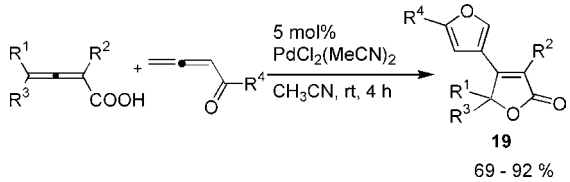

**Scheme 40**




**Scheme 41**




**Scheme 42**




The stereoelectronic effect of the two aryl groups in intermediate **13** may be responsible for the α-regioselectivity, and the steric effects of the two terminal substituents are the determining factor for the γ-regioselectivity, respectively (Scheme 35).[37]

## VI. Pd(0)-Catalyzed Coupling Cyclization of 1,2-Allenyl Ketones

Transition metal-catalyzed cycloisomerization of 1,2-allenyl ketones leading to furan derivatives has been extensively studied by Marshall[30b,38] and Hashmi[39] (Scheme 36).

Hashmi also demonstrated the $AuCl_3$-[39c] or Pd(II)-catalyzed[39b,40] dimeric cyclization of 1,2-allenyl ketones (Scheme 37).

When we applied the coupling−cyclization concept to the synthesis of polysubstituted furans, a mixture of coupling-cyclization product **14** and cycloisomerization product **15** was formed. Here again, a catalytic amount of $Ag^+$, i.e., $Ag_2CO_3$, is essential for the selective formation of coupling−cyclization product. Otherwise, the cycloisomerization product was formed in significant amounts (Scheme 38).[41] Compared with the cycloisomerization protocol, an extra substituent may be easily introduced into the 3-position of furans.

The reaction of *tert*-butyl-substituted 1,2-allenyl ketone 16 also afforded the corresponding products **17** in good yields, indicating that the carbonyl oxygen atom is nucleophilic enough to participate the coupling cyclization reaction (Scheme 39).

With the above-discussed protocol, only arylic and vinylic halides can be applied. For the synthesis of 3-allyl furans, the Pd-catalyzed coupling−cyclization reactions of 1,2-allenyl ketone with allylic bromides were also developed (Scheme 40).[42]

It is interesting to observe that the reaction with 3-phenyl-2(*E*)-propenyl bromide afforded 2,3-dimethyl-4-(3′-phenyl-2′(*E*)-propenyl)furan as the only product. The formation of 2,3-dimethyl-4-(1′-phenyl-2′-propenyl)furan was not observed, indicating a direct replacement of bromide by the $sp^2$ C−Pd species **18** or an oxidative addition−reductive elimination process (Scheme 41). [42]

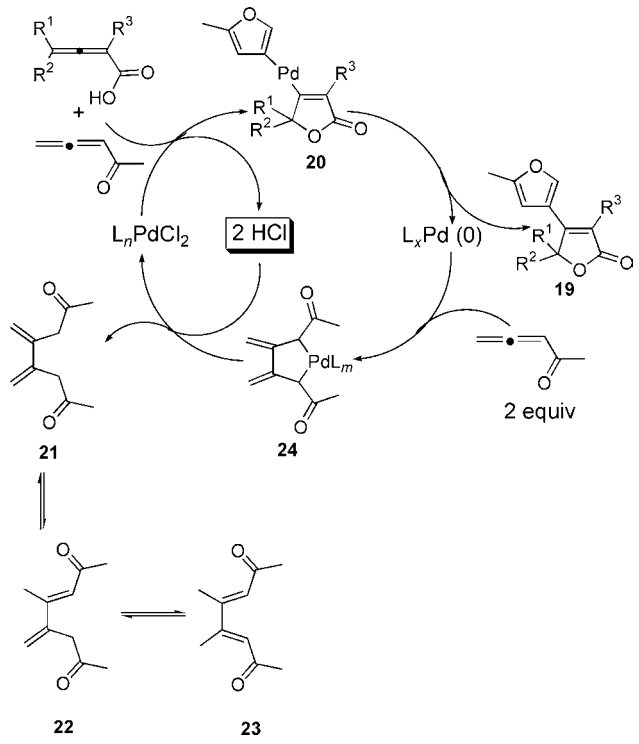
1,2-Allenyl ketone can also be applied as a partner in the Pd(II)-catalyzed biallene approach for the synthesis of dumbbell-type bicyclic compounds **19** (Scheme 42).[43]

Here an excess of 1,2-allenyl ketone was required not only for the bicyclization reaction itself but also for the regeneration of the catalytically active species. This was proved by the isolation of three 1,6-diketones **21**, **22** ,and **23**, which were formed by the protonolysis of cyclometalated intermediate **24**. The HCl formed in situ in the first step is also crucial for the catalytic cycle. The matched reactivities of 2,3-allenoic acids and 1,2-allenyl ketone are the key for the formation of intermediate **20** (Scheme 43).[39a,43]

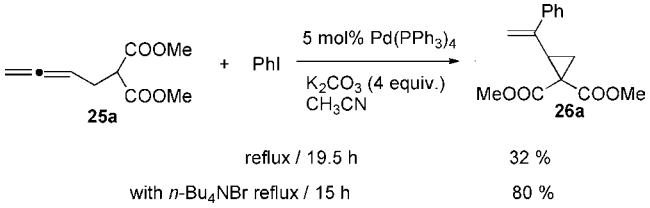
## VII. Pd(0)-Catalyzed Coupling-Cyclization of 2′-(2′,3′-Butadienyl)malonates with Organic Halides—Tuning the Regioselectivity

Cazes reported the Pd(0)-catalyzed coupling-cyclization of 2-(2′,3′-butadienyl)malonates and organic halides.[44] Except in a few limited cases, the reaction afforded five-

**Scheme 43**




**Scheme 44**




membered products highly selectively. We have observed that under the catalysis of $Pd(PPh_3)_4$ (5 mol %), the reaction of dimethyl 2-(2′,3′-butadienyl)malonate and PhI in the presence of $K_2CO_3$ (4 equiv) produced the three-membered vinylic cyclopropane derivative in $CH_3CN$ exclusively, albeit in a low yield. With the addition of *n*-$Bu_4NBr$, the three-membered product was formed in 80% yield as the only product (Scheme 44).[45]

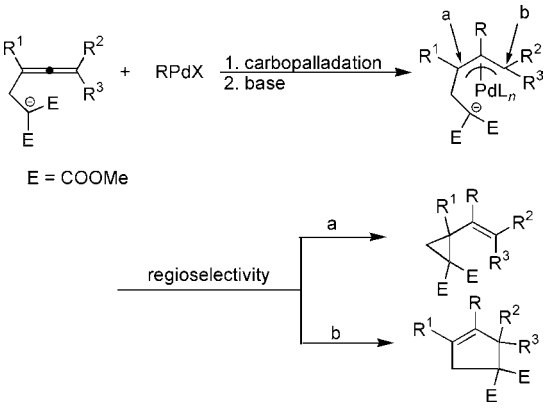
Thus, we attempted to develop different reaction conditions for the control of regioselectivity of this reaction (Scheme 45).[46]

The same reaction in THF afforded the three-membered product exclusively even in the absence of *n*-$Bu_4NBr$. Under conditions A, even with dimethyl 2-(2′-benzyl-2′,3′-butadienyl)malonate, the reaction afforded the cyclopropane derivative highly selectively. The formation of cyclopentene derivative was limited to 2−3% (Scheme 46).[46]

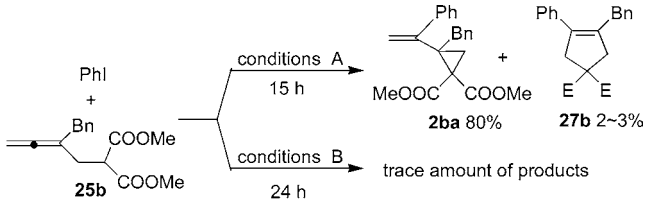
By tuning the solvent and base, reaction conditions (conditions C) for the highly selective formation of cyclopentene derivatives were also found (Scheme 47). However, conditions C can only be perfectly applied to the 2′-substituted malonate.[46]

The reactions with 2-(2′-unsubstituted-2,3-butadienyl)malonates under conditions C afforded a mixture of

**Scheme 45**



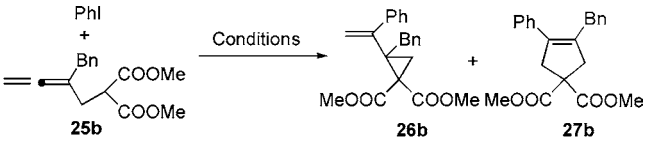

**Scheme 46**




**Conditions A** = 5 mol % $Pd(PPh_3)_4$, $K_2CO_3$ (4 equiv.), 10 mol % of n-$Bu_4NBr$, $CH_3CN$, reflux

**Conditions B** = 5 mol % $Pd(PPh_3)_4$, $K_2CO_3$ (4 equiv.), THF, reflux

**Scheme 47**



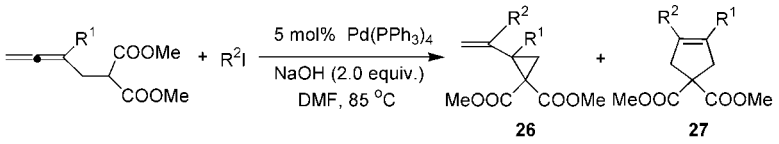

| Conditions | 26b | 27b |
|---|---|---|
| 2 mol % $Pd_2(dba)_3{\cdot}CHCl_3$, 4 mol % dppe, $K_2CO_3$ (4.0 equiv.), 10 mol % of *n*-$Bu_4NBr$, and DMSO, 85 °C, 24 h | 49% | 13% |
| 2 mol % $Pd_2(dba)_3{\cdot}CHCl_3$, 4 mol % dppe, NaH (1.1 equiv.), DMSO, 85 °C 12.5 h | 14% | 58% |
| **Conditions C**, (5 mol % $Pd(PPh_3)_4$, NaH (1.1 equiv.), DMSO, 85 °C), 12 h | 0 | **88%** |

three-membered and five-membered products. Conditions D then were developed, under which the reaction produced cyclopentene derivatives exclusively. With this set of reaction conditions, the selectivity problem under conditions C was also addressed nicely (Scheme 48).[46]

Furthermore, it is interesting to observe that the steric effect of organic halides also has an obvious impact on the regioselectivity. Under conditions A, the reaction of dimethyl (2′-benzyl-2′,3′-butadienyl)malonate with PhI afforded three-membered product **26b**, while the same reaction except that *o*-methylphenyl iodide was used instead of PhI afforded five-membered product **27c** exclusively (Scheme 49).

It is proposed that the cyclopropane derivative may be formed via the intermediate *syn*-**28** while the five-

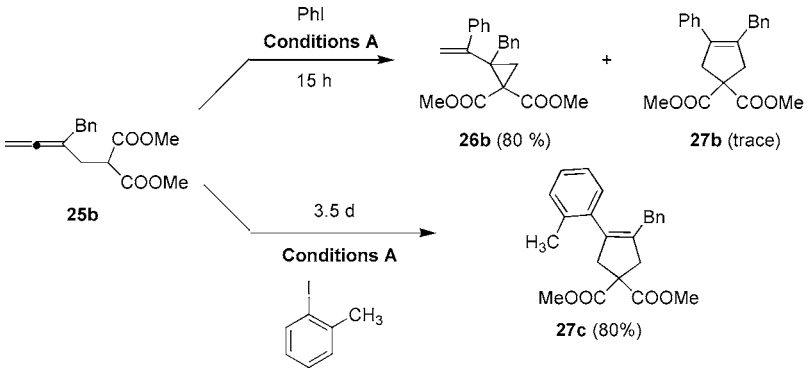
**Scheme 48**



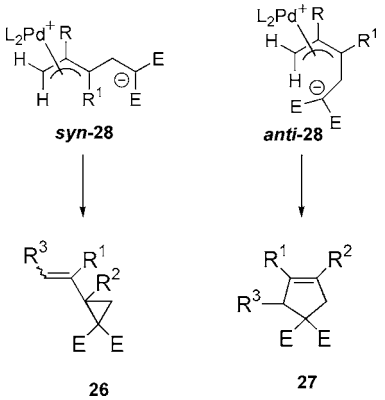

| entry | $R^1$ | $R^2$ | Conditions D | | Conditions C | |
|---|---|---|---|---|---|---|
| | | | **26** (%) | **27** (%) | **26** (%) | **27** (%) |
| 1 | H | *p*-$MeC_6H_4$ | 0 | 63 | - | - |
| 2 | H | *p*-$MeOC_6H_4$ | 0 | 57 | - | - |
| 3 | *n*-Pr | *p*-$MeOC_6H_4$ | 0 | 51 | 7 | 47 |
| 4[a] | *n*-Pr | *p*-$MeOC_6H_4$ | 0 | 70 | - | - |
| 5 | *n*-Pr | *p*-$MeO_2CC_6H_4$ | 0 | 52 | 8 | 54 |

[a] NaH (1.1 equiv.) was used instead of NaOH as the base.

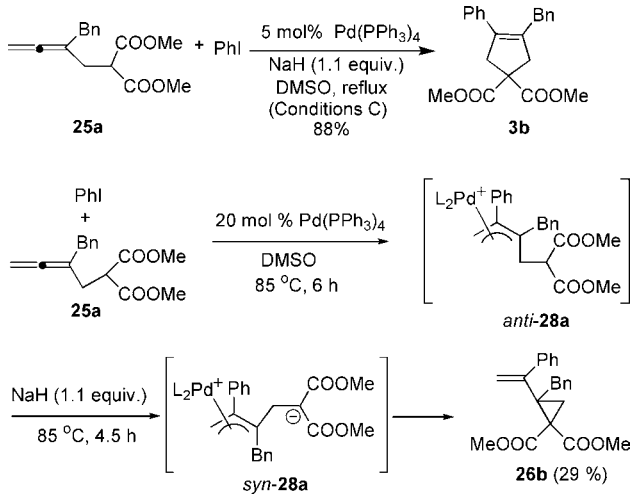
**Scheme 49**




**Scheme 50**




**Scheme 51**




membered product was formed via the intermediate *anti*-**28** (Scheme 50).

According to this assumption, it is believed that the syn-intermediate **28** is thermally more stable than the anti-intermediate **28**.[47] Thus, if enough time is allowed, the latter will convert to the former. This was proved by the experimental data. When a mixture of PhI and 2-(2′-benzyl-2′,3′-butadienyl)malonate was treated with 20 mol % $Pd(PPh_3)_4$ in DMSO at 85 °C for 6 h first, followed by the addition of NaH (1.1 equiv), this process afforded the three-membered product **26b** in 29% yield, a result in contrast to the same reaction, except that $Pd(PPh_3)_4$ and NaH were added simutaneously (Scheme 51).

## VIII. Concluding Remarks and Perspectives

We have demonstrated that allenes with a nucleophilic functionality connected to the α-carbon atom are versatile starting materials for some cyclic and acyclic compounds of synthetic and biological importance. Due to the substituent-loading capability and diversity of the functionalities, these methodologies are efficient, selectivity tunable, and diverse. Due to the chirality of the allene moiety and any chiral elements in the starting compounds, synthesis of compounds with optical activity is possible, depending on the availability of the optically active starting materials and the efficiency of chirality transfer. Future attention must be focused on the enantioselective synthesis of optically active allenes with a functionality.[34,48] Attention should also be directed to the influence of the nature of the tether between the allene moiety and the functionality on tuning the reactivity and selectivity,

polycomponent coupling cyclization reaction, new reaction patterns with different metal catalysts, etc. More research will be carried out to demonstrate the potentials of allenes.

*This research was supported by the State Basic Research Development Program (Grant G2000077500), the National Natural Science Foundation of China, Chinese Academy of Sciences, Shanghai Municipal Committee of Science and Technology, and Hong Kong Qiu Shi Foundation of Science and Technology (1999-2003) (Qiu Shi Award for Young Chinese Scientific Workers). I am grateful to my co-workers, whose names are cited in the references, for their hard work.*

## Note Added after ASAP Posting

This paper first appeared on the Web with an error in Scheme 14. The correct version was published 6/25/2003.

## References

(1) Burton, B. S.; Pechman, H. V. Ueber die Einwirkung von Chlorphosphor auf Acetondicarbonsäureäther. *Chem. Ber.* **1887**, *20*, 145−149.

(2) Jones, E. R. H.; Mansfield, G. H.; Whiting, M. C. Research on Acetylenic Compounds. Part XLVII. The Prototropic Rearrangement of Some Acetylenic Dicarboxylic Acids. *J. Chem. Soc.* **1954**, 3208−3212.

(3) Staudinger, H.; Ruzicka, L. InsektentÖtende Stoffe I. Über Isolierung und Konstitution des Wirksamen Teiles des Dalmatinischen Insektenpulvers. *Helv. Chim. Acta* **1924**, *7*, 177−201.

(4) (a) In *Allenes in Organic Synthesis*; Schuster, H. F.; Coppola, G. M., Eds.; John Wiley & Sons: New York, 1984. (b) In *The Chemistry of Ketenes, Allenes, and Related Compounds Part 1*; Patai, S., Ed.; John Wiley & Sons: New York, 1980.

(5) For some of the most recent publications, see: (a) Kang, S.-K.; Ha, Y.-H.; Ko, B.-S.; Lim, Y.; Jung, J. Palladium-Catalyzed Regio- and Diastereoselective Tandem Silastannylation/Allyl Addition of Allene Aldehydes and Allene Ketones: Synthesis of cis Cyclopentanols and Cyclohexanols. *Angew. Chem., Int. Ed.* **2002**, *41*, 343−345. (b) Ha, Y.-H.; Kang, S.-K. Palladium-Catalyzed Tandem Cyclization of Allenyl-Aldehydes and -Ketones with Aryl Iodides and $Bu_3SnSnBu_3$. *Org. Lett.* **2002**, *4*, 1143−1146. (c) Liu, G.; Lu, X. Palladium(II)-Catalyzed Tandem Reaction of Intramolecular Aminopalladation of Allenyl N-Tosylcarbamates and Conjugate Addition. *Org. Lett.* **2001**, *3*, 3879−3882. (d) Dieter, R. K.; Yu, H. Synthesis of 3-Pyrrolines, Annulated 3-Pyrrolines, and Pyrroles from α-Amino Allenes. *Org. lett.* **2001**, *3*, 3855−3858. (e) Kang, S.-K.; Kim, K.-J.; Yu, C.-M.; Hwang, J.-W.; Do, Y.-K. Ru-Catalyzed Cyclocarbonylation of α- and β-Allenic Sulfonamides: Synthesis of γ- and δ-Unsaturated Lactams. *Org. Lett.* **2001**, *3*, 2851−2853. (f) Bates, R. W.; Satcharoen, V. S. Diastereoselective Cobalt-mediated Acylation-cyclization of Allenes. *Synlett* **2001**, 532. (g) Kang, S.-K.; Kim, K.-J. Palladium(0)-Catalyzed Carbonylation-Coupling-Cyclization of Allenic Sulfonamides with Aryl Iodides and Carbon Monoxide. *Org. Lett.* **2001**, *3*, 511−514. (h) Karstens, W. F. J.; Klomp, D.; Rutjes, F. P. J. T.; Hiemstra, H. *N*-Acyliminium ion chemistry and palladium catalysis: a useful combination to obtain bicyclic heterocycles. *Tetrahedron* **2001**, *57*, 5123−5130.

(6) For reviews, see: (a) Zimmer, R.; Dinesh, C. U.; Nadanan, E.; Hhan, F. A. Palladium-Catalyzed Reactions of Allenes. *Chem. Rev.* **2000**, *100*, 3067−3126. (b) Yamamoto, Y.; Radhakrishnan, U. Palladium Catalysed Pronucleophile Addition to Unactivated Carbon−Carbon Multiple Bonds. *Chem. Soc. Rev.* **1999**, *28*, *199*. (c) Hiemstra, Allenes in Novel Palladium-Catalyzed and Acid-Mediated Cyclization Process. *Curr. Trends Org. Synth.* **1998**. (d) Reissig, H.-U.; Hormuth, S.; Schade, W.; Amombo, M. O.; Watanabe, T.; Pulz, R.; Hausherr, A.; Zimmer, R. Stereoselective Syntheses of Heterocycles with Lithiated Methoxyallene. *J. Heterocyclic Chem.* **2000**, *37*, 597. (e) Reissig, H.-U.; Schade, W.; Amombo, G. M. O. Pulz, R. Hausherr, A. Stereoselective syntheses of heterocycles via metalated alkoxyallenes. *Pure Appl. Chem.* **2002**, *74*, 175−180. (f) Ma, S.; Li, L. An Efficient New Methodology for the Synthesis of 1-Functionalized 2-Halo-2-alkenes via Hydrohalogenation Reaction of Electron-Deficient Allenes. *Synlett* **2001**, 1206−1213. **(**g) Hashmi, A. S. K. Palladium-Catalyzed Reactions of Allenes. *Angew. Chem., Int. Ed.* **2000**, *112*, 3590−3593. Ma, S. *Carbopalladation of allenes*. In *Handbook of Organopalladium Chemistry for Organic Synthesis*; Negishi, E. Ed.; Wiley-Interscience: New York, 2002; p 1491.

(7) Ma, S.; Shi, Z. Pd(0)/$Ag^+$-Cocatalyzed Cyclization Reaction of 1,2-Allenic Carboxylic Acids with Aryl/Alkenyl Halides-An Efficient Synthesis of Butenolides. *J. Org. Chem*. **1998**, *63*, 6387−6389 and references therein.

(8) Shimizu, I.; Tsuji, J. Palladium-Catalyzed Synthesis of 2,3-Disubstituted Allylamines by Regioselective Aminophenylation or Aminoalkenylation of 1,2-Dienes. *Chem. Lett.* **1984,** 233−236; Ahmar, M.; Cazes, B.; Gore, J. Synthese de Dienes-1,3- et de Styrenes Fonctionalises par Carbopalladation Catalytique D'allenes. *Tetrahedron Lett.* **1984**, *25*, 4505−4508.

(9) Ma, S.; Shi, Z.; Wu, S. Enantioselective Synthesis of β-Arylbutenolides via Palladium(0)-Catalyzed Asymmetric Coupling-Cyclization Reaction of Racemic Allenic Carboxylic Acids with Aryl Iodides. *Tetrahedron: Asymmetry* **2001**, *12*, 193−195.

(10) Marshall, J. A.; Wolf, M. A.; Wallace, E. M. Synthetic Routes to Allenic Acids and Esters and Their Stereospecific Conversion to Butenolides. *J. Org. Chem.* **1997**, *62*, 367−371.

(11) For some seminal papers in this area, see: (a) For drug discovery: Balkenhohl, F.; Bussche-Hünnefeld, C.; Lansky, A.; Zechel, C. Combinatorial Synthesis of Small Organic Molecules. *Angew. Chem., Int. Ed.* **1996**, *35*, 2288−2337. (b) For material screening: Xiang, X.-D.; Sun, X.; Briceño, G.; Lou, Y.; Wang, K.-A.; Chang, H.; Wallace-Freedman, W. G.; Chen, S.-W.; Schultz, P. G. A Combinatorial Approach to Materials Discovery. *Science* **1995,** *268*, 1738. Briceño, G.; Chang, H.; Sun, X.; Schultz, P. G.; Xiang, X.-D. A Class of Cobalt Oxide Magnetoresistance Materials Discovered with Combinatorial Synthesis. *Science* **1995**, *270*, 273. Danielson, E.; Golden, J. H.; McFarland, E. W.; Reaves, C. M.; Weinberg, W. H.; Wu, X. D. A combinatorial approach to the discovery and optimization of luminescent materials. *Nature* **1997**, *389*, 944. Wang, J.; Yoo, Y.; Gao, C.; Takeuchi, I.; Sun, X.; Chang, H.; Xiang, X.-D.; Schultz, P. G. Identification of a Blue Photoluminescent Composite Material from a Combinatorial Library. *Science* **1998**, *279*, 1712. Brocchini, S.; James, K.; Tangpasuthadol, V.; Kohn, J. A Combinatorial Approach for Polymer Design. *J. Am. Chem. Soc.* **1997**, *119*, 4553. Akporiaye, D. E.; Dahl, I. M.; Karlsson, A.; Wendelbo, R. Combinatorial Approach to the Hydrothermal Synthesis of Zeolites. *Angew. Chem., Int. Ed. Engl.* **1998**, *37*, 609. (c) For catalyst screening: Reddington, E.; Sapienza, A.; Gurau, B.; Viswanathan, R.; Sarangapani, S.; Smotkin, E. S.; Mallouk, T. E. Combinatorial Electrochemistry: A Highly Parallel, Optical Screening Method for Discovery of Better Electrocatalysts. *Science* **1998**, *280*, 1735. Senkan, S. M. High-throughput screening of solid-state catalyst libraries. *Nature* **1998**, *394*, 350. Boussie, T. R.; Coutard, C.; Turner, H.; Murphy, V.; Powers, T. S. Solid-Phase Synthesis and Encoding Strategies for Olefin Polymerization Catalyst Libraries. *Angew. Chem. Int. Ed.* **1998**, *37*, 3272. Hinderling, C.; Chen, P. Rapid Screening of Olefin Polymerization Catalyst Libraries by Electrospray Ionization Tandem Mass Spectrometry. *Angew. Chem., Int. Ed.* **1999**, *38*, 2253.

(12) Ma, S.; Duan, D.; Shi, Z. Palladium(0)-catalyzed Cyclization Reaction of Polymer-Supported Aryl Iodides with 1,2-Allenyl Carboxylic Acids. A Facile Solid-Phase Synthesis of Butenolides. *Org. Lett.* **2000**, *2*, 1419−1422.

(13) Ma, S.; Duan, D.; Wang, Y. Palladium(0)-Catalyzed Coupling-Cyclization Reaction of Polymer-Supported Aryl Iodides with 1,2-Allenyl Carboxylic Acids. Solid Phase Parallel Synthesis of Butenolides. *J. Comb. Chem.* **2002**, *4*, 239−247.

(14) In *Metal-Catalyzed Cross-Coupling Reactions*; Stang, P., Diederich, F., Eds.; VCH: Weiheim, 1998.

(15) Ma, S.; Shi, Z.; Yu, Z. Synthesis of β-Halobutenolides and Their Pd(0)-Catalyzed Cross-Coupling Reactions with Terminal Alkynes. A General Route to β-(1′-Alkynyl)butenolides. *Tetrahedron Lett.* **1999**, *40*, 2393−2396.

(16) Ma, S.; Shi, Z.; Yu, Z. Synthesis of β-Halobutenolides and Their Pd(0)−Catalyzed Cross-Coupling Reactions with Terminal Alkynes and Organozinc Reagents. A General Route to β−Substituted Butenolides and Formal Synthesis of *cis*-Whisky Lactone. *Tetrahedron* **1999**, *55*, 12137−12148.

(17) Ma, S.; Shi, Z. Synthesis of 4-Halo-2(5*H*)-furanones and Their Suzuki-Coupling Reactions with Organoboronic Acids. A General Route to 4-Aryl-2(5*H*)-furanones. *Chin. J. Chem.* **2001**, *19*, 1280−1284.

(18) Ma, S.; Wu, S. $CuX_2$-Mediated Cyclization Reaction of 2,3-Allenoic Acids. An Efficient Route to β-Halobutenolides. *J. Org. Chem.* **1999**, *64*, 9314−9317.

(19) Ma, S.; Yu, Z.; Wu, S. CuCl-Catalyzed Cycloisomerization Reaction of 1,2-Allenyl Carboxylic Acids. A Cost-Effective Synthesis of β-Unsubstituted Butenolides. *Tetrahedron* **2001**, *57*, 1585−1588.

(20) Runge, W.; Kresze, G.; Liebigs, Darstellung von Allencarbonsauren nach der phosphonatmethode und inre Enantiomerentrennung. *Ann. Chem.* **1975**, 1361−1378.
(21) Ma, S.; Wu, S. Novel $CuX_2$-Mediated Cyclization of Acid-Base Salts of (L)-Cinchonidine or (D)-/(L)-α-Methylbenzylamine and 2,3-Allenoic Acids in Aqueous Medium. An Efficient Entry to Optically Active β-Halobutenolides. *Chem. Commun.* **2001**, 441−442.
(22) Ma, S.; Shi, Z. Mechanistic Switch Leading to Highly Efficient Chirality Transfer in Pd(0)-Catalyzed Coupling-Cyclization of Aryl Iodides with 1:1 Acid-Base Salts of 2,3-Allenoic Acids and L-(−)-Cinchonidine or D-(+)-/L-(−)-α-Methylbenzylamine. Enantioselective Synthesis of Highly Optically Active 3-Aryl Polysubstituted Butenolides. *Chem. Commun.* **2002**, 540−541.
(23) Ma, S.; Wu, S. $CuBr_2$-Mediated Direct Aqueous Bromolactonization of 2,3-Allenoates. An Efficient access to β-Bromobutenolides. *Tetrahedron Lett.* **2001**, *42*, 4075−4077.
(24) Claesson, A.; Sahlberg, C.; Luthman, K. Allenes and Acetylenes. XVIII. Synthesis of 3-Pyrronlines by Silver(I)-catalyzed Cyclization of Allenic Amines. *Acta Chem. Scand., Ser. B* **1979**, *33*, 309−310.
(25) Ohne, H.; Toda, A.; Miwa, Y.; Taga, T.; Osawa, E.; Yamaoka, Y.; Fujii, N.; Ibuka, T. First Palladium-Catalyzed Aziridination Reaction of Amino Allenes. *J. Org. Chem.* **1999**, *64*, 2992−2993. Anzai, M.; Toda, A.; Ohno, H.; Takemoto, Y.; Fujii, N.; Ibuka, T. Palladium-catalyzed Regio- and Stereoselective Synthesis of N-Protected 2,-Dialkylated Azacyclobutanes from Amino Allenes. *Tetrahedron Lett.* **1999**, *40*, 7393−7397. Ohno, H.; Anzai, M.; Toda, A.; Ohishi, S.; Fijii, N.; Tanaka, T.; Takemoto, Y.; Ibuka, T. Stereoselective Synthesis of 2-Alkenylaziridines and 2-Alkenylazetidines by Palladium-Catalyzed Intramolecular Amination of α- and β-Amino Allenes. *J. Org. Chem.* **2001**, *66*, 4904−4914.
(26) (a) Wooldridge, T. A.; Lightner, D. A. Syntheses of "Oxidized" Hemopyrrole and Kryptopyrrole: Porphyric Monopyrroles. *J. Heterocyclic Chem.* **1977**, *14*, 1283−1284. (b) Semonský, M.; Černý, A.; Kotva, R.; Zikán, V.; Kakáč, B. Substances with Antineoplastic Activity XXV. Some γ-Alkyl-α,β-Dichloro(Dibromo)-α,β-crotonolactones; Products of Cordensation of γ-Methyl-α,β-Dibromo-α,β-Crotorolactone with Some Primary Amine. *Collect. Czech. Chem. Commun.* **1968**, *33*, 2698−2705. (c) For isolation and testing, see: Wiedhopf, R. M.; Trumbull, E. R.; Cole, J. R. Antitumor Agents from Jatropha macrorhiza (Euphorbia-ceae) I: Isolation and characterization of Jatropham. *J. Pharm. Sci.* **1973**, *62*, 1206−1207. For the revision of the structure, see: Yakushijin, K.; Kozuka, M.; Ito, Y.; Suzuki, R.; Furukawa, H. Ring Transformation of 2-Furylcarbamates To 5-Hydroxy-3-pyrrolin-2-ones. Revised Structure of Jatropham. *Heterocycles* **1980**, *14*, 1073−1076.
(27) Ma, S.; Xie, H. Unexpected Facile Sequential Halolactamization-Hydroxylation of 2,3-Allenamides with $CuX_2$ for the Efficient Synthesis of 4-Halo-5-hydroxypyrrol-2(5H)-ones. *Org. Lett.* **2000**, *2*, 3801−3803.
(28) Ma, S.; Xie, H. Steric Hindrance-Controlled Pd(0)-Catalyzed Coupling-Cyclization of 2,3-Allenamides and Organic Iodides. An Efficient Synthesis of Iminolactones and γ-Hydroxy-γ-lactams. *J. Org. Chem.* **2002**, *67*, 6575−6578.
(29) Olsson, L.-I.; Claesson, A. Synthesis of 2,5-Dihydrofurnas and 5,6-Dihydro-2H-pyrans by Silver(I)-Catalyzed Cyclization of Allenic Alcohols. *Synthesis* **1979**, 743−745.
(30) (a) Marshall, J. A.; Pinney, K. G. Stereoselective Synthesis of 2,5-Dihydrofurnas by Sequential SN2′-Cleavage of Alkynyloxiranes and $Ag^+$-catalyzed Cyclization of the Allenylcarbinol Products. *J. Org. Chem.* **1993**, *58*, 7180−7184. (b) Marshall, J. A.; Sehon, C. A. Synthesis of Furans and 2,5-Dihydrofurans by Ag(I)-Catalyzed Isomerization of Allenoates, Alkynyl Allylic Alcohols, and Allenylcarbinols. *J. Org. Chem.* **1995**, *60*, 5966−5968.
(31) Shimizu, I.; Sugiura, T.; Tsuji, J. Facile Synthesis of β-Aryl or β-Alkenyl- methyl α,β-unsaturated Carbonyl Compounds by Palladium-Catalyzed Reaction of 1,3-Dien-4-ols with Aryl or Alkenyl Halides. *J. Org. Chem.* **1985**, *50*, 537−539.
(32) Ma, S.; Zhao, S. Pd(0)-catalyzed Insertion-Cyclization Reaction of 2,3-Allenols with Aryl or Alkenyl Halides. Diastereoselective Synthesis of Highly Optically Active trans-2,3-Disubstituted Vinylic Oxiranes. *J. Am. Chem. Soc.* **1999**, *121*, 7943−7944.
(33) Kang, S.-K.; Yamaguchi, T.; Pyun, S.-J.; Lee, Y.-T.; Baik, T.-G. Palladium-Catalyzed Arylation of α-Allenic Alcohols with Hypervalent Iodonium Salts: Synthesis of Epoxides and Diols Carbonates. *Tetrahedron Lett.* **1998**, *39*, 2127−2130.
(34) Xu, D.; Xu, Y.; Li, L.; Ma, S. Efficient Preparation of Highly Optically Active (*S*)-(−)-2,3-Allenols and (*R*)-(+)-2,3-Allenyl Acetates via a Clean Novozym-435-Catalyzed Enzymatic Separation of Racemic 2,3-Allenols. *Chem. Eur. J.* **2002**, *8*, 5012−5018.
(35) Ma, S.; Gao, W. Efficient Synthesis of 4-(2′-Alkenyl)-2,5-dihydrofurans via $PdCl_2$-catalyzed Coupling-Cyclization Reaction of 2,3-Allenols with Allylic Halides. *Tetrahedron Lett.* **2000**, *41*, 8933−8936.
(36) Ma, S.; Gao, W. Efficient Synthesis of 4-(2′-Alkenyl)-2,5-dihydrofurans, and 5,6-Dihydro-2H-pyrans via the Pd-Catalyzed Cyclizative Coupling Reaction of 2,3- or 3,4-Allenols with Allylic Halides. *J. Org. Chem.* **2002**, *67*, 6104−6112.
(37) Ma, S.; Zhao, S. Novel Substituent and Chelating Effects in the Pd-Catalyzed Reaction of 2,3-Allenols, Aryl Iodides, and Amines. Highly Regio- and Stereo-selective Synthesis of 2−Amino-3-alken-1-ols or 4−Amino-2(*E*)-alken-1-ols. *J. Am. Chem. Soc.* **2001**, *123*, 5578−5579.
(38) (a) Marshall, J. A.; Robinson, E. A Mild Method for the Synthesis of Furans. Application to 2,5-Bridged Furano Macrocyclic Compounds. *J. Org. Chem.* **1990**, *55*, 3450−3451. (b) Marshall, J. A.; Wang, X. Synthesis of Furans by Ag(I)-Promoted Cyclization of Allenyl Ketones and Aldehydes. *J. Org. Chem.* **1991**, *56*, 960−969. (c) Marshall, J. A.; Wang, X. Synthesis of 2,5-Furanocycles through Intraannular Cyclization of Macrocyclic Allenones. *J. Org. Chem.* **1993**, *57*, 3387−3396. (d) Marshall, J. A.; Bartley, G. S. Observations Regarding the Ag(I)-Catalyzed Conversion of Allenones to Furans. *J. Org. Chem.* **1994**, *59*, 7169−7171.
(39) (a) Hashmi, A. S.; Ruppert, T. L.; Knöfel, T.; Bats, J. W. C−C Bond Formation by the Palladium-Catalyzed Cycloisomerization/Dimerization of Terminal Allenyl Ketones: Selectivity and Mechanistic Aspects. *J. Org. Chem.* **1997**, *62*, 7295−7304. (b) Hashmi, A. S. K.; Schwarz, L. *Chem. Ber./Recueil* **1997**, *130*, 1449−1456. (c) Hashimi, A. S. K. Schwarz, L.; Choi, J.-H.; Frost, T. M. A New Gold-Catalyzed C−C Bond Formation. *Angew. Chem., Int. Ed.* **2000**, *39*, 2285−2288.
(40) Hashmi, A. S. K. Transition Metal Catalyzed Dimerization of Allenyl Ketones. *Angew. Chem. Chem., Int. Ed.* **1995**, *34*, 1581−1583.
(41) Ma, S.; Zhang, J. Pd(0)-catalyzed Cyclization Reaction of Aryl or 1-Alkenyl Halides with 1,2-Dienyl Ketones. A General and Efficient Synthesis of Polysubstituted Furans. *Chem. Commun.* **2000**, 117−118.
(42) Ma, S.; Li, L. Palladium(II)-Catalyzed Cyclization Reaction of Allylic Bromides with 1,2-Dienyl Ketones. An Efficient Synthesis of 3-Allylic Polysubstituted Furans. *Org. Lett.* **2000**, *2*, 941−944.
(43) Ma, S.; Yu, Z. Oxidative Cyclization-Dimerization Reaction of 2,3-Allenoic Acids and 1,2-Allenyl Ketones. An Efficient Synthesis of 4-(3′-Furanyl)butenolide Derivatives. *Angew. Chem., Int. Ed.* **2002**, *41*, 1775−1778.
(44) (a) Ahmar, M.; Cazes, B.; Gore, J. Carbopalladation of β-allenylmalonates: A Way to Cyclopentenyl or Vinylcyclopropyl Derivatives. *Tetrahedron Lett.* **1985**, *26*, 3795−3798. (b) Ahmar, M.; Cazes, B.; Gore, J. Palladium-catalysed Alkylative Cyclisation of 2,3-Butadienylmalonates to γ-Lactones. *Tetrahedron* **1987**, *43*, 3453−3456. (c) Resson, L.; Bazin, J.; Gore, J., Cazes, B. Formation de Dedrives Cyclopenteniques et Vinylcyclopropaniques Lors de la Carbopalladation de Diesters et D'α-sulfonylesters Alleniques. *Tetrahedron Lett.* **1994**, *35*, 2881−2884. (d) Gamez, P.; Ariente, C.; Gore, J., Cazes, B. Stereoselectivity of the Carbopalladation-Functionalization of Allenic Compounds: a Mechanistic Study. *Tetrahedron* **1998**, *54*, 14835−14844.
(45) Ma, S.; Zhao, S. Reverse of Regioselectivity in Intramolecular Nucleophilic Substitution of π−Allyl Palladium Species. Highly Selective Formation of Vinylic Cyclopropanes via the Pd(0)-Catalyzed Coupling-Cyclization Reaction of Organic Iodides with 2-(2′,3′-Dienyl)malonates. *Org. Lett.* **2000**, *2*, 2495−2497.
(46) Ma, S.; Jiao, N.; Zhao, S.; Hou, H. Control of Regioselectivity in Pd(0)-Catalyzed Coupling-Cyclization Reaction of 2-(2′,3′-Allenyl)-malonates with Organic Halides. *J. Org. Chem.* **2002**, 67, 2837−2847.
(47) Frost, C. G.; Howarth, J.; Williams, J. M. J. *Tetrahedron: Asymmetry* **1992**, *3*, 1089−1122.
(48) Ma, S.; Hou, H.; Zhao, S.; Wang, G. Efficient Synthesis of Optically Active 2,3-Allenols via the Simple CuBr-Mediated Reaction of Optically Active Propargylic Alcohols with Paraformaldehyde. *Synthesis* **2002**, 1643−1645.

AR020133K